Encyclopedia of Functional Foods in Health and Disease

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Editorial Assistant: Amanda Conte, University of Miami, Coral Gables, Florida, USA

Encyclopedia of Functional Foods in Health and Disease

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Important Notice:
This publication is neither a medical guide nor a manual for self-treatment. If you should suspect that you suffer from a medical problem, you should seek competent medical care. The reader should consult his or her health professional before adopting any of the suggestions in this book. Never disregard professional medical advice due to something you read in this textbook. This book only offers important information on functional foods and nutrition in overall health and wellness. Nonetheless, readers should be aware that nutrition and medicine are expanding fields and should continue to educate themselves on preventative measures. Their primary care provider and the patient are responsible for determining the best plan of care. The authors, editors, and publisher take no liability for any injury or illness that may arise by using the materials from this text.

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Introduction

Founded in 2011, the Functional Foods in Health and Disease (FFHD) journal has been publishing cutting-edge biomedical research and embarking on the development of functional foods. Their purpose is to provide research that expands on functional food science and lead to the development of functional food products. This journal is an excellent resource for PhD students, professors, public health professionals, medical doctors, dieticians, nutritionists, government representatives (FDA, MIH, USDA) and the general public for information pertaining to the latest developments for the prevention, treatment and management of chronic diseases or their symptoms by way of functional foods and bioactive compounds.

This book is a compilation of the abstracts from all articles published in Volumes 1 through 11. It has been created in chronological order from February 2011 to present. This book will not only provide easy access to the full journal articles, but it will provide other authors a large reference for all things related to functional food. Additionally, the proper citation has been provided with every abstract, making the use of the article as simple as possible. Published as an e-book, finding information via topic, author or keyword has been made very easy. This book can also be provided as a supplement to any of the Functional Food Center Inc. textbooks.

Danik Martirosyan, PhD, Founder of Functional Food Center, Functional Food Institute, Dallas, TX, USA

Bioactive compounds of bitter melon genotypes (*Momordica charantia* L.) in relation to their physiological functions

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ABSTRACT

Background: Bitter Melon (*Momordica charantia* L) is one of the most popular cooked vegetables in many Asian countries. Its experimental use in mice has indicated improvement in glucose tolerance against Type II diabetes and reduction in blood cholesterol. However, it has not been proven which alkaloids, polypeptides, or their combinations in the Bitter Melon extract are responsible for the medicinal effects. Green and white varieties of Bitter Melon differ strikingly in their bitter tastes, green being much more bitter than white. It is not yet known whether they are different in their special nutritional and hypoglycemic properties. Nutritional qualities of Bitter Melons such as protein, amino acids, minerals, and polyphenolics contents were determined using four selected varieties such as Indian Green [IG], Indian White [IW], Chinese Green [CG], and Chinese White [CW] grown at the University of Arkansas at Pine Bluff [UAPB] Agricultural Research Center. Results indicated that protein levels of IW were significantly higher than IG in both flesh and seed.

Methods: Four Bitter Melon varieties, Indian Green [IG], Indian White [IW], Chinese Green [CG] and Chinese White [CW] were used for phytochemical analyses to determine protein contents, protein hydrolysis, amino acids contents, and their antioxidant and antimutagenic activities. All analyses were conducted following standard methods. Statistical analyses were conducted using JMP 5 software package [SAS]. The Tukey's HSD procedure was used for the significance of differences at the 5% level.

Results: Moisture contents across the four varieties of Bitter Melon flesh ranged between 92.4 and 93.5%, and that of seed ranged between 53.3 and 75.9%. Protein contents of the flesh were highest in IW [9.8%] and lowest in CG [8.4%]. Seed protein contents were the highest in IW [31.3%] and lowest in IG [27.0%]. Overall, white varieties had higher protein contents than the green varieties. Compared with soy protein, most of the essential amino acid contents of Bitter Melon were similar as in soy proteins. Some amino acids such as Alanine, Glycine, and Valanine were relatively higher in Bitter Melon flesh than in soy protein. Phenolics contents of the flesh, seed, and seed coat tissue [SCT] were significantly different [$p<0.05$] among the four varieties. The four varieties were similar in their antioxidant activities of the flesh tissues; however, they were significantly different in their antioxidant activities in the seed and seed coat tissues [SCT]. Bitter melon varieties IW and CG, tested for antimutagenic effects, both flesh and seed had considerably high activities against benzo[a]pyrene with *Salmonella* TA98 [92-100% inhibition] and S*almonella* TA100 [79-86% inhibition].

Conclusion: Based on these studies, Bitter Melon is a good source of phenolic compounds. All four varieties tested

showed considerably high antioxidant and antimutagenic activities. Therefore, these natural plant phenolics can be a good source of biologically active compounds that may be applied in many food systems to enhance food values and special nutritional qualities. Further studies will be needed using more genetically diverse varieties to pinpoint the bioactive and functional compounds and their physiological properties.

Key words: *Momordica charantia*, protein, polyphenolics, antioxidant, antimutagenicity

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Morinda citrifolia L. (noni) improves the Quality of Life in adults with osteoarthritis

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Running title: Noni improves the QoL of adults with osteoarthritis

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ABSTRACT

Background: *Morinda citrifolia Linn (noni),* as a "pain killer", has been used as a traditional medicine by Polynesians for over 2000 years. It was reported to have a broad range of therapeutic effects including analgesic and anti-inflammation. The *in-vitro* and *in vivo* anti- inflammatory and analgesic properties of noni juice (NJ) suggest that NJ may be a useful adjunctive treatment for osteoarthritis (OA). In this pilot study we explored whether NJ improves the symptoms and Quality of Life (QoL) for adults with OA. We also sought to evaluate the tolerability and safety of NJ for patients with OA in a primary care setting.

Methods: This was an open label three-month intervention pilot study. Data were collected by pre/post intervention survey and laboratory testing. Inclusion criteria were: adults of both sexes aged 40 to 75, with a diagnosis of OA on the hip or knee by x-ray examination provided by their primary care physician, not on prescription medicine for OA, and who were willing to drink 3 oz of NJ a day for 90 days.

Results: Of the 64 questions measuring different aspects of QoL asked on the pre/post survey, 49 (77%) had significant pre/post mean scale differences as measured by independent *t*-test. The OA patients reported being significantly more satisfied with their current health conditions including mobility, walking and bending, hand, finger, and arm functions, household tasks, social activity, arthritis pain, work ability, level of tension, and mood. The study participants were also more positive about their future health and reported taking less over-the-counter (OTC) pain relievers. Pre/post laboratory testing including: lipid panel, liver and kidney functions were in the normal ranges. High Sensitive C Reactive Protein (hsCRP), an inflammatory biomarker, was reduced by 10% after the intervention.

Conclusion: As a nutritional supplement, NJ demonstrated a potential therapeutic effect and improved the symptoms and the QoL for adults with OA. A larger, double blinded, and placebo controlled clinical trial study is needed to confirm these benefits. NJ has the potential to become an adjunctive therapy for OA patients.

Clinical trial registration number: NCT01070264.
Key words: *Morinda citrifolia (noni),* Noni juice (NJ), Osteoarthritis, Quality of life (QoL), pain scales

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Metabolic Syndrome: The complex relationship of diet to conditions of disturbed metabolism

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ABSTRACT

The widespread prevalence and deleterious effects of metabolic syndrome have become a major public health challenge as it is associated with the development of type 2 diabetes and cardiovascular disease. Lifestyle modification focusing on diet has shown promise for managing cardiovascular disease risk, and clinical studies provide evidence that a Mediterranean diet supplemented with phytochemicals is a successful interventional approach. The role of phytochemicals in regulating gene expression and modulating intracellular kinase activity has only recently begun to be appreciated. Clinical studies investigating the effects of specific phytochemicals in metabolic syndrome patients have produced encouraging results, including normalization of metabolic function, reduction of cardiovascular risk, and resolution of metabolic syndrome. As research advances our understanding of the evolutionary relationships between plants and humans, details are emerging about the mechanisms by which phytochemicals regulate insulin signaling and inflammatory responses. This expanding field of research is likely to lead to novel, effective clinical approaches for combating chronic diseases such as metabolic syndrome.

Key words: Metabolic syndrome, Mediterranean diet, xenohormesis, phytochemicals, low-glycemic load diet, *Humulus lupulus*, *Acacia nilotica*

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A nutritional approach to the Metabolic Syndrome

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ABSTRACT

Poor diet and sedentary lifestyle contribute to the development of metabolic syndrome (MetS); addressing both is crucial for its management. A diet featuring the Mediterranean dietary pattern or low glycemic load has been shown to prevent and ameliorate MetS. Plant compounds, including soy protein and phytosterols, have been associated with reduced cardiovascular disease (CVD) risk. Recently, phytochemicals from hops and *acacia* were identified as lipogenic, anti- inflammatory compounds that reduced serum insulin and glucose levels in animals. A 12-week, randomized lifestyle intervention study in overweight and obese women with LDL ≥3.37 mmol/L (130 mg/dL) compared a Mediterranean-style, low-glycemic-load diet and soy/phytosterol-based medical food to an AHA low-fat diet. The modified Mediterranean diet with medical food was superior in reducing markers of MetS and CVD risk. A subsequent, randomized 12-week study in men and women with MetS and LDL ≥3.37 mmol/L (130 mg/dL) showed that supplementation with soy/phytosterol-based medical food plus phytochemicals enhanced the benefits of a Mediterranean-style low-glycemic-load diet and aerobic exercise. At the completion of the study, 43% of participants receiving medical food and phytochemicals exhibited net resolution of MetS compared with only 22% of those on diet and exercise alone. A subanalysis of participants at high risk (MetS + LDL ≥4.14 mmol/L [160 mg/dL]) indicated minimal benefit from lifestyle change alone but marked benefits with the addition of medical food and phytochemicals. Case studies illustrate long-term benefits of this supplemented lifestyle change program. In conclusion, institution of a phytochemical-enhanced lifestyle intervention promises to be a clinically useful approach in MetS management.

Key words: metabolic syndrome, low-glycemic-load diet, rho iso-alpha acids, Acacia nilotica, Humulus lupulus, lifestyle modification, medical food, phytosterol, phytochemicals

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A Clinician's perspective on incorporating therapeutic lifestyle change into clinical practice

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Running title: Clinician‟s perspective on implementing TLC program

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ABSTRACT

This article describes the unique perspective of a clinician who was originally trained as an acute care specialist but in recent years had the opportunity to witness the positive impact of therapeutic lifestyle change (TLC) programs in managing chronic diseases. Through experience gained from conducting a multi-center clinical trial investigating the effects of TLC program in people with metabolic syndrome, Dr. Mark S. McIntosh discusses various aspects and challenges pertinent to implementing a successful TLC program. Patients, physicians, lifestyle counselors, work places, and home environment are all critical in forming an alliance for transforming the current sick-care approach to preventive, wellness-focused approach that is far more efficient, rewarding, and financially sustainable.

Key words: therapeutic lifestyle change, lifestyle counselor, lifestyle medicine, metabolic syndrome, dietary modification

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Molecular basis of the anti-cancer effects of genistein isoflavone in LNCaP prostate cancer cells

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ABSTRACT

Background: Prostate cancer is the most common form of non-skin cancer within the United States and the second leading cause of cancer deaths. Survival rates for the advanced disease remain relatively low, and conventional treatments may be accompanied by significant side effects. As a result, current research is aimed at alternative or adjuvant treatments that will target components of the signal transduction, cell-cycle and apoptosis pathways, to induce cell death with little or no toxic side effects to the patient. In this study, we investigated the effect of genistein isoflavone, a soy derivative, on expression levels of genes involved in these pathways. The mechanism of genistein-induced cell death was also investigated. The chemosensitivity of the LNCaP prostate cancer cells to genistein was investigated using ATP and MTS assays, and a caspase binding assay was used to determine apoptosis induction. Several molecular targets were determined using cDNA microarray and RT-PCR analysis.

Results: The overall data revealed that genistein induces cell death in a time- and dose- dependent manner and regulates expression levels of several genes involved in carcinogenesis and immunity. Several cell-cycle genes were down-regulated, including the mitotic kinesins, cyclins and cyclin-dependent kinases. Various members of the Bcl-2 family of apoptotic proteins were also affected. The DefB1 and the HLA membrane receptor genes involved in immunogenicity were also up regulated.

Conclusion: The results indicate that genistein inhibits growth of the hormone-dependent prostate cancer cells, LNCaP, via apoptosis induction through regulation of some of the genes involved in carcinogenesis of many tumors, and immunogenicity. This study augments the potential phytotherapeutic and immunotherapeutic significance of genistein isoflavone.

Key words: Genistein isoflavone, prostate cancer, expression of genes, phytotherapeutic adjuvant, immunotherapy and chemotherapy

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Effect of Mixed-Tocotrienols in Hypercholesterolemic Subjects

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ABSTRACT

Background: Studies on the cholesterol lowering activity of tocotrienols have yielded mixed results, with some showing cholesterol lowering effect while some showing no activity.

Aim: A randomized, double-blind, parallel group study was conducted to investigate the cholesterol lowering activity of tocotrienols.

Methods: Thirty-two hypercholesterolemic subjects were randomly assigned to orally receive either 300 mg of mixed tocotrienols capsules daily or placebo capsules containing 300 mg of soya bean oil for a period of 6 months. The subjects were monitored before supplementation and monthly thereafter for their serum cholesterol as well as tocotrienol and tocopherol concentrations.

Results: The serum total cholesterol and low density lipoprotein (LDL) cholesterol of the subjects in the tocotrienol supplementation group were decreased significantly by 8.9 ± 0.9% and 12.8 ± 2.6% respectively after 4 months of supplementation and the reduction persisted till the end of the 6-month study, with a reduction of 10.8 ± 1.0% and 17.3 ± 1.8%, respectively from baseline. Moreover, there was a 22fold increase in the total tocotrienol concentrations from baseline during supplementation compared to the placebo group, while the concentration of tocopherol recorded only a modest increase. On the other hand, the serum cholesterol, total tocotrienol and tocopherol concentrations of subjects in the placebo group remained essentially unchanged.

Conclusions: Supplementation with mixed tocotrienols at dose of 300 mg per day resulted in the lowering of the serum total and LDL cholesterol levels after 5 months of supplementation.

Keywords: tocotrienols, cholesterol-lowering, total cholesterol, LDL cholesterol, tocopherols

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Antioxidant Protection against Pathological Mycotoxins Alterations on Proximal Tubules in Rat Kidney

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ABSTRACT

Background: Ochratoxin A (OTA) was one of the mycotoxins and received attention worldwide because of the hazard it posed to human and animal health, where the kidney was the primary target organ for OTA toxicity. In the other hand, dates served as a good source of natural antioxidants and could potentially be considered as a functional food.

Methods: The study was performed in the department of biology in King Abdulaziz University. Animals were gavage administrated and divided into four groups: first group received (sodium bicarbonate), second group received (289 µg OTA /kg B.W. /day), third group received (1mg Ajwa/kg B.W. / day) and fourth group received (289 µg OTA /kg B.W./day+ 1mg Ajwa /kg B.W. / day). Serum (creatinine - urea) levels were measured in each group at the time of tissue collection , some biopsies were fixed in 10% buffered formalin solution for light microscopy processing stained with Haematoxylin and Eosin (H& E.), Periodic Acid-Schiff (PAS) and Masson´s Trichrome (M.T.).Other biopsies were immediately collected into electron microscopy processing.

Results: After 28 days, a significant decrease in body weight, kidney weight and relative weight was detected in OTA treated group. Also, Serum (creatinine - urea) level were elevated .The normal cyto-architecture of proximal tubules were lost exhibiting damaged bruch border, degenerated, binucleated and karyomegalic cells. The most destructed ultra- structure was the mitochondria which severely swollen with disintegrated membranes. In Ajwa Date extract-group the proximal tubules were normal, whereas in Ajwa date extract + OTA -group the severity of the lesions was significantly reduced.

Conclusion: The present results indicated that, Ajwa date have protective effects and ameliorated the lesions of Ochratoxin nepherotoxicity which might lead to kidney failure.

Key words: Ochratoxin A., Ajwa date, proximal tubules, light –structure, ultra –structure, biochemical analysis, morphometry.

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/135/273

Lipid Replacement Therapy: A functional food approach with new formulations for reducing cellular oxidative damage, cancer-associated fatigue and the adverse effects of cancer therapy

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ABSTRACT

Background: Cancer-associated fatigue and the chronic adverse effects of cancer therapy can be reduced by Lipid Replacement Therapy (LRT) using membrane phospholipid mixtures given as food supplements.

Methods: This is a review of the published literature on LRT and its uses.

Results: LRT significantly reduced fatigue in cancer patients as well as patients suffering from chronic fatiguing illnesses and other medical conditions. It also reduced the adverse effects of chemotherapy, resulting in improvements in incidence of fatigue, nausea, diarrhea, impaired taste, constipation, insomnia and other quality of life indicators. In other diseases, such as chronic fatigue syndrome, fibromyalgia syndrome and other chronic fatiguing illnesses, LRT reduced fatigue by 35.5-43.1% in different clinical trials and increased mitochondrial function.

Conclusions: LRT formulations appear to be useful as non-toxic dietary supplements for direct use or placed in functional foods to reduce fatigue and restore mitochondrial and other cellular membrane functions. Formulations of LRT phospholipids are suitable for addition to various food products for the treatment of a variety of chronic illnesses as well as their application in anti-aging and other health supplements and products.

Keywords: nutritional supplements, NT factor®, Coenzyme Q_{10}, cancer fatigue, mitochondria

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Mushrooms as a functional food mediator in preventing and ameliorating diabetes

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ABSTRACT

Diabetes is a major health problem predisposing to markedly increased complications. Despite the numerous preventative strategies and armories of medication, the management of diabetes remains grossly unsatisfactory. Diabetes is emerging as a pandemic. Therefore it is important to identify novel nutraceuticals or drugs for curing or preventing diabetes, which have fewer side effects. The present paper reviewed scientific information on mushrooms with regards to its anti-diabetic active compounds and/or pharmacological test results, which are commonly used as functional foods and ingredients used in the traditional medical system and which have demonstrated experimental or/and clinical anti-diabetic effectiveness. These functional foods might have a big potential for the prevention or cure of diabetes more than in other plant species. However, still scientific or clinical studies are not sufficient for hypoglycemic effect for mushrooms use as ‗official' drug. Therefore, it is proposed that a close attention be paid to carry out further research of functional mushrooms for preventive and curative measures for diabetes and its complications.

Keywords: Diabetes, Mushrooms, Functional foods, Hypoglycemic, and Nutraceuticals

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Plant flavonoids as angiotensin converting enzyme inhibitors in regulation of hypertension

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ABSTRACT

Background: Angiotensin converting enzyme (ACE) is a key component in the renin angiotensin aldosterone system (RAAS) which regulates blood pressure. As the over expression of RAAS is associated with vascular hypertension, ACE inhibition has become a major target control for hypertension. The research on potential ACE inhibitors is expanding broadly and most are focused on natural product derivatives such as peptides, polyphenolics, and terpenes. Plant polyphenolics are antioxidant molecules with various beneficial pharmacological properties. The current study is focused on investigating and reviewing the ACE inhibitory property of fruit flavonoids. An apple skin extract (ASE) rich in flavonoids, the major constituents of the extract and their selected metabolites were assessed for the ACE inhibitory property *in vitro*. It is important to investigate the metabolites along with the flavonoids as they are the constituents active inside the human body.

Objective: To investigate whether flavonoids, flavonoid rich apple extracts and their metabolites could inhibit ACE *in vitro.*

Method: The samples were incubated with sodium borate buffer (30 µL, pH 8.3), 150 µL of substrate (Hip-His-Liu) and ACE (30 µL) at 37 ^{o}C for 1 h. The reaction was stopped by addition of 150 µL of 0.3M NaOH. The enzyme cleaved substrate was detected by making a fluorimetric adduct by adding 100 µL of o-phthaladehyde for 10 min at room temperature. Reaction was stopped by adding 50 µL of 3M HCl. Fluorescence was measured by using a FluoStar Optima plate reader at excitation of 350 nm and emission of 500 nm.

Results: The extract and the compounds showed a concentration dependant enzyme inhibition. Increasing concentrations from 0.001 ppm to 100 ppm of ASE showed an increment of 29% to 64% ACE inhibition. The IC_{50} (concentration of test compound which gives 50% enzyme inhibition) values of ASE, quercetin, quercetin-3-glucoside, quercetin-3-galactoside, cyanidin-3- galactoside were 49 µg/mL, 151 µM, 71 µM, 180 µM, 206 µM, respectively. The major constituents of the ASE that were tested separately showed effective ACE inhibition. From the three metabolites tested, only quercetin-3-glucuronic acid showed concentration dependant ACE inhibition. The ACE inhibition of 0.001 ppm to 100 ppm of quercetin-3-glucuronic was in the range of 43% and 75% and the IC_{50} value was 27 µM.

Conclusion: The results demonstrated that flavonoids have a potential to inhibit ACE *in vitro* and the inhibitory property varies according to type of sugar moiety attached at C-3 position. The results also revealed that the major

contributing compounds of ASE for ACE inhibition belong to flavonoids. Among the tested compounds, the lowest IC_{50} value is associated with the quercetin- 3-glucuronic acid, a major *in vivo* metabolites of quercetin and its glycosides. The results suggest that certain dietary flavonoids may possess properties of blood pressure regulation.

Key words: Hypertension, renin angiotensin system (RAS), angiotensin converting enzyme (ACE), flavonoids, apple

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Using food grade Lye "omushelekha" in the formulation of health products from commonly consumed African Indigenous vegetables and vegetable combinations

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ABSTRACT

Background: Lye, sodium hydroxide and potassium hydroxide has been used over the years in food preparation including the preparation of vegetables and dried meat products, washing or chemical peeling of fruits and vegetables, cocoa processing, caramel production, poultry scalding and cooking among others. Lye is believed to improve the organoleptic properties and also enhances the nutritional value to the products.

Objective: To assess the effect of food grade lye on the levels of copper and iron in the raw, boiled and boiled-fried single vegetables and vegetable combinations treated with and without food grade lye.

Methods: Single vegetables, *Crotalaria occroleuca, Solanum scabrum, Vigna unguiculata* and *Amaranthus blitum* and their combinations were cooled and kept in the fridge at 4^{o}Cs. Elemental analysis was done for the raw, boiled and boiled-fried samples using Atomic Absorption Spectrophotometry (AAS) under standard conditions using wavelengths of 248.3nm for iron and 324.2nm for copper. Paired t-test was used to compare the iron and copper levels of the boiled and boiled-fried vegetables while the independent t-test was done to assess the levels of iron and copper in the raw, boiled and boiled fried samples.

Results: Boiled-fried samples recorded higher content of iron and copper than the boiled ones. A combination of *Amaranthus blitum-Crotolaria occloreuca* boiled without lye boiled-fried with lye, and boiled-fried without lye had the highest copper contents of 1.66mg/100gram, 4.56mg/100gram, and 4.56mg/100gram respectively, compared to *Amaranthus blitum* alone (3.48mg/100gram) and *Crotolaria occloreuca* (0.42mg/100gram). A combination of *Amaranthus blitum-Crotolaria occloreuca* boiled in non-lye water, and those boiled-fried with and without lye had the highest extractable iron of 557mg/100g, 859.2mg/100g, and 859.2mg/100g respectively. Iron content was high in the *Solanum scabrum* (281.1mg/100g), and *Crotolaria occloreuca* (110/100g), *Amaranthus blitum* (108mg/100g) boiled-fried with lye. It was possible that iron was leached from the cooking utensils and absorbed by the vegetables.

Conclusion: The results of this study clearly demonstrated that vegetable combinations of *Amaranthus blitum-Crotolaria occloreuca* had a higher content of copper. Vegetable combinations exposed to different treatments had higher levels of iron and copper. This could be attributed different nutrient-nutrient interactions between different vegetables combinations.

Key Words: *Food grade lye, Crotalaria occroleuca, Solanum scabrum, Vigna unguiculata, Amaranthus blitum*, iron, copper.

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Dietary supplementation of fructooligosaccharides reduces hepatic steatosis associated with insulin resistance in obese Zucker rats

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ABSTRACT

Background: One in five adults in the United States is obese as defined by a body mass index of 30 kg/m^2. Obesity is associated with metabolic syndrome, a combination of medical conditions including cardiovascular disease, type 2 diabetes, hypertension, hypercholesterolemia, and hypertriglyceridemia. These conditions present challenges to the medical care system and require a multifaceted approach through a variety of interventions. This study investigated the effects of fructooligosaccharides (FOS) at the level of 5 % (w/w) in alleviating the complications associated with metabolic syndrome.

Methods: The study was carried out using thirty-six, three-month old female lean and obese Zucker rats housed in an environmentally controlled laboratory. The Zucker rats were divided into three groups (N=12): Lean (L-CTRL) and obese controls (O-CTRL) and obese-FOS (O- FOS). The controls received AIN-93M purified rodent diet and the animals in the O-FOS group were fed AIN-93M diet modified to contain 5.0% FOS (w/w). After 100 days of treatment, the rats were fasted for 12 hours and sacrificed. Tissue and organs of interest, and blood were collected for analysis. Serum concentrations of the following were determined: glucose, glycosylated hemoglobin (HbA1c), total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), triglycerides (TG), and insulin. Gravimetric quantification of liver lipids was performed and peroxisome proliferator-activated receptor-□ (PPAR-□) gene expression was determined in white adipose tissue by qRT-PCR.

Results: No significant differences were observed in the serum lipids, fasting blood glucose, HbA1c and PPAR-□ gene expression in white adipose tissue of O-FOS group compared to O- CTRL group. FOS supplementation significantly lowered the percent total liver lipids by 12% with a subsequent reduction in the liver weights compared to O-CTRL rats. Serum insulin concentrations were lowered 3.6 fold in O-FOS group compared to O-CTRL ($P < 0.05$).

Conclusion: Based on these findings we conclude that dietary supplementation of 5% FOS (w/w) may reduce hepatic steatosis and the risk for non-alcoholic fatty liver disease (NAFLD) associated with insulin resistance without changes in blood lipids and glucose levels.

Key words: Dietary fiber, Fructooligosaccharide, Hepatosteatosis, Liver lipids, Non-alcoholic fatty liver disease (NAFLD), Zucker.

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Metabolic syndrome among obese patients attending the medical clinics of the three teaching hospitals at Sana's City, Yemen

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ABSTRACT

Background: Yemen faces major challenges in improving the health status of its population as it is entering an epidemiological transition with rising non- communicable diseases e.g. obesity, diabetes and cardiovascular diseases (CVDs). We designed this study to find out the prevalence of Metabolic Syndrome (MS) and its components among obese Yemeni patients.

Methods: All obese (waist circumference >102 cm (40 inch) in male and >88 cm (35 inch) in female) attending the outpatients medical clinics at the three teaching hospitals in Sana'a city, were examined and their blood pressure (BP), fasting samples of plasma glucose, triglycerides, and HDL cholesterol were measured. The prevalence of MS obtained based on the Adult Treatment Panel III and presence of at least 3 of the following: systolic BP ≥130 mm Hg and/or diastolic BP ≥ 85 mm Hg or on treatment for high BP, fasting glucose ≥110 mg/dl or on diabetes treatment, triglycerides ≥150 mg/dl, and HDL cholesterol <40 mg/dl in men and <50 mg/dl in women.

Results: 200 obese were identified during study period with an overall MS prevalence of 46%. The metabolic co-morbidities were raised BP (68%), high triglycerides (66%), reduced high density lipoprotein (64%), and raised fasting blood glucose (40%).

Conclusion: Prevalence of MS is high among obese Yemeni patients and high BP was the commonest co-morbidity. These findings highlight an urgent need to develop strategies for prevention, detection, and treatment of MS that could contribute to decreasing the rising incidence of CVD and diabetes.

Keywords: Metabolic syndrome, obesity, cardiovascular diseases, diabetes mellitus, Yemen.

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Functional food availability, a limitation to peoples' health on Islands

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ABSTRACT

Background: All foods are imported to markets in smaller islands in the Caribbean. Before export of foods to these destinations, the foods are subjected to several preservative procedures like irradiation, pesticide spray and prolonged refrigeration etc., to last the extended transport periods. This reduces availability of protective elements and the nutrient contents of the foods to scanty levels, especially to common people with low and middle incomes. Hence the majority of people in these categories on the small islands become vulnerable to ill health.

Aims and Objectives: To assess 1. Food availability 2. Normal transport period for foods to reach from the suppliers, and 3. Current level of prevalence of non-infective chronic diseases in the area.

Methods: Data were collected from two sources. One set of data was collected from the three supermarkets on the island to obtain information on source, transport time and nature of foods imported; and the second from 200 randomly selected responses of diseased persons for information on the age, gender and cause of death.

Results: All the foods were imported and the time taken for the food (including protective foods) to reach the island was about 3 weeks. The major causes of death were malignancy (30%), diabetes and its complications (25%), cardio vascular diseases (19.5%), STD / HIV (8.5%) and other causes (17.0%). A review of prevalence of chronic diseases like hypertension, diabetes, heart diseases, arthritis and associated functional limitations, in the region reveals that their prevalence is proportionately high on the island compared to nearby developed mainland regions. Body mass index of ≥25 was reported to be as high as 58.3%. The health care facilities available are seen to be limited and public health activity to prevent or manage the prevailing chronic health issues, appeared to be meager.

Conclusion: There is a need to address the problem through public health actions to lower the incidence of the chronic degenerative diseases in the area: 1. Educate the community about the ways to improve their nutrition and life styles, 2. Make available health and nutrition promoting foods to all the people living in the islands, 3. Strengthen health services to tackle chronic degenerative diseases in the region.

Key Words: Foods, Nutrition, Chronic diseases, Mortality, Protective foods, Functional foods

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Antioxidant activity and mechanism of protocatechuic acid *in vitro*

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ABSTRACT

Background: Protocatechuic acid (PCA) is a natural phenolic acid widely distributed in plants and is considered as an active component of some traditional Chinese herbal medicines such as *Cibotium barometz* (L.) J.Sm, *Stenoloma chusanum* (L.) Ching, *Ilex chinensis* Sims. PCA was reported to possess various pharmacological effects which may be closely correlated with its antioxidant activities. However, the antioxidant of PCA has not been investigated systematically yet.

Methods: In the study, the antioxidant activities of protocatechuic acid were measured *in vitro* using various antioxidant assays including 1,1-diphenyl-2-picryl-hydrazyl (DPPH•), 2,2'-azino-bis (3-ethylbenzthiazoline-6-sulfonic acid) ($ABTS^{+}$•), superoxide anion radicals (•O_2^-) and hydroxyl radical (•OH) scavenging activity, ferric ions (Fe^{3+}) and cupric ions (Cu^{2+}) reducing power, ferrous ions (Fe^{2+}) and cupric ions (Cu^{2+}) chelating activity, compared with the positive controls Trolox or BHT.

Results: In all assays, PCA along with positive controls exhibited dose-dependently antioxidant ability. Comparing to a standard antioxidant Trolox, the relative antioxidant activity of PCA (i.e. the ratio of $IC_{50(Trolox)}/IC_{50(PCA)}$) was calculated as 2.8, 2.3, 3.7, 6.1, 4.2, 1.0, 2.7, 1.5, respectively, for DPPH, ABTS, reducing power (Fe^{3+}), reducing power (Cu^{2+}), superoxide anion radical-scavenging, hydroxyl radical-scavenging, chelating ability (Fe^{2+}) and chelating ability (Cu^{2+}).

Conclusion: Comparing to Trolox, PCA shows much more effective antioxidant activity *in vitro* in both lipid and aqueous media. Hence, it could therefore be used in pharmacological or food industry as a natural antioxidant. It may exhibit antioxidant activity by both chelating metal transition ions as well as by scavenging free radicals via donating hydrogen atom (H•) or electron (e).

Keywords: Protocatechuic acid, antioxidant, reducing power, free radical-scavenging, chelating ability.

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Lipid Replacement Therapy drink containing a glycophospholipid formulation rapidly and significantly reduces fatigue while improving energy and mental clarity

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ABSTRACT

Background: Fatigue is the most common complaint of patients seeking general medical care and is often treated with stimulants. It is also important in various physical activities of relatively healthy men and women, such as sports performance. Recent clinical trials using patients with chronic fatigue have shown the benefit of Lipid Replacement Therapy in restoring mitochondrial electron transport function and reducing moderate to severe chronic fatigue.

Methods: Lipid Replacement Therapy was administered for the first time as an all-natural functional food drink (60 ml) containing polyunsaturated glycophospholipids but devoid of stimulants or herbs to reduce fatigue. This preliminary study used the Piper Fatigue Survey instrument as well as a supplemental questionnaire to assess the effects of the glycophospholipid drink on fatigue and the acceptability of the test drink in adult men and women. A volunteer group of 29 subjects of mean age 56.2±4.5 years with various fatigue levels were randomly recruited in a clinical health fair setting to participate in an afternoon open label trial on the effects of the test drink.

Results: Using the Piper Fatigue instrument overall fatigue among participants was reduced within the 3-hour seminar by a mean of 39.6% ($p<0.0001$). All of the subcategories of fatigue showed significant reductions. Some subjects responded within 15 minutes, and the majority responded within one hour with increased energy and activity and perceived improvements in cognitive function, mental clarity and focus. The test drink was determined to be quite acceptable in terms of taste and appearance. There were no adverse events from the energy drink during the study.

Conclusions: The Lipid Replacement Therapy functional food drink appeared to be a safe, acceptable and potentially useful new method to reduce fatigue, sustain energy and improve perceptions of mental function.

Keywords: functional food drink, NT Factor®, NT Factor Lipids®, fatigue, mitochondrial function, mental function

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The effects of intravenous vitamin C administration on hs-CRP and Tumor Necrosis Factor-α levels in Haemodialysis Patients

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ABSTRACT

Background: It has been proved that pre-inflammatory factors increase mortality and morbidity of cardio-vascular diseases especially in hemodialysis patients. There is a great evidence for the increase of pre-inflammatory factors and vitamin C deficiency in dialysis patients. Limited data, however, are available regarding the effects of vitamin C supplementation on reduction of inflammatory markers in such patients.

Objectives: The aim of this study is to determine the changes of hs-CRP and Tumor Necrosis Factor-α (TNF-α) levels after administration of vitamin C in End Stage Renal Disease patients (ESRD) on Hemodialysis

Methods and Materials: In this clinical trial, vitamin C was administered intravenously (IV), (500 mg two times per week) for 2 months in 41 chronic hemodialysis patients and the hs-CRP and TNF-α levels of these patients were compared with a control group with no vitamin C as treatment. Besides hs-CRP and TNF-α, detailed laboratory results were evaluated before and after the study. The statistical analysis was performed using SPSS version 16 at the end of the study.

Results: The hs-CRP and TNF-α levels reduced significantly in hemodialysis patients after vitamin C supplementation (hs-CRP decreased from 7.27±3.70 to 6.60± 3.75, P< 0.001 and TNF-α decreased from 25.61±12.28 to 22.82±22.83, P= 0.006), whereas the levels of these pro-inflammatory factors increased in hemodialysis patients without vitamin C supplementation (hs-CRP increased from 7.13±3.56 to 7.73±3.83, P= 0.049 and TNF-α increased from 21.32±5.64 to 23.63±15.59, P= 0.353). Vitamin C supplementation also reduced ESR level and increased Hb level significantly but it had no influence on lipid profile.

Conclusion: According to the findings of this study, it seems that vitamin C administration can reduce hs-CRP and TNF-α level in hemodialysis patients and as a result prevent atherosclerosis. It can be concluded that administration of vitamin C supplementation is beneficial in hemodialysis patients.

Key words: hemodialysis, hs-CRP, TNF-α, Vitamin C
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Effect of dietary fiber in lowering serum glucose and body weight in sprague dawley rats

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ABSTRACT

Introduction: The present study evaluated the hypoglycemic perspectives and weight loss significance of dietary fiber. Dietary fiber was supplemented in commercial wheat flour (atta) for the preparation of chapaties, a staple diet of South Asia. Male Sprague Dawley rats (n = 100) were randomly divided into 4 diet groups (n = 25 per group). The control group was fed basal diet that included commercial wheat flour chapati, cornstarch, corn oil, salt and vitamin mixture in such a way that 10% of the protein was available from the final diet. To the basal diet of other 3 groups, chapaties supplemented with 2% guar gum (GG 2%), 3% guar gum (GG 3%) and 5% chickpea + 1% guar gum (CP5%+GG1%) were added, respectively. All diets were fed to the rats for a period of 8 weeks to perceive the impact of respective compositions. Rats fed on CP 5% + GG 1%, showed maximum glucose reduction (14.57%) followed by GG 3% (11.64%) and GG 2% (9.60%) as compared to control diet. Likewise, rats fed on 3% GG showed maximum decline (7.90%) in body weight. It was concluded that chapaties prepared from selected treatments provide an additional dietary fiber that could be supportive for diabetic and obese individuals.

Results: The results indicated that addition of dietary fiber influenced the physical characteristics of chapati non-significantly. Maximum glucose concentration was found to be 112.50 mg/dL in control group followed by 101.70 and 99.41 mg/dL in groups fed on guar gum 2% and guar gum 3%, respectively. Lowest glucose concentration (96.11 mg/dL) was observed in rats fed on the combination of chickpea 5 %+ guar gum 1%. Maximum serum protein concentration was found to be 6.39 g/dL in rats fed on combination of chickpea 5 % + guar gum 1% whilst the remaining three groups showed non significant variations with respect to each other. Means for serum protein were 6.33, 6.30 and 6.32 g/dL for control, guar gum 3%, and guar gum 2%, respectively. Maximum serum albumin concentration was found to be 3.63 g/dL in rats fed on combination of chickpea 5%+ guar gum 1% showing non-significant differences than that of control (3.60 g/dL).

Conclusion: Soaring cost of medication and their side effects demand new ways against the existinng malady of diabetes. Diet based strategy is a right approach as it is economical and assessable to avoid the health risks. The present research explored that diet diversification is an effective tool for the management of serum glucose and body weight. Role of legumes is indispensable to enhance the dietary fiber. Ingestion of chapaties prepared from selected compositions of composite flours providing an additional dietary fiber would be supportive to reduce hyperglycemia and obesity.

Keywords: Sprague Dawley rats, Dietary fiber, Composite flour, Chapati, Serum glucose, Insulin glucose indices.

Effects of Portabella mushrooms on collagen-induced arthritis, inflammatory cytokines, and body composition in dilute brown non-agouti (DBA1) mice

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ABSTRACT

Background: Exotic mushrooms have long been used in Asia for treatment and/or prevention of chronic diseases due to their immunomodulatory properties. However, the health benefits of portabella mushrooms (PM) (brown Agaricus bisporous), on collagen-induced arthritis (CIA) and associated complications, (i.e. loss of lean mass, increased fat mass and inflammatory cytokines), have not been previously investigated.

Methods: We investigated CIA pathogenesis, body composition and plasma levels of IL- 6, TNF-α and sICAM1 in DBA1 female mice fed either the AIN76 diet or the same diet fortified with 5% lyophilized PM (n=19-20/group). Ten mice/group were immunized with 100 µg bovine collagen type II on day 42 of the protocol, followed by 50 µg lipopolysaccharides on day 62, and euthanized on day 73-74. Cytokines were measured by ELISA.

Results: Compared to baseline diet, PM had: no protective effect from CIA since all collagen immunized mice developed severe edema, bone erosion, and mononuclear cell infiltration in paws. In mice with and those without CIA, feeding a PM-fortified diet resulted in higher percent of body fat than feeding the baseline diet ($p<0.05$). After CIA induction, PM provided the following beneficial effects: (a) a smaller reduction in lean mass and absolute thymus weight; (b) a higher fat mass loss; and (c) lower plasma TNF-α levels ($p <0.05$). PM-fortification did not alter plasma IL-6 and sICAM1 regardless of CIA status; but it increased in vitro IL-6 secretion by mitogen- treated spleen cells.

Conclusion: Our data suggest that PM may reduce plasma TNF-α, attenuate lean mass loss and thymus atrophy associated with arthritis, and protect spleen cell function assessed by IL-6 secretion. However, PM-fortification did not attenuate overall CIA pathogenesis which may be due to lack of effect on plasma IL-6. Decreased TNF-α without alterations in IL-6 may reduce the risk of other conditions associated with chronic inflammation such as cardiovascular disease.

Key words: portabella mushrooms, inflammatory cytokines, collagen-induced arthritis, body composition, TNF-α, IL-6, thymus, DBA1 mice.

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Anti-jugular vein thrombotic effect of *Morinda citrifolia L.* [noni] in male SD rats

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ABSTRACT

Background: Venous thromboembolism (VTE) is a common and serious medical condition, which is estimably responsible for more than 300,000 hospital admissions annually in the USA. Pulmonary embolism (PE) is a major complication of VTE, which contributes to 12% death of hospitalized patients. Heparin is the most common anti-coagulant, but severe allergic reactions, bleeding, and thrombocytopenia limit its use. Thus, seeking a botanical, nontoxic antithrombotic alternative is an interesting area. *Morinda citrifolia L.* [noni] is a medicinal plant used in folk remedies by Polynesians for over 2,000 years. It has been reported to have a broad range of therapeutic and preventive effects. The bioactivities of NJ have been continuously discovered with antioxidative, anti-inflammatory, analgesic, and immune modifying activities. Our novel hypothesis is whether NJ has an anti-venous thrombotic effect in rodents. To examine our hypothesis, this study was designed to examine the anti-thrombotic effect of NJ on the jugular vein thrombosis model induced by ferric chloride in SD rats.

Material and Methods: NJ and placebo used in this study were donated by Morinda Holding Inc. NJ was formulated with grape juice and blue berry juice. Placebo was prepared by using the same procedure of NJ preparation, but without NJ in it. Thirty-six male SD rats were divided into six groups. Anti-venous thrombotic activities of 5% NJ, 10% NJ, heparin, and 10% NJ plus heparin were examined and compared with the positive and blank controls. Thrombosis was induced by application of a filter paper soaked in 50% ferric chloride on the right jugular vein. A2-cm fragment of the occluded vein (thrombus) was removed and weighed after 1-hour maturation. Blood samples were collected for platelet count, aPTT, and PT tests.

Results: The weight of a 2-cm fragment of normal jugular vein was 9.9 ± 2.1 mg, while the weight of the occluded vein in positive controls was 30.7 ± 12 mg [p=0.001], 24.7 ± 6.5 mg in heparin [p=0.16], 25.5 ± 6.5 mg in 5% NJ [P=0.15], 20.0 ± 5 mg in 10% NJ [P=0.04], and 16.1 ± 5.0 mg in heparin plus 10% NJ [P=0.02], respectively. The activity of aPTT was significantly increased in heparin, 60.0 ± 10.0 sec [p=0.002] compared with 16.83 ± 4.9 sec in blank control. There was a significant increase in 5% NJ [34.24 ± 9.6 sec, p=0.01], a slight increase in 10% NJ [24.0 ± 5.4 sec, p=0.06]. The activity of PT was significantly increased in heparin group only [36.52 ± 3.0 sec vs 26.85 ± 0.4 sec in blank control, p=0.01). There was no significant change in NJ groups. Clearly, the reduced thrombus weight by heparin may be partially due to the activation of aPTT and PT. The slight inhibition of NJ on aPTT activity may explain

the possible additive antithrombotic effect of NJ with heparin. The platelet count was slightly reduced to 775,700 in the heparin group compared with blank control, there was no changes observed in other groups.

Conclusion: NJ has an anti-jugular vein thrombotic effect and a possible additive antithrombotic effect with heparin by activating aPTT without induction of thrombocytopenia. We wonder whether NJ has an anti-platelet function activity. The mechanisms for anti-venous thrombotic effects of NJ needs further study.

Key words: *Morinda citrifolia L.* [noni], noni juice (NJ), jugular vein thrombosis, heparin, antithrombosis, anticoagulant, activated partial thromboplastin time [aPTT], prothrombin time [PT].

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Developing an effective food supplement for the prevention of osteoporosis

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ABSTRACT

Background: Aging is accompanied by a gradual loss of bone mineral contents which might lead to a higher rate to fractures. In the past twenty years, many pharmaceuticals are created to prevent bone loss. Most effective drugs only suppress bone resorption, the result of which is a loss of the normal balance of bone metabolism. Anti-resorptive drugs have already shown complications arising from the loss of balanced metabolism. Therefore it becomes clear now that prevention of bone mineral loss through a natural maintenance process will be more beneficial for those not under special risks. Drug treatment could be researched for those who already developed severe osteoporosis. There are many medicinal herbs in Chinese Medicine known to be supporting bone health. Three of those herbs, *Herba Epimedii, Fructus Ligustri Lucidi* and *Fructus Psoralea* (ELP) were chosen to make a formula for the prevention of osteoporosis.

Result: One hundred and fifty postmenopausal osteopenic women were recruited, randomized and allocated to the herbal group (ELP) or placebo group. After 12 months of consumption of herbal formula, bone mineral maintenance was found when the bone mineral density (BMD) of the femur and tibia were as assessed using Dual-energy X-ray Absorptiometry (DEXA) and Peripheral Quantitative Computed Tomography (pQCT) machines. No adverse effects were found.

Conclusion: The clinical study using ELP was designed as a randomized controlled trial to test the efficacy of the agent used. The results showed positive support on the BMD of all bone tested. However statistical difference between the herbal and placebo group reached the significant level only in the proximal tibia and those who experienced menopause for more than ten years. This finding well indicates that ELP is good for preventive but does not satisfy the demand of a treatment agent. ELP could be recommended to those under the early threat of osteoporosis, i.e. osteopenia, to be used as a preventive agent.

Keywords: Osteoporosis, post-menopause women, herbal supplement, functional food.

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Nutrigenomics of Neuradaptogen Amino-Acid-Therapy and Neurometabolic Optimizers: Overcoming carbohydrate bingeing and overeating through neurometabolic mechanisms

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ABSTRACT

Despite progress that has been made in the treatment of obesity, the epidemic continues to rise worldwide. While pharmacological treatment of obesity may be effective, medications may have significant side effects and can be potentially fatal. This review will provide significant evidence to substantiate the existence of *Reward Deficiency Syndrome* in Obesity and the role of catecholaminergic pathways in aberrant substance seeking behavior, in particular cravings for carbohydrates. The genetic basis for generalized craving behavior will be established. Evidence to support the augmentation of precursor amino acid therapy and enkephalinase, MOA and COMT inhibition leading to enhanced levels of neurotransmitters: serotonin, enkephalins, GABA and dopamine/norepinephrine as well increasing insulin sensitivity (affecting dopamine neuronal synthesis regulation) through the use of certain neurometabolic optimizers will also be provided. This review article cites many published studies to support a conceptual paradigm shift towards the use of this proposed nutrigenomic formula. The analysis and research preceding this formulation is outlined. This formulation has a generalized anti-craving effect and can inhibit carbohydrate bingeing, inducing significant healthy fat loss and prevention of relapse. This is the first time that components of this formula have been combined, at the dosage levels indicated with the goal of promoting successful and sustainable body recomposition. We are encouraging other laboratories to further evaluate Neuroadtagen Amino-Acid Therapy (NAAT)/Nurometabolic optimizers as a putative anti-obesity complex in larger controlled blinded studies and await interpretation of must these needed studies.

Keywords: NAAT, Dopamine, Genes, Polymorphisms, Obesity, Craving Behavior, Overeating, Reward Deficiency

Syndome, Nutrigenomics**.**

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Fermentation by gut microbiota cultured in a simulator of the human intestinal microbial ecosystem is improved by probiotic *Enterococcus faecium* CRL 183\

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ABSTRACT

Background: Enterococci are used in a large number of dairy products, such as starter cultures in food supplements and in foods considered functional. *In vitro* gut fermentation models present an unmatched opportunity of performing studies frequently allenged in humans and animals owing to ethical concerns. A dynamic model of the human intestinal microbial ecosystem (SHIME) was designed to better simulate conditions intestinal microbiota.

Methods: The SHIME model **was** used to study the effect of *Enterococuus faecium* CRL 183 on the fermentation pattern of the colon microbiota. Initially, an inoculum prepared from human feces was introduced into the reactor vessels and stabilized over 2 wk using a culture medium. This stabilization period was followed by a 2-wk control period during which the microbiota were monitored. The microbiota were then subjected to a 4-wk treatment period by adding 10^8 CFU/mL of the *Enterococcus faecium* CRL 183 to vessel one (the stomach compartment).

Results: The addition resulted into an overall increase of bacterial marker populations (Enterobacteriaceae, *Lactobacillus* spp., *Bifidobacterium* spp. and *Clostridium* spp.), with a significant increase of the *Lactobacillus* sp. and Bifidobacterium sp populations. The short- chain fatty acid (SCFA) concentration increased during the supplementation period; this was due mainly to a significant increase in the levels of acetic, butyric and propionic acids. Ammonium concentrations increased during the supplementation period.

Conclusions: Results showed that the major effect of *E. faecium* CRL 183 was found in the ascendant and transverse colon.

Key words: Gut microbiota, *Enterococcus*, Gastrointestinal resource management, Simulator of Human Intestinal Microbial Ecosystem (SHIME)

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Wound healing activity of *Ipomoea batatas* tubers (sweet potato)

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ABSTRACT

Background: *Ipomoea batatas* (L.) Lam. from the family Convolvulaceae is the world's sixth largest food crop. The tubers of *Ipomoea batatas* commonly known as sweet potato are consumed as a vegetable globally. The tubers contain high levels of polyphenols such as anthocyanins and phenolic acids and vitamins A, B and C, which impart a potent antioxidant activity that can translate well to show wound healing effects. To check their effects on wound healing, the peels and peel bandage were tested on various injury models in rats in the present study.

Methods: The methanolic extracts of the peels and peel bandage of *Ipomoea batatas* tubers (sweet potato) were screened for wound healing by excision and incision wound models on Wistar rats. Three types of gel formulations were prepared, viz., gel containing 3.0% (w/w) peel extract, gel containing 6.0% (w/w) peel extract and gel containing 10% (w/w) peel extract. Betadine (5% w/w povidone iodine cream) was used as a reference standard. In the incision wound model, Tensile strength of the skin was measured. Epithelization time, wound contraction, hydroxyproline content of the scab, and ascorbic acid and malondialdehyde content of the plasma were determined in the excision wound model.

Results: In the incision wound model, high tensile strength of the wounded skin was observed in animals treated with the peel extract gels and the peel bandage when compared with wounded control animals. The increase in tensile strength indicates the promotion of collagen fibers and that the disrupted wound surfaces are being firmly knit by collagen. In the excision wound model, significant wound closure was observed on the 4th day in rats treated with all three gel formulations when compared with the wounded control rats. A significant increase in hydroxyproline and ascorbic acid content in the gel-treated animals and a significant decrease in malondialdehyde content in the animals treated with gel as well as peel bandage was observed when compared with the wounded control animals.

Conclusion: It may be concluded that the peels of *Ipomoea batatas* tubers possess a potent wound healing activity, which may be due to an underlying antioxidant mechanism.

Key Words: Sweet potato peels, excision wound, incision wound, wound healing

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Screening of less known two food plants for comparison of nutrient contents: Iranian and Indian vegetables

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ABSTRACT

Background: Greater consumption of fruits and vegetables is associated with reduced risk of cardiovascular disease, stroke, and cancers. The most important nutrients present in plants are carbohydrates, such as the starch and free sugars, oils, proteins, minerals, ascorbic acid, and the antioxidant phenols. Plants are an essential component of the universe. Human beings have used those as medicine from the very beginning of time.

Methods: The proximate composition and mineral constituents of *Asparagus officinalis* stem and *Momordica dioica* fruit were evaluated in order to scientific standard methods of Association for Official and Analytical Chemists (AOAC).

Results: The stem contained ashes: 10.70% crude protein: 32.69%, crude lipid: 3.44%, crude fiber: 18.50%, and carbohydrates: 34.67%. Stem also have high energy value (384.27kcal/100g) dry weight. Mineral ranges (mg/100g dry weight, DW) were: K (10.94), Na (1.84), Ca (0.67), Fe (0.19), and Zn (2.60). The fruits contained ashes: 9.1%, crude protein: 5.44%, crude lipid: 3.25%, crude fiber: 22.9%, and carbohydrates: 59.31%. The fruits also have high energy value (288.25kcal/100g) dry weight. Mineral ranges (mg/100g dry weight, DW) were: K (4.63), Na (1.62), Ca (7.37), Fe (5.04), and Zn (3.83).

Conclusion: Comparing proximate and minerals contents of the stem and the fruit, the results indicated that *Asparagus officinalis* stem could be a good supplement for some nutrients such as protein, lipid, potassium and zinc, fibre and carbohydrates while *Momordica dioica* fruit was good source of lipid, crude fiber, carbohydrates, iron and zinc.

Keywords: *Asparagus officinalis* stem; *Momordica dioica*; Micronutrients; Proximate and Mineral composition.

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Total dietary fiber, and selected vegetable, fruit, legume and cereal fiber intake and risk of heart attack in periodontitis subjects

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ABSTRACT

Background: Epidemiological studies have found an association between periodontal disease and coronary artery disease(Arbes, Slade et al. 1999; Beck, Elter et al. 2001; Genco, Offenbacher et al. 2002), and have even implicated periodontal disease as a risk factor(Arbes, Slade et al. 1999; Beck, Elter et al. 2001), however have not proven causality(Hujoel, Drangholt et al. 2000). Although dietary amounts, sources, and types (soluble versus insoluble) of fiber have been shown to reduce the risk of heart attack (Liu, Buring et al. 2002; Negri, Vecchia et al. 2003), this author is unaware of studies that have examined the association between food sources of dietary fiber and heart attack risk in subjects with periodontitis. This study was designed to determine whether total dietary fiber and fiber from different plant sources (vegetables, fruits, legumes, or cereals) modified self-reported HA risk, as well as acute-phase inflammatory responses in subjects with periodontitis using NHANES III data.

Objectives: The objective of this study was to investigate the association between total dietary fiber intake levels, and selected vegetables, fruits, legumes, and cereal fiber intake and the risk of self-reported history of heart attack (HA) in periodontitis subjects using data available in the Third National Health and Nutrition Examination Survey (NHANES III).

Materials and Methods: Adult participants in NHANES III were used in this study. Zero to thirty three (0-33) percent of sites with periodontal attachment loss > 3 mm was considered a healthy periodontium, while greater than thirty three percent (>33) of sites with periodontal attachment loss of > 3 mm as periodontitis. The outcome variable was the self-reported history of HA. Total dietary fiber, and monthly selected vegetable, fruit, legume and cereal consumption were divided into low and adequate levels. Data was analyzed by Kruskal-Wallis, ANOVA and multivariate analyses using SPSS ®. $P<0.05$ was used to reject the null hypothesis.

Results: Individuals with periodontitis, that consumed low levels of the selected vegetables and fruits had a significantly increased risk of self-reported HA for: low total dietary fiber intake levels($P<0.005$); low levels of selected vegetables - low broccoli and any other vegetables($P<0.01$); Brussels sprouts, carrots, cabbages, spinach and tossed salads($P<0.05$), and low selected fruits – citrus fruits, peaches/nectarines and any other fruits($P<0.05$), adjusting for confounders of both diseases and energy (Kcal). Adjusting the model further for serum antioxidants, dietary cholesterol and other fat intake maintained a significantly higher HA risk for: low total dietary fiber intake levels($P<0.05$); low levels of selected vegetables - low broccoli, spinach($P<0.05$) and any other vegetables($P=0.05$); but significantly increased HA risk with low all-bran cereal($P<0.05$). Serum CRP and creatinine, and plasma fibrinogen, were significantly affected by fiber quantity and source in periodontitis versus healthy periodontium subjects, and in periodontitis and healthy periodontium subjects individually($P<0.05$)

Conclusions: It is theorized that subjects with periodontitis that consume inadequate levels of total dietary fiber, and inadequate fiber from selected vegetables, fruits, legumes, and cereals are likely to increase their risk of heart attack.

Keywords: Dietary Fiber, Periodontitis , Heart Attack

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The protective effect of soybean phytochemicals on androgen responsive human prostate cancer cells LNCaP is likely mediated through modulation of hormone/cytokine-dependent pathways

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ABSTRACT

Background: Population studies suggested that consumption of a soy rich diet provides protective effects against several chronic diseases, including prostate cancer. However, the active components in soy as well as the mechanisms of action of soy's protective effects remain unclear. It would be important to elucidate these questions to support the use of soy in the prevention of chronic disease.

Methods: A cell culture model and molecular techniques were used as tools to identify a molecular signature induced by soy-derived phytochemicals.

Results: Soy phytochemicals inhibit growth of androgen responsive prostate cancer cells. Global gene expression analysis using DNA microarray and real time PCR analysis identified multiple pathways affected by the soy-derived phytochemicals genistein, daidzein, equol, and glyceollins in the androgen responsive human prostate cancer cell LNCaP. These pathways included androgen receptor-dependent pathways, insulin-like growth factors pathways, and cell cycle- related pathways. Soy-derived phytochemicals modulated these pathways in a concentration- dependent fashion.

Conclusion: Taking into consideration the physiological achievable concentration of diet- derived soy phytochemicals, we propose the concentration-dependent cancer protective effect is likely mediated through modulation of hormone/cytokine-dependent pathways.

Key Words: androgen, estrogen, cancer prevention, cell cycle, gene expression

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Effect of Polyphenols in enhancing the swimming capacity of rats

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ABSTRACT

Background: Increased physical activities elevate reactive oxygen species (ROS) leading to dysfunction and integrity of cells thus inducing oxidative stress which intern may affect overall physical performance. Polyphenols are well known for their excellent antioxidant potency. In this study, the effect of selected polyphenols with established health benefits viz., catachin, chlorogenic acid, ellagic acid and quercetin was investigated with respect to swimming performance in rats.

Methods: The animals were force fed with aqueous mixture of polyphenols at 25 mg/rat/day and subjected to swimming exercise until exhaustion.

Results: Rats fed with poly phenols showed a significant increase in swimming time, and the activities of Lactic dehydrogenase (LDH) and creatine pyruvic kinase (CPK) were lowered. Polyphenols increased the concentration of Adenosine triphosphate (ATP), glycogen in muscle lowered the activities of and. Polyphenols increased the concentration of Adenosine triphosphate (ATP) and glycogen in muscle and reduced MDA levels in the liver, muscle and blood but increased DNA and RNA concentration in muscle.

Conclusion: The results clearly demonstrated combination of polyphenols used enhanced the swimming performance of the rats.

Keywords: Polyphenols, Exercise capacity, ROS, ATP, Catachin, Chlorogenic acid, Ellagic acid and Quercetin.

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Immunodetection and quantification of insulin-like antigens in sprouts: development of an efficient functional food

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Running title: Sprouts can be a good source of insulin

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ABSTRACT

Background: Hormone Insulin is a drug used for the treatment of type 1 and type 2 Diabetes Mellitus. Insulin used in this experiment is derived from bovine and pork pancreas, as well as through recombinant technology. Patients with diabetes mellitus face an inability to utilize glucose from blood due to either less secretion of insulin, or the inability of the insulin to act; As a result of this glucose levels in the blood rise. The prevention and treatment of type 2 Diabetes Mellitus one is world's major public health issues. Natural alternatives have a big role to play in this field. This study aims at discovering functional foods rich in Insulin like proteins. Here we are reporting Insulin-like proteins synthesizing during the embryo development stage of *Glycine max*: soybean, *Vigna radiata*: moong and *Vigna unguiculata*: cowpea seeds. Hence, germination transforms these seeds containing human insulin like proteins.

Methods: In our investigation we have provided protein extraction with Enzyme-linked immunosorbent assay (ELISA). The plant materials weighing 1g were crushed in mortar and pestle, and the protein from the plant materials was extracted with 20 ml of 0.05 M sodium phosphate buffer (pH 7.6). The suspensions were centrifuged at 6000 rpm for 15 min, and the clear supernatants were subjected to Enzyme linked immunosorbent assay (ELISA) for the detection of insulin-like proteins. We have used USDA nutritional data sources for the analysis of new products.

Results: Our results demonstrate that Insulin is not expressed in dry mature dormant seeds, but is expressed only during the embryo development stage. Dry mature dormant seeds and the seeds germinated for 24 hours, 48 hours, 72 hours, and 96 hours of *Glycine max*, *Vigna radiata* and *Vigna unguiculata,* were investigated for expression of insulin through immunodetection using anti-insulin antibodies. Dry dormant seeds of all the three seeds showed zero expression at 450 nm for insulin, while significant presence of insulin showing positive immuno-reactivity towards anti-insulin antibodies were observed at 24 hours, 48 hours, 72 hours, and at 96 hours of germination.

Conclusion: The study is suggesting that insulin-like proteins are synthesized only during the process of embryo development, the sprouts of such legumes, particularly soybeans, can be a good source of insulin.

Key words: Germination, insulin, seed embryo development, sprouts.

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Living life the natural way – Wheatgrass and Health

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ABSTRACT

The Human diet is enriched with young parts of plants (so called ―green foods‖), which can improve nutrient balance intake in natural way. Wheatgrass (*Triticum aestivum*) refers to young grass of the common wheat plant, which belongs to Poaceae family. This is the most commonly found herb in India, although its nativity is currently unknown. This plant is believed to have many nutritional values; it has been shown to have anti-inflammatory, antioxidant, anti- carcinogenic, immunomodulatory, laxative, astringent, diuretic, antibacterial and anti-aging properties. Its use in acidity, colitis, kidney malfunctions, atherosclerosis and swelling has been shown to be beneficial. Wheatgrass juice helps in building red blood cells and stimulates healthy tissue cell growth. 100 g of wheatgrass powder is equal to 23 kg of fresh vegetables. Ideally, wheatgrass should be taken about an hour prior to meal. This allows the body to fully metabolize it without competing with other foods, and it may also curb hunger. It is recommended that lot of water (at least a liter) should be consumed with the juice to reap its maximum nutritional benefits. Taking wheatgrass as a supplement in the mid-morning or mid-afternoon is a great time for this "green" energy boost.

Keywords: wheatgrass, anti-carcinogenic, detoxification, health.

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Functional foods in the treatment of type 2 diabetes: olive leaf extract, turmeric and fenugreek, a qualitative review

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ABSTRACT

Almost 30% of US residents ages 65 and older have diabetes. The cost of diabetes care was estimated at $174 billion in 2007, including $116 billion in additional medical costs, and $58 billion in reduced productivity. Globally, the estimated cost of diabetes care was $376 billion in 2010, representing 12% of health expenditures. Many individuals with diabetes make use of functional foods, nutritional supplements, and/or herbal remedies to manage their disease. The functional foods olive leaf extract, turmeric, and fenugreek are commonly used in traditional medicine systems to manage diabetes. All three of these functional foods have antioxidant and anti-inflammatory properties as well as specific insulin sensitizing qualities. In vitro studies offer proof of mechanism, and animal studies consistently show treatment efficacy for all three foods. The few human studies that have been conducted, however, use surrogate rather than clinical endpoints. The establishment of these and other functional foods as evidence based interventions for diabetes requires well designed, adequately powered, and randomized controlled pivotal trials with clinical endpoints.

Keywords: type 2 diabetes, olive leaf extract, turmeric, and fenugreek

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Supplementation of powdered black cumin (*Nigella sativa*) seeds reduces the risk of hypercholesterolemia

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ABSTRACT

Background: Functional and nutraceutical foods are gaining immense popularity among the masses. Plants and their bioactive molecules are of prime importance. Although various plants from different geographical areas have been tested in the past, many horizons still need to be addressed. Black cumin (*Nigella sativa* L.) is one such example that is quite popular in South Asia and the Middle East.

Context and purpose: The present research study was designed to expedite the role of black cumin seed in reducing the risk of hypercholesterolemia. For the purpose, thirty Sprague dawley rats were procured from the National Institute of Health (NIH) in Islamabad, Pakistan, and further split up into three groups, (10 rats each). Experimental diets were prepared using powdered black cumin (PBC) at 1% and 2%, and compared with the placebo.

Results: The results revealed that PBC was effective in reducing the serum cholesterol, triglycerides, and low-density lipoproteins (LDL). Additionally, the experimental diets resulted in a non-significant increase in high-density lipoprotein (HDL). Overall, powdered black cumin at 1% and 2% reduced cholesterol level by 6.73, and 4.48%, LDL by 24.79, and 24.32% respectively. However, the supplementation of PBC at 2% resulted in marked variations as increasing tendency, which was recorded for cholesterol and triglycerides contents after 28 days of study.

Conclusion: Present research investigation brightened the prospects of using powdered black cumin seed in diet based therapies to improve the lipid profile. Further studies are still required to assess the phytochemistry of the plants and indeed the functional ingredients responsible for such health benefits. Such studies would bring meticulousness for utilization of black cumin seeds as a functional food.

Keywords: Functional foods, black cumin, lipid profile, cholesterol, triglycerides

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Curcumin and EGCG suppress apurinic/apyrimidinic endonuclease 1 and induce complete remission in B-cell non-Hodgkin's lymphoma patients

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ABSTRACT

Background: Follicular lymphoma (FL) is the most common subtype of indolent lymphoma. FL is still considered to be an incurable disease and palliation of symptoms is an acceptable approach to the expected pattern of repeated relapses due to developing resistance to chemotherapy agents. Apurinic/apyrimidinic endonuclease/redox factor-1 (APE1/Ref-1) is a multifunctional protein involved in DNA base excision repair (BER) of oxidative DNA damage and in redox regulation of a number of transcription factors. It was observed that cytoplasmic APE1 induced COX-2 expression through NF-κB activation. It has been shown that chemopreventive agents potentiate the efficacy of chemotherapy through the regulation of multiple signaling pathways, including NF-κB, c-Myc, cyclooxygenase-2, apoptosis, and others, suggesting a multitargeted nature of chemopreventive agents. We hypothesized that curcumin, a polyphenolic antioxidant derived from the spice turmeric, and epigallocatechin gallate (EGCG) from green tea would potentiate the effect of chemotherapy in B-cell lymphoma.

Objective: We examined the role of human apurinic/apyrimidinic endonuclease 1 (APE1) in resistance and prognosis in patients with FL. Our major objective was to update the safety and efficacy results of the antitumor effect of combination of curcumin and EGCG therapy in relapsed or resistant indolent or transformed non-Hodgkin follicular lymphoma patients and their peripheral blood mononuclear cells (PBMCs) compared with healthy donors' controls.

Methods: Thirty patients with FL with over-expression of constitutive active NF-κB in their PBMCs received regular CHOP and consumed capsules compatible with curcumin doses between 0.9 and 5.4 g daily for up to 9 months and 9.0 g/day green tea whole extract "1000 mg tablets of green tea whole extract containing 200 mg EGCG. We designed a dose-escalation study to explore the efficacy of CHOP in combination with curcumin and the green tea extract epigallocatechin-3 gallate (EGCG) on the viability of patients' peripheral blood mononuclear cells (PBMCs) lymphocytes.

Results: Treatment of patients with the combination of curcumin and EGCG, significantly lower cytoplasmic APE1 and the levels of the transcription factor were lower than those predicted from the effects of the CHOP agents (cyclophosphamide, doxorubicin, vincristine, and prednisone) alone, especially with a blunting of the remarkable increases in NF- κB activation induced by CHOP. Eighteen of the patients had a CR (18/30), and twelve patients had PR (12/30) within 9 month treatment and followed up to 12 months. They remain disease-free a mean of 8.6 y (range, 7.9–9.2 y) after this combination therapy.

Conclusion: Optimal patient benefit might be obtained in follicular lymphoma when administering curcumin up-front in combination with chemotherapy and EGCG treatment. The combination of curcumin with EGCG resulted in a synergistic antitumor activity and that with CHOP agents in additivity or sub-additivity, down-regulated the expression of all NF-κB regulated gene products, leading to the suppression of angiogenesis, metastasis and entering in complete remission as indicated by β2-microglobulin and lactate dehydrogenase (LDH) levels.

Key words: Curcumin, EGCG, B- cell NHL, NF-κB, VEGF, APE1, lymphoma

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A combination of various functional food ingredients as a weight management program: randomized, placebo-controlled, and double-blind human clinical studies

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ABSTRACT

Background: *Lycium barbarum* increased the postprandial energy expenditure (PPEE). Negative energy balance caused by the systematic procedure (TAI*slim*® System), including increasing metabolic rate through physical activity, use of *Lycium barbarum*-containing TAI*slim* (Product A), and decreasing caloric intake by consuming a chewable confection (TAI*slim* SKINNY=Product B), and a meal replacement shake (TAI*slim* SHAKE=Product C), would be successful for weight loss.

Methods: We examined TAI*slim* System on anthropometrics, appetite in Study 1 and PPEE in Study 2, both in a randomized, placebo-controlled, double-blind manner. **1**) A total of 67 participants were randomized into 2 groups (placebo or TAI*slim* System). Intake procedures were: Product A, 60 ml (20 kcal) b.i.d. immediately before breakfast and lunch, Product B, 1 chew (20 kcal) t.i.d. between meals and after dinner; Product C, 40.5 g (158 kcal) as breakfast. A calorie-restricted diet with multi-vitamin supplementation and daily exercise was required. Anthropometric parameters were assessed at baseline, 4, 8, and 12 w. **2**) Appetite was measured using a subjective visual analog scale during the initial 3-7 days of intake. **3**) For PPEE evaluation, 12 participants consumed a single bout of TAI*slim* System products or placebo, and took part in 6 study sessions. EE was measured by an indirect calorimeter immediately before (baseline) and at 1, 2, and 4 h post-intake of samples.

Results: 1) Body weight was significantly reduced by 6.2±0.7%, compared to pre-intervention with TAI*slim* System ($P<0.01$). Waist circumference, total body fat, blood pressure, and fasting blood glucose levels were also significantly reduced by TAI*slim* System, in a range of 3.8-9.9%. TAI*slim* System was significantly more effective than the placebo ($P<0.05$). The placebo group showed -0.1-3.9% reduction from pre-intervention with no significant difference. **2**) TAI*slim* System also significantly suppressed appetite, by 39%, compared to the baseline and placebo ($P<0.05$) (11% reduction in the placebo). **3**) PPEE was significantly increased by TAI*slim* System compared to placebo and baseline levels. Compared to the baseline EE, placebo increased only by 0.8±0.9%, but 7.2±1.2 % with TAI*slim* System ($P<0.01$).

Conclusions: It is suggested that TAI*slim* System exhibits significant weight loss and stimulating effects on caloric expenditure, and thus may be a useful and effective weight loss program.

Keywords: *Lycium barbarum*, Goji, Fiber, Phenylalanine, N-Acetyl-L-Tyrosine, Tea, Polyphenols, Human clinical trial, Energy expenditure, Resting metabolic rate, Waist circumference, Appetite, Body mass index, TAI*slim*.

Health promotion by antioxidants

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ABSTRACT

Background: Various antioxidnats from daily foods are expected to prevent lifestyle-related diseases. For example, natural carotenoid beta-cryptoxanthin seems to be a promising antioxidant, and based upon epidemiological data it was shown to be a possible cancer preventing agent. For this reason, we chose to study beta-cryptoxanthin more extensively.

Methods and Results: From the result of clinical trial using beta-cryptoxanthin-enriched Mandarin orange juice, it was proven to potentiate the preventive activity of multi-carotenoid mixture against liver cancer in the patients with chronic viral hepatitis-induced liver cirrhosis. Furthermore, beta-cryptoxanthin also has preventive activity against alcohol-induced gamma- GTP elevation, and obesity.

Conclusion: An antioxidant beta -cryptoxanthin seems to be valuable for health promotion.

Key words: beta-Cryptoxanthin, Health promotion, Liver cancer prevention, Prevention of alcohol-induced gamma-GTP elevation, Prevention of obesity.

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/105/216

Neuroprotective and immune effects of active forms of vitamin D_3 and docosahexaenoic acid in Alzheimer disease patients

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ABSTRACT

Neurodegenerative diseases, in particular Alzheimer disease (AD), afflict an increasing proportion of the older population with aging. Decreased exposure to sunlight and decreased consumption of fish, fruits, and vegetables, are two epidemiological factors that appear to be related to the pandemic of AD. In addition to replacing simple with complex carbohydrates and avoiding saturated fat, two nutritional components, vitamin D (acting through the endogenous hormonal form 1□,25 dihydroxyvitamin D, 1,25D) and docosahexaenoic acid (DHA) (acting through the docosanoid lipidic modulators resolvins and neuroprotectins) have high potential for prevention of Alzheimer disease. 1,25D is a neuroprotective, it acts both directly and indirectly in neurons by improving the clearance of amyloid-beta by macrophages/microglia. Resolvins and neuroprotectins inhibit amyloidogenic processing of amyloid-precursor protein, inflammatory cytokines, and apoptosis. It is likely that the increased consumption of vitamin D and fish oil could prevent neurodegeneration in some subjects by maintaining adequate endocrine, paracrine, and/or autocrine production of 1,25D and the DHA-derived lipidic modulators. Before firm recommendations of the dosage can be proposed, however, the in vivo effects of vitamin D_3 and DHA supplementation should be investigated by prospective studies.

Key words: Alzheimer disease, vitamin D3, DHA, fish oil

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The enhancing effect of γ-Cyclodextrin inclusion on γ-Tocotrienol-dependent negative growth control of mesothelioma cells in a xenograft model

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ABSTRACT

Background: Malignant mesothelioma is an aggressive cancer with no effective treatment options. Of phytochemicals, tocotrienol (T3), a member of vitamin E, is one of the most potent anti-mesothelioma agents, but the effectiveness *in vivo* is quite limited, due to its low bioavailability. In this study, we investigated if the oral treatment of □-T3 inclusion with □-cyclodextrin (CD) could improve the bioavailability and anticancer activity of the T3.

Findings: Using nude mice bearing MSTO-211H cells (a human malignant mesothelioma cell line), the effect of □-T3 inclusion with □-CD on □-T3 level in tumor tissues, tumor growth, and its related mRNA levels were examined. The difference of tumor growth between the two groups had no statistical significance, but the latter showed a lower tendency compared with the former. In linked with this observation, the level of vascular endothelial growth factor mRNA required for *in vivo* tumor growth in □-T3 inclusion with □-CD group was lower than that in □-T3 group, on the contrary, the level of □-T3 level showed an opposite tendency.

Conclusion: Our study demonstrated that the bioavailability of □-T3 was improved by an oral administration of a novel □-T3 inclusion complex with CD. Furthermore, the improvement of the bioavailability contributed to the increase of anticancer activity of □-T3 *in vivo*.

Key words: Anti-cancer agent, bioavailability, cyclodextrin, mesothelioma, tocotrienol.

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Lipid Replacement Therapy functional food formulation with NT Factor for reducing weight, girth, body mass, appetite and fatigue while improving blood lipid profiles

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ABSTRACT

Background: Lipid Replacement Therapy using NT Factor® plus kidney bean alpha-amylase inhibitor (Healthy Curb®) was used in a two month weight loss clinical trial to reduce weight and improve fatigue without changing easting or exercise patterns and without use of drugs, stimulants or herbs.

Objectives: To determine the effects of an all-natural functional food, NT Factor® plus alpha-amylase inhibitor (Healthy Curb®), on weight loss, body girth, body mass and index, basal metabolic rate, appetite, carvings for sweets and fatigue as well as blood lipid profiles during a 2-month open label clinical trial without food restrictions or increases in physical activity.

Methods: Thirty subjects (Mean Age = 56.8 ± 1.8; 24 females and 6 males) used the functional food containing NT Factor® (500 mg) and alpha-amylase inhibitor (500 mg) 30 min before each meal in tablet form. Participants were told to eat and exercise normally. Weight, waist and hip measurements were taken weekly. Appetite and sweet cravings were assessed weekly by standard methods. Fatigue was determined using the Piper Fatigue Scale. Blood samples were taken prior to and at the end of the trial for lipid and chemical analyses.

Results: Sixty-three percent of the participants lost an average of 6.11 ± 0.28 pounds (2.77 ± 0.12 Kg) ($p<0.001$) along with average reductions of 2.51 ± 0.05 inches (6.4 ± 0.13 cm) ($p<0.0001$) and 1.5 ± 0.04 inches (3.8 ± 0.10 cm) ($p<0.0001$) from waist and hip circumferences, respectively. The entire group lost an average of 3.63 ± 0.13 pounds (1.65 ± 0.11 Kg) ($p<0.001$) with average reductions of 1.59 ± 0.03 inches (4.04 ± 0.06 cm) ($p<0.0001$) and 1.13 ± 0.02 inch (2.87 ± 0.05 cm) ($p<0.0001$) from waist and hip circumferences, respectively. Weight loss and body measurement decreases were gradual, consistent and significant, along with reductions in body mass index (BMI) and basal metabolic rate (BMR) measurements. Overall hunger was reduced 44.5% ($p<0.001$), with reduced cravings for sweets and fats, and there was a 23.9% reduction in fatigue ($p<0.009$). Along with fatigue reduction there was a 26.8% perceived improvement ($p<0.004$) in cognition and ability to concentrate, remember and think clearly. Blood lipid profiles at the end of the trial suggested improved cardiovascular lipid profiles, and there were no adverse events from the product.

Conclusions: The participants lost weight, showed significant decreases in waist and hip measurements and had reduced average overall body mass. Their fatigue was significantly reduced, and they experienced marked appetite suppression and reduced cravings for sweets and fats. Healthy Curb® was completely safe and well tolerated and appeared to be an effective functional food product to manage weight and appetite without changing eating or exercise patterns.

Keywords: NT Factor®, alpha-amylase inhibitor, weight loss, girth, body mass index, fatigue, hunger, appetite, mitochondrial function, blood lipoproteins

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Therapeutic application of diacylglycerol oil for obesity: serotonin hypothesis

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ABSTRACT

Characteristics for the serum lipid abnormalities in the obesity/metabolic syndrome are elevated fasting, postprandial triglyceride (TG), and decreased high-density lipoprotein-cholesterol (HDL-C). Diacylglycerol (DAG) oil ingestion has been reported to ameliorate postprandial hyperlipidemia and prevent obesity by increasing energy expenditure, due to the intestinal physiochemical dynamics that differ from triacylglycerol (TAG). Our study demonstrated that DAG suppresses postprandial increase in TG-rich lipoprotein, very low-density lipoprotein (VLDL), and insulin, as compared with TAG in young, healthy individuals. Interestingly, our study also presented that DAG significantly increases plasma serotonin, which is mostly present in the intestine, and mediates thermogenesis, proposing a possible mechanism for a postprandial increase in energy expenditure by DAG. Our other study demonstrated that DAG suppresses postprandial increase in TG, VLDL-C, and remnant-like particle-cholesterol, in comparison with TAG in an apolipoprotein C-II deficient subject, suggesting that DAG suppresses postprandial TG-rich lipoprotein independently of lipoprotein lipase. Further, to understand the molecular mechanisms for DAG-mediated increase in serotonin and energy expenditure, we studied the effects of 1-monoacylglycerol and 2-monoacylglycerol, distinct digestive products of DAG and TAG, respectively, on serotonin release from the Caco-2 cells, the human intestinal cell line. We also studied effects of 1- and 2-monoacylglycerol, and serotonin on the expression of mRNA associated with β-oxidation, fatty acids metabolism, and thermogenesis, in the Caco-2 cells. 1-monoacylglycerol significantly increased serotonin release from the Caco-2 cells, compared with 2-monoacylglycerol by approximately 40%. The expression of mRNA of acyl-CoA oxidase (ACO), fatty acid translocase (FAT), and uncoupling protein-2 (UCP-2), was significantly higher in 1-MOG-treated Caco-2 cells, than 2-MOG-treated cells. The expression of mRNA of ACO, medium-chain acyl-CoA dehydrogenase, FAT, and UCP-2, was significantly elevated in serotonin-treated Caco-2 cells, compared to cells incubated without serotonin. In conclusion, our clinical and in vitro studies suggested a possible therapeutic application of DAG for obesity, and obesity-related metabolic disorders.

Key words: Diacylglycerol, intestine, obesity, serotonin, thermogenesis

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Glycemic Index values of some Jaffna fruits

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ABSTRACT

Background: The incidence of diabetes mellitus has recently increased in developing countries. Scientific data on glycemic index values of common meals is essential to modify the diets for diabetes mellitus patients. This study aimed to evaluate the glycemic index (GI) values of fruits such as 'Kathali' (Yellow plantain), 'Kappal' (Golden plantain), and 'Itharai' (Green plantain) varieties of plantains, jack fruit and papaya. The results will be helpful to physicians and the general public to decide the benefits of the consumption of fruits, particularly by diabetic and coronary heart disease patients.

Methods: Healthy volunteers (20 Nos.) of 21.05(±0.92) years, 53.90 (±9.36) kg body weights, 153.92 (±9.15) m heights, and 20.55 (±2.22) kgm^{-2} body mass indexes were selected with their written consent. After overnight fasting, 75g glucose and each test fruit containing 75g digestible carbohydrate were administered at different instances and blood glucose levels were measured half hourly for two hours. The glycemic response and GI values were calculated and analyzed by Randomized Complete Block Design using SAS analytical package.

Results: The mean GI values of the 'Kathali', 'Kappal', 'Itharai' varieties of plantains, jack fruit and papaya were 54.45 (±9.26), 50.43 (±5.79), 48.47 (±10.13), 65.36 (±8.00) and 34.80 (±12.78) % respectively. The GI value of papaya differed significantly ($P<0.05$) from other fruits. The GI value of 'Itharai' variety of plantain differed significantly ($P<0.05$) from other fruits except the 'Kappal' variety of plantain.

Conclusion: The three varieties of plantains and papaya were low GI fruits, and jack fruit was found to be an intermediate GI fruit. The presence of dietary fiber, esp. soluble fiber, reduces the glycemic response and glycemic index of foods.

Keywords: Glycemic index, glycemic response, fiber, fruits.

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Glycophospholipid formulation with NADH and CoQ10 significantly reduces intractable fatigue in Western blot-positive 'Chronic Lyme Disease'

Patients: Preliminary Report

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ABSTRACT

Background: An open label 8-week preliminary study was conducted in a small number of patients to determine if a combination oral supplement containing a mixture of phosphoglycolipids, coenzyme Q10 and microencapsulated NADH and other nutrients could affect fatigue levels in long-term, Western blot-positive, multi-symptom „chronic Lyme disease" patients (also called „post-treatment Lyme disease" or „post Lyme syndrome") with intractable fatigue.

Methods: The subjects in this study were 6 males (mean age = 45.1 ± 12.4 years) and 10 females (mean age = 54.6 ± 7.4 years) with „chronic Lyme disease" (determined by multiple symptoms and positive Western blot analysis) that had been symptomatic with chronic fatigue for an average of 12.7 ± 6.6 years. They had been seen by multiple physicians (13.3 ± 7.6) and had used many other remedies, supplements and drugs (14.4 ± 7.4) without fatigue relief. Fatigue was monitored at 0, 7, 30 and 60 days using a validated instrument, the Piper Fatigue Scale.

Results: Patients in this preliminary study responded to the combination test supplement, showing a 26% reduction in overall fatigue by the end of the 8-week trial ($p < 0.0003$). Analysis of subcategories of fatigue indicated that there were significant improvements in the ability to complete tasks and activities as well as significant improvements in mood and cognitive abilities. Regression analysis of the data indicated that reductions in fatigue were consistent and occurred with a high degree of confidence ($R^2 = 0.998$).

Conclusions: The combination supplement was a safe and effective method to significantly reduce intractable fatigue in long-term patients with Western blot-positive „chronic Lyme disease."

Keywords: Lyme disease, Lipid Replacement Therapy, NT Factor, mitochondria, chronic fatigue, NADH, coenzyme Q10

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Anti-ulcer activity of *Ipomoea batatas* tubers (sweet potato)

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ABSTRACT

Background: Peptic ulcers occur in that part of the gastrointestinal tract which is exposed to gastric acid and pepsin, i.e., the stomach and duodenum. Gastric and duodenal ulcers are common pathologies that may be induced by a variety of factors such as stress, smoking and noxious agents including non-steroidal anti-inflammatory drugs. *Ipomoea batatas* tubers (sweet potato) contain ample amounts of antioxidants. It has been proven already by many scientific studies that antioxidants have ulcer healing properties. In reference to this, we tried assessing the ulcer healing effect of *Ipomoea batatas* tubers.

Methods: The anti-ulcer activity of the tubers of *Ipomoea batatas* (sweet potato) was studied in cold stress and aspirin-induced gastric ulcers in Wistar rats. Methanolic extracts of *Ipomoea batatas* tubers (TE) at two doses, viz., 400 and 800 mg /kg were evaluated in cold stress and aspirin-induced gastric ulcer models using cimetidine and omeprazole respectively as standards. The standard drugs and the test drugs were administered orally for 7 days in the cold stress model and for 1 day in the aspirin-induced gastric ulcer model. Gastroprotective potential, status of the antioxidant enzymes {superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and glutathione reductase(GR)} along with GSH, and lipid peroxidation were studied in both models.

Results: The results of the present study showed that TE possessed gastroprotective activity as evidenced by its significant inhibition of mean ulcer score and ulcer index and a marked increase in GSH, SOD, CAT, GPx, and GR levels and reduction in lipid peroxidation in a dose dependant manner.

Conclusion: The present experimental findings suggest that tubers of *Ipomoea batatas* may be useful for treating peptic ulcers.

Key Words: Sweet potato tubers, cold stress, aspirin, ulcer, antioxidants.

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Evaluation of dietary Intake and Food Patterns of Adolescent Girls in Sistan and Baluchistan Province, Iran

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ABSTRACT

Background: The evidence suggests a relationship between lifestyle and diet-related risk factors.

Objective: This study assessed the dietary intake and habits of high school girls in Sistan and Bluchistan province, in southeastern Iran**.**

Methods: In a cross-sectional, descriptive study, 753 high school girls aged 14-18 years old were enrolled by a clustered random sampling method. Dietary intake and food habits were evaluated by a two-day, 24-hour dietary recall, and a food frequency questionnaire (FFQ).

Results: The analysis of dietary intakes showed that energy, calcium, zinc, vitamin C and folate intake, compared to the Dietary Reference Intake (DRI), were found to be lower. The, infrequent intake of milk and dairy products, fruits and vegetables, and a high consumption of empty calorie foods e.g. salty snacks, sweets, soft drinks and junk foods were seen among adolescents.

Conclusions: The adolescent girls had an improper dietary intake and food habits. Thus, the implementation of nutrition education programs in schools and the designing of proper patterns towards healthier food choices could help improve eating behaviors, the health maintenance of adolescents, and also prevent diet- related diseases in adulthood.

Key words: Adolescent girls, Dietary intake, Food habits.

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Differential effects of tea extracts on growth and cytokine production by normal and leukemic human leukocytes

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ABSTRACT

Background: Tea is one of the world's most highly consumed beverages, second only to water. It is affordable and abundant and thus has great potential for improving health of those in both developed and developing areas. Green, oolong, and black teas differ in the extent of fermentation and types of bioactive polyphenols produced. Green tea and its major polyphenol decrease growth of some cancer cells and effect production of immune system cytokines. This study compares the effects of different types of tea extracts on viability and cytokine production by normal and leukemic human T lymphocytes. Generation of the toxic reactive oxygen species H_2O_2 by extracts was also examined.

Methods: The Jurkat T lymphoblastic leukemia cells and mitogen-stimulated normal human peripheral blood mononuclear cells were used in this study. Cell viability was determined by (3- 4,5-dimethylthiamizol-2-yl)-diphenyltetrazolium bromide) assay and production of interleukin-2 by Enzyme-Linked ImmunoSorbent Assay. Levels of H_2O_2 generated by tea extracts were determined using the xylenol-orange method.

Results: We found that green, oolong, and black tea extracts differentially effect the growth and viability of T lymphoblastic leukemia cells and normal peripheral blood mononuclear cells, substantially decreasing both growth and viability of leukemic T lymphocytes and having much lesser effects on their normal counterparts. Tea extracts also had differential effects on the production of the T lymphocyte growth factor interleukin 2, significantly decreasing production by leukemic cells while having only minor effects on normal cells. All three extracts induced H_2O_2 generation, with green and oolong tea extracts having the greatest effect. Leukemic cells were much more susceptible to growth inhibition and killing by H_2O_2 than normal lymphocytes.

Conclusions: The three tea extracts studied altered leukemic T lymphocyte functions, decreasing cell viability, growth, and production of a major cell growth factor and the H_2O_2 generated by solutions of extracts may be partially responsible. Normal cells were affected to a far lesser degree by tea extracts and are also more resistant to killing by H_2O_2 than leukemic cells. This study has implications for using tea extracts for chemotherapeutic and immunomodulatory purposes.

Key Words: Tea extracts, interleukin-2, hydrogen peroxide, leukemia, T lymphocytes

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Chemical composition of water buffalo milk and its low-fat symbiotic yogurt development

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ABSTRACT

Background: Water buffalos are the second most widely available milk source in countries around the world. While typical average milk compositions are readily available, information on seasonal variation in chemical composition of buffalo milk is limited -especially in the Northeastern region of the United States. Data collected in this study can be useful for the manufacture of a wide variety of specialty dairy products such as symbiotic buffalo milk yogurt. To analyze functionality, symbiotic low fat buffalo milk yogurt prototypes (plain and blueberry) were developed using a commercial starter containing probiotics.

Methods: During a one-year cycle, physicochemical and mineral contents of buffalo milk were analyzed. Prototype yogurts were manufactured commercially and samples of the yogurt prototypes were analyzed for physicochemical and microbiological properties and for the survivability of probiotics during ten weeks of storage.

Results: Average contents of total solids, fat, lactose, crude protein, ash, specific gravity, and conjugated linoleic acid in the milk ranged from 16.39-18.48%, 6.57-7.97%, 4.49-4.73%, 4.59-5.37%, 0.91-0.92%, 1.0317-1.0380%, and 4.4-7.6 mg/g fat, respectively. The average mineral contents of calcium, phosphorous, potassium, magnesium, sodium, and zinc in the milk were 1798.89, 1216.76, 843.72, 337.20 and 7.48 mg/kg, respectively, and remained steady throughout the year. The symbiotic low fat buffalo milk yogurts evaluated in this study contained higher amounts of protein, carbohydrates, and calcium than similar yogurts manufactured with cows' milk. During refrigerated storage, the probiotic *Lactobacillus acidophilus* was viable (>1×10^6 CFU/g) for the first two weeks, while *Bifidobacterium spp.* and *Lactobacillus casei* remained viable during the entire ten weeks. Reducing the acidity and enhancing the flavor of the yogurts could improve the overall acceptability.

Conclusion: The results indicated that the low fat buffalo milk yogurt are a rich source of nutrients and are nutritionally preferable to cows' milk yogurts. The shelf life analysis indicated it to be a good vehicle for developing symbiotic yogurt.

Keywords: Buffalo milk, conjugated linoleic acid, symbiotic yogurt, probiotic survivability, physicochemical properties, acceptability.

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Amino acid profile of raw and locally processed seeds of *Prosopis africana* and *Ricinus communis*: potential antidotes to protein malnutrition

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ABSTRACT

Background: Increasing incidence of malnutrition occasioned by high incidence of hunger, worsening food situation in the world, insufficient availability and high cost of animal protein sources, has necessitated extensive research into and use of alternative plant protein sources especially underexploited leguminous seeds.

Methods: Flours from raw, boiled and fermented seeds of *Prosopis africana* and *Ricinus communis* were evaluated for crude protein and amino acid (AA) profiles, and their protein qualities determined.

Results: Fermentation improved the protein contents of raw seeds of *P. africana* and *R. communis* by 18.70% and 3.95% respectively. In the raw and fermented *P. africana* seeds, glutamate at 132.60 ± 1.30 and 182.70 ± 3.02 mg/g crude protein (mg/gcp) was the most abundant amino acid (AA), while leucine (62.80 ± 0.60 and 79.50 ± 2.01 mg/gcp) was the most concentrated essential amino acid (EAA). Aspartate (151.90 ± 2.01 and 170.10 ± 2.00 mg/gcp) and arginine (72.80 ± 2.01 and 78.60 ± 2.00 mg/gcp) were the most concentrated and abundant non-essential amino acid (NEAA) and EAA in the raw and fermented samples of *R. communis* respectively. The total AA concentrations (mg/gcp) of raw and fermented *P. africana* were 733.00 and 962.60 respectively, while those of *R. communis* were 823.50 and 894.10 respectively. The total EAA contents (mg/gcp) for *P. africana* were 311.00 (raw) and 404.50 (fermented), and for *R. communis;* 401.10 (raw) and 430.30 (fermented). Threonine was the limiting EAA in raw and fermented *P. africana,* whereas lysine was the limiting EAA in *R. communis* raw sample. Fermentation significantly ($p<0.05$) increased the individual AA compositions of *P. africana* and *R. communis* by 94% and 53% respectively, while boiling reduced these parameters significantly ($p<0.05$) by 47% and 82% respectively.

Conclusion: *P. africana* and *R. communis* seeds are potentially important plant sources of protein and essential amino acids, and so could be of great importance in combating malnutrition and food security problems generally.

Key words: Amino acid score; condiments; crude protein; fermentation; legumes; nutrition.

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Therapeutic efficacy of Genistein-Cytoreg® combination in breast cancer cells

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ABSTRACT

Background: In spite the heavy investments in therapeutic research breast cancer still impacts the lives of women globally. The projected incidence of new cases of in situ breast cancer in the USA for 2011 is 57,650, with estimated 39,520 deaths. The phytoestrogen, genistein and the synthetic compound, Cytoreg® have been shown to inhibit growth and proliferation in many cancer cell lines.

Purpose of the Study: In this study, we investigated the therapeutic efficacy of Cytoreg®- genistein combination on growth inhibition in the MCF-7 human breast cancer cells.

Method: MCF-7 cells were treated with genistein and Cytoreg® single and combination treatments for 24-48hrs; and post treatment chemosensitivity assessed, using: Trypan Blue exclusion and MTT assays for cell viability, Ethidium bromide/Acridine orange to assess apoptosis induction, and FAM Poly-Caspase binding assay for mechanism of action.

Results: The overall data indicated dose- and time- dependent cell death in the MCF-cells and apoptosis as the major means of treatment-induced growth inhibition with all the treatment regimens.

Conclusion: Comparatively, the genistein-Cytoreg® combination treatment was significantly more efficacious in growth inhibition in the MCF cells than either genistein or Cytoreg® alone. Genistein seems to act additively with Cytoreg® in combination treatment-induced apoptosis in MCF-7 cells. The normal human breast epithelial cells were not significantly inhibited by either single or the combination treatments.

Key words: Cytoreg®, Genistein, Combination treatment, MCF- cancer cells, apoptosis

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Impact effect of lycopene and tomato-based products network on cardio- protective biomarkers *in vivo*

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ABSTRACT

Background: Dietary intake plays an important role as nutritional supplements are known to provide potential health benefits in cardiovascular disease. Recent studies suggest that the dietary intake of tomatoes and tomato products containing lycopene are associated with a decreased risk of cardiovascular disease. In order to substantiate these facts, the present study was undertaken to investigate the effectiveness of lycopene from tomato products on the potential effects of oxidative stress and atherosclerosis *in vivo*, focusing on early atherosclerotic events.

Methods: Thirty male albino rats were assigned randomly into 5 groups; group C was the negative control group fed a basal diet, group H was the positive control fed a high-fat diet (HFD), group TS (HFD) was fed a 8% lyophilized tomato paste, group TW (HFD) was fed a 24% lyophilized raw tomato, and group L (HFD) was fed 0.1% mg pure lycopene. The level of serum; total cholesterol (TC), total triglyceride (TG), high-density lipoprotein cholesterol (HDL-$_c$), and low-density lipoprotein cholesterol (LDL-$_c$) was measured after 8 weeks of experimental treatment. Malondialdehyde (MDH) plasma levels were measured in heart tissue homogenate. Furthermore, pathologic changes of the heart and aorta were also assessed.

Results: We found that TC, TG, LDL-$_c$ and MDH, levels were significantly increased in group H ($P < 0.05$) compared to the negative control group. Administration of TS, TW and L demonstrated significant changes in these parameters ($P < 0.05$). The TW group (fed 24% of lyophilized raw tomato components) had more positive effects than the TS & L groups. Furthermore, morphologic changes of heart and aorta revealed that TW and TS had a similar preventive effect against the development of atherosclerosis. **Conclusion:** Our study indicated that raw tomatoes have a higher potential effect when compared to tomato paste or lycopene alone. This potential effect includes the ability to attenuate and/or reverse oxidative stress and other atherosclerosis related parameters induced by the consumption of a high-fat diet.

Key words: Cardioprotective, Lipid profile, Lycopene, Oxidative stress, Tomatoes products

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Voluntary ingestion of natural cocoa extenuated hepatic damage in rats with experimentally induced chronic alcoholic toxicity

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ABSTRACT

Background: Chronic ethanol ingestion causes hepatic damage imputable to an increased oxidative stress engendered by alcoholic toxicity. Polyphenols in cocoa have antioxidant properties, and natural cocoa powder (NCP) contains the highest levels of total antioxidant capacity when compared to all other kinds of edible cocoa products. This study tested the hypothesis that dietary supplementation with NCP mitigates hepatic injury resulting from chronic ethanol consumption. Three groups of eight randomized Sprague-Dawley rats were fed standard rat food and treated daily for 12 weeks as follows: (i) the Ethanol-water group was given unrestricted access to 40% (v/v) ethanol for 12 hours (at night) followed by water for the remaining 12 hours (daytime), (ii) the Ethanol-cocoa group had similarly unrestricted access to 40% ethanol for 12 hours followed by 2% (w/v) NCP for 12 hours, and (iii) the control group was not given alcohol and had unrestricted access to only water which was synchronously replenished every 12 hours as it was for the ethanol treated animals.

Results: Qualitative structural liver damage evidenced by hepatocyte cytoplasmic fatty accumulation, nuclear alterations, and disruption of general liver micro-architecture, was severe in the ethanol-water group when compared with the ethanol-cocoa group of rats. Design-based stereologic assessment yielded a significantly greater volume (Tukey's HSD, p = 0.0005) of undamaged hepatocytes (9.61 ml, SD 2.18 ml) in the ethanol-cocoa group as opposed to the ethanol-water group of rats (2.34 ml, SD 1.21 ml). Control rats had 10.34 ml (SD 1.47 ml) of undamaged hepatocytes, and that was not significantly greater (Tukey's HSD, p=0.659) than the value for the ethanol-cocoa group of rats. Relative to controls, therefore, histomorphometry showed 93% hepatocyte preservation from alcoholic injury in rats that voluntarily imbibed NCP suspension compared with 23% in animals that drank water.

Conclusions: Ethanol-induced structural liver injury was qualitatively and quantitatively milder in rats which chronically imbibed alcohol then afterward drank NCP beverage in place of water. The antioxidant and anti-inflammatory properties of polyphenols in NCP are postulated in mitigating the damage of rat liver due to chronic ethanol consumption. Thus, it is suggested from these findings that regular drinking of NCP beverage may slow progression of alcoholic liver disease in dipsomaniacs.

Key words: natural cocoa powder, chronic alcoholic toxicity, total antioxidant capacity, polyphenols

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Novel concepts on functional foods and nutrigenomics in healthy aging and chronic diseases: a review of fermented papaya preparation research progress

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ABSTRACT

Functional foods are an emerging research field corresponding with genomical, epidemiological and clinical studies integrated with the food industry in accordance with the consumer demands. Consequently, the features of the functional foods are being discussed by various researchers and related institutions, and a common view has been pointed out about the availability and the nature of the components of functional foods. Recently, the outcomes of functional foods are being assessed by the help of all the available scientific tools. Genomic medicine is one of the most promising areas of research to reveal the benefits of functional foods and the bioactive ingredients. Nutrigenomics aims at studying the genetic and epigenetic interactions with a nutrient or the functional component in order to lead to a phenotype change and therefore to the cell metabolism, differentiation or even apoptosis. Papaya and its fermentation product are specific products derived from the technologically advanced and controlled environmental- friendly bio-fermentation process.

It has been well known for a long time that the natural anti-oxidant properties of papaya, mainly depending on vitamins A and C in addition to certain amino acids, were consistent both in the fruit and derived from the papain enzyme which is no longer present in the fermented product. In this article, functional foods in genomic medicine are discussed in review of the fermented papaya preparation research progress. Clinical evidences about fermented papaya as a functional food are reported as supported by various research protocols and experimental models. The benefits of fermented papaya preparation are also discussed in nutrigenomic basis and it is reported to have an important antioxidant and transcriptomic potential which deserves further investigation. As a conclusion, fermented papaya preparation represents a Functional Food highly compliant with the novel features of the new nutrigenomic-driven action plan strategy aimed to reduce the incidences of diseases and successful integration within specific pharmacological treatments.

Keywords: functional foods, fermented papaya preparation, nutrigenomics

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Biochemical evaluation of the effects of Nigerian polyherbal preparation on Wistar rabbits

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ABSTRACT

Background: Diabetes mellitus is a metabolic disorder with multiple etiologies. Its sufferers are generally at high risk of dyslipidemia characterized by hypercholesterolemia, hyper- triglyceridemia, hyperlipoproteinemia and low levels of high-density lipoprotein cholesterol. Globally, the estimated cost of diabetes care was $376 billion in 2010, representing 12% of health expenditures for that year.

Methods: The effects of the aqueous extracts of a little known Nigerian traditional polyherbal formula consisting of *Emilia coccinea, Acanthus montanus, Hibiscus rosasinensis* and *Asystasia gangetica* on serum glucose concentration, amylase activity and lipid profiles of normal, diabetic, and liver-damaged rabbits were studied using standard procedures. The mixture of the aqueous extracts of the four plants was orally administered in two doses – 120mg/kg body weight and 240mg/kg body weight for 28 days.

Results: The drug elicited dose- and duration-of-administration-dependent, significant ($p<0.05$) reductions in serum levels of glucose, total cholesterol, triacylglycerol and LDL-cholesterol; and significant ($p<0.05$) increases in the HDL-cholesterol concentrations with no changes in amylase activity.

Conclusion: These results confirm the hypoglycemic, antihyperlipidemic and hepatoprotective potentials of the crude drug and thus justify its application in ethnomedicine in the management of diabetes.

Key words: *Emilia coccinea, Acanthus montanus, Hibiscus rosasinensis, Asystasia gangetica*, antidiabetic, hepatoprotection.

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Phenotype microarray profiling of the antibacterial activity of red cabbage

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ABSTRACT

Background: Functional food can be a potent source of wide array of biocomonents with antimicrobial activity. We investigated the antibacterial activity of red cabbage (RC) extract on Gram negative and positive ATCC strains. Most intersting, we, for the first time, explored and analysed the complete phenotypic profile of RC-treated bacteria using Omnilog Phenotype Microarray.

Results: This study revealed that the phenotype microarray (PM) screen was a valuable tool in the search for compounds and their antibacterial mechanisms that can inhibit bacterial growth by affecting certain metabolic pathways. It was shown that RC exerted remarkable antibacterial effect on S. aureus and E. coli bacteria, and PM showed a wide range phenotypic profile of the exerted RC antibacterial activity. RC targeted the peptide, carbon, nutriontional assembly, and sulfur metbolic pathways altogether. The peptidoglycan synthesis pathway was inferred to be targeted by RC extract at a metabolic point different from other available cell wall-targeting drugs; these could be hot targets for the discovery of new therapy for many problematic microbes.

Conclusions: Taken together, the phenotype microarray for functional food and medicinal plants can be a very useful tool for profiling their antimicrobial activity. Moreover, extracts of functional food can exert antibacterial activity by hitting a wide range of metabolic pathways, at the same time leading to very difficult condition for bacteria to rapidly develop resistance. Therefore, using functional foods or medicinal plants as such, or as extracts, can be superior on mono-targeting antibiotics if the optimal concentrations and conditions of these functional foods were sought.

Key words: red cabbage, bacteria, antibacterial, phenotype microarray, Omnilog, Biology
Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/88/295

Lowbush blueberries, *Vaccinium angustifolium,* modulate the functional potential of nutrient utilization and DNA maintenance mechanisms in the rat proximal colon microbiota

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ABSTRACT

Background: The core gut microbiota encodes for a metabolic capacity that often surpasses the metabolic potential of its host. Lowbush wild blueberries (LWB) are a rich source of bioactive compounds, and the gut microbiota is an important modulator of their activity. The objective of this research is to study the effect of a diet enriched with LWB on the gastrointestinal microbiota's metabolic potential.

Methods: Nine three-week-old male Sprague Dawley rats were randomly assigned to two groups. The control group (*N*=4) was placed on the AIN93 diet, and the treatment group (*N*=5) was fed the same diet with 8% (w/w) LWB powder substituting for dextrose. The animals consumed the diets for six weeks, after which they were sacrificed. Functional profiles and metabolic potential of the colon microbiota in response to diet were analyzed using deep whole genome sequencing (WGS).

Results: Proteins predicted from WGS DNA sequences were assigned to 3,746 COG, 5,577 KEGG, and 4,474 Pfam families. Statistical comparisons of the protein-coding genes revealed significant changes in 25 Gene Ontology (GO), 186 KEGG, and 20 Pfam protein families representing 2.1%, 3.3%, and 0.02% of all hits identified, respectively. Overall, the combined inquires into these databases represented an emphasis on membrane trafficking, DNA regulation, modification and repair, and nutrient metabolism. Protein families that significantly increased by the enrichment of LWBs were involved with amino acid metabolism, 2,4-dienoyl-CoA reductase, metal ion binding, glutamate synthase, REDOX homeostasis, and aryl transferases. In contrast, protein families involved with integrase/recombinase, reverse transcriptase, and transposon/transposase were at a lower abundance.

Conclusions: The results from this study reflect the potential impact that LWBs have on the functional repertoire of bacterial communities in the proximal colon. The results demonstrate a higher potential for the metabolism of amino acids and a lower potential for horizontal integration of plasmids and lower phage/transposon activity in the LWB diet, suggesting that the genome at the time of sampling was more stable. This study helps unravel diverse mechanisms of microbial adaptation to LWBs in the diet of mammals and can provide guidance in optimizing functional diets.

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/87/187

Anti-cancer effect of *Angelica Sinensis* on women's reproductive cancer

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ABSTRACT

Objective: Danggui, the root of *Angelica Sinensis*, has traditionally been used for the treatment of women's reproductive disorders in China for thousands of years. This study was to determine whether Danggui have potential anti-cancer effect on women's cancer and its potential mechanism.

Methods: Danggui was extracted by ethanol. The Cell Titer 96® Aqueous Non-Radioactive Cell Proliferation Assay was used to compare the effects of Danggui on human breast (MCF-7 and 7368) and cervical (CaSki and SiHa) cancer cells with its effects on normal fibroblasts (HTB-125). A revised Ames test was used to test for antimutagenicity. The standard strains of Salmonella typhimarium (TA) 100 and 102 were used in the test. Methyl methane sulfonate (MMS) and UV light were used as positive mutagen controls and ethanol and double distilled water (DDW) as controls. The SAS statistical software was used to analyze the data.

Results: Danggui was found to be much more toxic to all cancer cell lines tested than to normal fibroblasts. There was a significant negative dose-effect relationship between Danggui and cancer cell viability. Average viability of MCF-7 was 69.5%, 18.4%, 5.7%, 5.7%, and 5.0% of control for Danggui doses 0.07, 0.14, 0.21, 0.32, and 0.64 ug/ul, respectively, with a $P_{trend} < 0.0001$. Half maximal inhibitory dose (ID_{50}) of Danggui for cancer cell lines MCF-7, CaSki, SiHa and CRL-7368 was 0.10, 0.09, 0.10 and 0.07 ug/ul, respectively. For the normal fibroblasts, ID_{50} was 0.58 ug/ul. At a dose of 0.32 ug/ul, Danggui killed over 90% of the cells in each cancer cell line, but at the same dose, only 12.3 % of the normal HTB-125 cells were killed. Revertants per plate of TA 100 decreased with the introduction of increasing doses of Danggui extracts with a $P_{trend} < 0.0001$ when UV light was used as a mutagen. There was no difference in revertants per plate between ethanol and DDW control groups.

Conclusions: Danggui could be used as a safe and effective adjuvant therapy to prevent and treat breast and cervical cancers. Anti-cancer effects may be due to its anti-mutagenicity. Danggui should be investigated as a potential

adjuvant anti-cancer therapy for women's cancer treatment and prevention of recurrence.

Key words: *Angelica Sinensis*, Danggui, cancer, women's reproductive disorders

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Development of functional food products in relation to obesity

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ABSTRACT

The development of new eating habits, as well as actual trends in production and consumption, has a health, environmental and social impact. The entire world is fighting diseases characteristic of the modern age such as obesity, osteoporosis, cancer, diabetes, allergies, and dental problems. With a global increase in the prevalence of obesity, both nutrition and exercise play key roles in its prevention and treatment. Natural product (nutraceutical) interventions are currently being investigated on a large-scale basis as potential treatments for obesity and weight management. With advancing nutritional sciences, several nutrients such as; low-glycemic-index carbohydrates, 5-hydroxytryptophan, green tea extract, and chromium have been shown to promote weight loss. The first two nutrients decrease appetite, green tea increases the 24 hr energy expenditure, and chromium promotes the composition of the weight lost to be fat rather than lean tissue. These have been assembled, in efficacious doses, into a new functional food product and described in this review. Each component has already been shown to promote weight loss independently in clinical trials.

Key words: obesity, weight loss, functional foods

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Flavonoids and phenolic acids from pearl millet (*Pennisetum glaucum*) based foods and their functional implications

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ABSTRACT

Background: Pearl millet (*Pennisetum glaucum*), considered a poor man's cereal, may be a repository of dietary antioxidants, especially flavonoids and phenolic acids, which provide bioactive mechanisms to reduce free radical induced oxidative stress and probably play a role in the prevention of ageing and various diseases associated with oxidative stress, such as cancer, cardiovascular, and neurodegenerative diseases.

Objective: The present study focused on the identification of individual flavonoids and phenolic acids from seven commercial varieties of pearl millet and five samples of pearl millet-based traditional recipes of Banaskantha, Gujarat, India.

Methods: Total phenols were determined by the Folin-Ciocalteu method, and individual polyphenol separation included the isolation and identification of (a) flavonoids, (b) phenolic acids, and (c) glycoflavones involving interaction with diagnostic reagents and paper chromatographic separation of compounds and their UV-visible spectroscopic studies including hypsochromic and bathchromic shifts with reagents such as AlCl3, AlCl3/HCl, NaOMe, NaOAc, and NaOAc/H3PO3. Five traditional recipes consumed in the pearl millet producing belt of Banaskantha, Gujarat, India, were standardized in the laboratory and analyzed for phenol and individual flavonoids.

Results: Total phenols in raw samples ranged from 268.5 - 420mg/100g of DW and 247.5 - 335mg/100g of DW in cooked recipes. The commonly identified flavonoids were tricin, acacetin, 3, 4 Di-OMe luteolin, and 4-OMe tricin. Five phenolic acids were identified: namely vanilic acid, syringic acid, melilotic acid, para-hydroxyl benzoic acid, and salicylic acid.

Conclusion: The presence of flavonoids, such as tricin, acacetin, 3, 4 Di-OMe luteolin, and 4- OMe tricin, indicate the chemopreventive efficacy of pearl millet. They may be inversely related to mortality from coronary heart disease and to the incidence of heart attacks in the pearl millet consuming belts of the world.

Keywords: Polyphenols, Antioxidant, Flavonoids, Total Phenols, Pearl Millet (raw and cooked) *(Pennisetum glaucum),* Banaskantha, Gujarat.

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An open-label, randomized clinical trial to assess the immunomodulatory activity of a novel oligosaccharide compound in healthy adults

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ABSTRACT

Background: Rice Bran Arabinoxylan Compound (RBAC) is a nutritional supplement produced by enzymatic hydrolysis of hemicellulose B derived from rice bran. Several *in vitro* studies and clinical reports have shown RBAC to possess promising immunomodulating effects, specifically with respect to natural killer cell and cytokine activity. The concept of a true immunomodulator is an agent possessing a broad range of activity dependent upon the existing state of health and immunity in the individual host. The present study investigated the immunomodulatory effect of RBAC in a healthy adult human population over 60 days by assessing changes in natural killer cell cytotoxicity (NKCC) and cytokines and growth factors. Subjects participated in a two-group, randomized intervention, where one group (n=10) consumed 1 gram/day and the other (n=10) consumed 3 gram/day. Safety and tolerability of RBAC were assessed with total bilirubin, total protein, creatinine, and liver function tests.

Results: We found that both groups had similar responses for NKCC, cytokines, and growth factors. The NKCC peaked at 1 week, whereas interferon-γ, tumor necrosis factor-α, interleukins-1α, -1β, -8, and -10, and epidermal growth factor peaked at 30 days. All subjects tolerated the supplement without any adverse reactions.

Conclusions: Our results showed transient, bi-directional, immune marker effects consistent with true, multifactorial immunomodulation rather than simply immunostimulation or immunosuppression. Given our findings, the immunomodulatory activity of RBAC merits study in conditions where the immune system is functionally compromised (e.g., otherwise-healthy smokers and HIV/AIDS or cancer patients). RBAC may not only help to destroy tumor cells and viruses directly, but also increase the activity of immune cells, thereby optimizing the immune system, especially NKCC, which can increase the chance and speed of host recovery.

Keywords: Rice bran, arabinoxylan compound, activity of immune cells, immunomodulation, HIV/AIDS, and cancer

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Starch digestibility and predicted glycemic index of fried sweet potato cultivars

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ABSTRACT

Background: Sweet potato (*Ipomoea batatas L*.) is a very rich source of starch. There is increased interest in starch digestibility and the prevention and management of metabolic diseases.

Objective: The aim of this study was to evaluate the levels of starch fractions and predicted glycemic index of different cultivars of sweet potato.

Material and Method: French fries produced from five cultivars of sweet potato ('Ginseng Red', 'Beauregard', 'White Travis', 'Georgia Jet clone #2010' and 'Georgia Jet') were used. The level of total starch (TS), resistant starch (RS), digestible starch (DS), and starch digestion index starch digestion index in the samples were evaluated. *In vitro* starch hydrolysis at 30, 90, and 120 min were determined enzymatically for calculation of rapidly digestible starch (RDS), predicted glycemic index (pGI) and slowly digestible starch (SDS) respectively.

Results: The RS content in all samples had an inversely significant correlation with pGI (- 0.52; $P<0.05$) while RDS had positive and significant influence on both pGI ($r=0.55$; $P<0.05$) and SDI ($r= 0.94$; $P<0.01$). 'White Travis' and 'Ginseng Red' had higher levels of beneficial starch fractions (RS and SDS) with low pGI and starch digestion Index (SDI), despite their higher TS content. Generally, all the cultivars had products with low to moderate GI values.

Conclusion: The glycemic index of these food products highlights the health promoting characteristics of sweet potato cultivars.

Keywords: Sweet potato, *Ipomoea batatas L*, French fries, *in vitro* starch digestibility, glycemic index, resistant starch

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Preliminary study on the In-Vitro Susceptibility of *Mycobacterium tuberculosis Isolates* to Virgin Coconut Oil

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ABSTRACT

Background: Tuberculosis remains a major public health threat. Studies have shown that medium chain fatty acids (MCFA), such as, those found in Virgin Coconut Oil (VCO), possess activity against a wide range of microorganisms including *Mycobacterium tuberculosis*. The goal of the study was to determine the in-vitro susceptibility of *M. tuberculosis (TB) isolates* to two commercial brands of VCOs each containing different amounts of lauric acid and produced by two different extraction processes. Two brands of VCO were tested for their anti-TB actions compared to pure lauric acid and a negative control. Two replicate runs were done. VCO samples were inoculated with 0.1 mL of the H37RV strain of *M. tuberculosis* and incubated at 37^0C with shaking for 5 days. After incubation, the mixtures were diluted 10-fold up to 10^{-4} concentration to obtain countable colonies using Middlebrook 7H10 agar plates and Lowenstein- Jensen (L-J) slants. Colony growths of M. tuberculosis were examined in each dilution every week for three to eight weeks.

Results: Both brands of VCO at increasing dilution from 1:10 to 1:10000 lowered the colony counts of *M. tuberculosis* by 46% to 100 % on the Middlebrook 7H10 agar. Similar results were noted on L-J slants with colony counts decreasing by 25% to 96%. Lauric acid solution showed complete inhibition of bacterial growth in both the agar plates and LJ slants.

Conclusion: Different VCO preparations containing different amounts of lauric acid exhibited different degree of inhibition against *M. tuberculosis*. The result of the study suggests the potential of VCOs agent against the growth of *M. tuberculosis* Similar effect on other organisms is a possibility and should also be explored. But more studies are needed to replicate the studies using different concentrations of VCOs, lauric acid and other fatty acids in VCO such as myristic acid, caproic or caprylic acids.

Key words: Lauric acid, virgin coconut oil, tuberculosis, food supplement

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Effects of oral supplementation with pyrroloquinoline quinone on stress, fatigue, and sleep

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ABSTRACT

Seventeen adult male and female subjects participated in a clinical trial using an open-label trial to evaluate the effectiveness of pyrroloquinoline quinone (PQQ) on stress, fatigue, quality of life and sleep. They ingested 20 mg of PQQ daily for 8 weeks. Changes in stress, fatigue, quality of life measures and sleep were evaluated using various inventories and questionnaires. For example, the results of the Profile of Mood States-Short Form revealed that all six measures of vigor, fatigue, tension-anxiety, depression, anger-hostility and confusion were significantly improved following PQQ administration compared with scores for those measures before administration of PQQ. Measures for quality of life, appetite, sleep, obsession and pain, also improved significantly. The results of the Oguri-Shirakawa-Azumi Sleep Inventory (Middle Aged and Aged version) showed significant improvement in sleepiness at awakening, sleep onset and maintenance, and sleep duration. For validation, the Pittsburgh Sleep Quality Index Japanese version also showed significant improvement in sleep-related behavior. Furthermore, the changes in these global scores were correlated with changes in the cortisol awakening response (R = -0.55), i.e. the effects of PQQ on improvement of sleep quality are supported by a biomarker.

Keywords: Pyrroloquinoline quinone, stress, fatigue, quality of life, sleep

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Dialysis Free Protocol for Some End Stage Renal Disease Patients (Khosroshahi Protocol)

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ABSTRACT

Background: The number of patients with End Stage Renal Disease (ESRD) is growing annually around the world. Provision of renal replacement therapy in the form of dialysis and transplant is relatively expensive. Recent studies have shown no survival benefit of early initiation of dialysis. Given recent outcome data of the timing of dialysis treatment and the expenses and logistics of hemodialysis procedure have stimulated research on alternative strategies. The aim of this study is to introduce another type of renal replacement therapy for selective patients with advanced chronic kidney disease (CKD).

Methods: In a case series we used a so-called "dialysis free protocol" consisting of a low protein diet, uremic toxin adsorbents, and prebiotics for selective ESRD patients who had dialysis access constraints or did not agree placement of hemodialysis vascular access or peritoneal dialysis catheter.

Findings: clinical and biochemical results of this study showed that these patients were not deteriorating during the study period and Blood Urea Nitrogen (Bun) & serum creatinin levels were not elevated in these months. Participating patients were relatively well throughout the study without signs of florid uremia and without a need for emergent or urgent dialysis.

Conclusion: We conclude that our proposed dialysis free protocol reduces the need for dialysis treatment at least transiently. Whether this protocol can reduce the need for dialysis treatment requires additional studies.

Key words: End Stage Renal Disease, Low Protein Diet, Prebiotics, Activated Charcoal

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Green tea for the prevention of cancer: evidence of field epidemiology

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ABSTRACT

Background: Tea is derived from the leaf of *Camellia sinensis*, a natural beverage widely consumed around the world. Geological and botanical evidence suggests that the tea plant originated from China. Varying methods of processing tea leaves lead to green tea, black tea, or Oolong tea, which differ in their concentrations of polyphenols. Green tea polyphenols appear to have anti-tumorigenic properties, and form 30-40% of the dry weight of green tea compared with only 3-10% of black tea. Numerous studies in multiple animal models and different cancer cell lines have demonstrated the anti-tumorigenesis by green tea polyphenols. Despite the consistency of laboratory results, evidence of this effect occuring in humans has been inconclusive to date.

Objective: To investigate if green tea consumption was associated with longer survival rates in ovarian cancer patients, and a lower risk of ovarian, breast, and colorectal cancer, in addition to adult leukemia

Methods: We have conducted one prospective cohort study in ovarian cancer patients, and five case-control studies in ovarian, breast, and colorectal cancers, and leukemia over the past decade. Tea consumption was measured using a structured questionnaire by face-to-face interviews. The validity and reliability of the questionnaire was assessed in a preliminary study, and then evaluated by a test–retest. Cox proportional hazards regression models were used to obtain hazard ratios(HRs), 95% confidence intervals(95% CIs), and were adjusted for age at diagnosis, locality, body mass index(BMI), parity, International Federation of Gynecology and Obstetrics (IFGO) stage, histologic grade of differentiation, cytology of ascites, residual tumour, and chemotherapeutic status. Odds ratios(ORs) and 95% CIs were obtained using logistic regression analyses, which accounted for demographic, lifestyle, hormonal and family cancer factors, and potential confounders.

Results: Higher green tea consumption was consistently observed as being associated with a lower risk of mortality due to ovarian cancer, and a decreased risk of ovarian, breast, and colorectal cancers, and adult leukemia occurrences in our observational studies. The adjusted HR and 95% CI for case mortality from ovarian cancer was 0.40(0.18-0.90) in the patients who consumed green tea at the highest level compared with non-tea drinkers. Compared with never or seldom tea drinkers, the adjusted ORs ranged from 0.07 to 0.61 for ovarian, breast, and colorectal cancers, and adult leukemia in those who consumed green tea at the highest level. Significant inverse dose-response relationships were also observed for quantity, duration, and frequency of green tea consumed.

Conclusion: We concluded that regular consumption of green tea enhanced survival of ovarian cancer, and decreased risks of ovarian, breast, and colorectal cancers, and adult leukemia. Evidence from our observational studies supported the protective effect of green tea against cancers, and this evidence will provide a knowledge platform from which to launch interventional studies for cancer prevention in the next stage.

Key words: Green tea, nutrition epidemiology, case-control studies, cohort studies, risk factor, cancer survival, breast cancer, colorectal cancer, adult leukemia, ovarian cancer

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Optimization of an effective growth medium for culturing probiotic bacteria for applications in strict vegetarian food products

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ABSTRACT

Background: This study aimed to modify de Man Rogosa Sharpe culture medium (termed MRS) for selective cultivation of probiotics strain for the consumption by the strictly vegetarian human population. Vegetarian probiotic foods by definition must be free from all animal-derived ingredients. This not only includes the product ingredients but the probiotic inoculum as well. Probiotic starter cultures are traditionally grown and stored in media containing milk or meat- derived ingredients. The presence of these ingredients makes the probiotic cell concentrates unsuitable for use in vegetarian products and thus creates the need for a growth medium which is free from animal-derived ingredients. Present study investigated the growth of a strain of Lactobacillus lactis *in MRS.* The present invention relates in general to a bacterial culture media, and more specifically a complex microbial culture media, based on plant seed powder extract in place of animal extract for probiotic bacterial growth.

Methods: Lactobacillus lactis, a probiotic, was grown in standard MRS culture medium as well as in our various test media (TM) containing various vegetal source in place of beef extract, yeast extract and peptone as in case of MRS. The inoculated culture mediums were incubated at 37□C for 72 hours and growth of probiotic is recorded at regular intervals. The growth was recorded as Colony Forming Units (CFUs).

Results: The best growth of probiotic is observed in TM 2. TM 2 is the leguminous seed extract. Starter culture mediums for probiotics or other bacteria primarily contain protein from animal source. The possibility of using vegetal protein from TM 2 extract in place of peptones and meat extract for the nitrogen supplementation of culture media for the growth of lactic acid bacteria has been demonstrated.

Conclusion: The absolute vegetarian culture medium containing TM 2 is better than standard MRS for the growth of probiotics.

Abbreviations: de Man Rogosa Sharpe (MRS), Colony Forming Units (CFU), test media (TM), National Dairy Research Institute (NDRI), Tamarind seed powder (TSP), solid-state fermentation (SSF), Lactobacillus casei Shirota (LcS)

Keywords: probiotics, lactic acid bacteria, vegetarian.

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Bioinformatics approaches for identifying new therapeutic bioactive peptides in food

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ABSTRACT

The traditional methods for mining foods for bioactive peptides are tedious and long. Similar to the drug industry, the length of time to identify and deliver a commercial health ingredient that reduces disease symptoms can take anything between 5 to 10 years. Reducing this time and effort is crucial in order to create new commercially viable products with clear and important health benefits. In the past few years, bioinformatics, the science that brings together fast computational biology, and efficient genome mining, is appearing as the long awaited solution to this problem. By quickly mining food genomes for characteristics of certain food therapeutic ingredients, researchers can potentially find new ones in a matter of a few weeks. Yet, surprisingly, very little success has been achieved so far using bioinformatics in mining for food bioactives.

The absence of food specific bioinformatic mining tools, the slow integration of both experimental mining and bioinformatics, and the important difference between different experimental platforms are some of the reasons for the slow progress of bioinformatics in the field of functional food and more specifically in bioactive peptide discovery.

In this paper I discuss some methods that could be easily translated, using a rational peptide bioinformatics design, to food bioactive peptide mining. I highlight the need for an integrated food peptide database. I also discuss how to better integrate experimental work with bioinformatics in order to improve the mining of food for bioactive peptides, therefore achieving a higher success rates.

Keywords: bioactive peptides, bioinformatics, mining food, therapeutic properties, food proteins, functional food.

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/80/173

Red wine extract, resveratrol, on maintenance of organ function following trauma-hemorrhage

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ABSTRACT

Resveratrol, is a polyphenol that can be extracted from grapes and red wine, possess potential anti-inflammatory effects, which would result in the reduction of cytokine production, the alteration of the expression of adhesion molecule molecules, and the inhibition of neutrophil function. Resveratrol might also act as an antioxidant, anti-aging, and control of cell cycle and apoptosis. Resveratrol has been shown to have protective effects for patients in shock-like states. Such protective phenomenon is reported to be implicated in a variety of intracellular signaling pathways including the regulation of the mitogen-activated protein kinases (MAPK)/ hemeoxygenase-1 (HO-1) pathway, activates estrogen receptor (ER), and the mediation of pro-inflammatory cytokines, reactive oxygen species (ROS) formation and reactive. Moreover, through anti-inflammatory effects and antioxidant properties, the resveratrol is believed to maintain organ function following trauma-hemorrhage.

Key words: resveratrol, anti-inflammatory, trauma-hemorrhage.

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Maternal diet, LCPUFA status and prematurity in Indian mothers: A cross-sectional study

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ABSTRACT

Background: Recently, certain long chain polyunsaturated fatty acids (LCPUFA) have been shown to exert functional benefits with regards to gestational length. The present study examined the association of maternal LCPUFA intake, specifically Docosahexaenoic acid (DHA) and Arachidonic acid (ARA), and plasma status at delivery with duration of gestation and risk of premature delivery in Indian mothers.

Methods: In a cross-sectional nested case-control study, 191 mother-baby pairs [164 Full term (FT) and 27 Preterm (PT)] were examined for differences in maternal habitual diet pattern and plasma fatty acid composition in relation to the length of gestation.

Results: The frequency of intake of n-3 fatty acid rich varieties of fish was higher ($p<0.05$) in FT mothers compared to PT mothers. Maternal plasma fatty acid concentration of n-3 Alpha Linolenic acid (ALA), Eicosapentaenoic acid (EPA), DHA and total n-3 fatty acids at delivery was significantly associated with intake of vegetarian ALA sources such as millets, dark whole pulses, dry fruits like walnuts, and green leafy vegetables. Among age, parity, and neonatal sex matched case-control pairs, PT mothers had significantly ($p<0.01$) higher levels of n-6 ARA, but lower ($p<0.01$) levels of n-3 DHA and total n-3 fatty acids compared to FT mothers irrespective of socioeconomic group. In fact, mothers with plasma DHA levels below median (<3.0%) had ten times higher risk (OR-10.47; 95% CI: 3.03-36.48) of delivering prematurely compared to those who had plasma DHA levels above median.

Conclusion: Results underscore the importance of consuming varied sources of ALA and DHA for their role as functional lipids in determining gestational length.

Key words: LCPUFA, maternal diet, omega 3, DHA, preterm birth, relative risk

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/73/160

Anxiolytic activity of aerial part hydroethanolic extract of *Allium ascalonicum* Linn. (Liliaceae) in mice

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ABSTRACT

Background: *Allium ascalonicum* Linn. (Liliaceae) is a mildly aromatic annual herb used to flavor food. Ethnobotanical survey revealed application of *A. ascalonicum* in the treatment of central nervous system (CNS) disorders.

Objective: To investigate the anxiolytic activity of aerial part hydroethanolic extract of *A. ascalonicum*.

Methods: The hole-board, elevated plus maze, light/dark exploration, open field and social interaction tests were used in this study. Groups of mice were treated orally with distilled water (10 ml/kg), diazepam (1 mg/kg), and *A. ascalonicum* (50-400 mg/kg). Evaluations were done 1 h post-treatment and the duration of observation was mostly 5 min. In the hole-board test, mice were observed for number/duration of head dips and number of sectional crossings. In the elevated plus maze test, the time spent in the open/closed arms and the number of entries by mice were observed. In the light/dark exploration test, the latency of entry into the dark box, time spent in the light and dark compartments, number of rearing and assisted rearing were determined. In respect of the open field test, observations were made for the number of rearing, assisted rearing, and sectional crossings. In the social interaction test, pairs of mice were observed for number of interactions including sniffing, following, and partner grooming.

Results: In the hole-board test, *A. ascalonicum* significantly ($p<0.05$, 0.01) increased the number/duration of head dips and number of sectional crossings. In the elevated plus maze test, *A. ascalonicum* significantly ($p<0.05$) increased the number of entries into the open arm with corresponding reduction in number of entries into the closed arm. In the light/dark exploration test, *A. ascalonicum* significantly ($p<0.05$, 0.01) increased the latency of entry into the dark box, time spent in the light box, and number of rearing and assisted rearing. In respect of the open field test, *A. ascalonicum* significantly ($p<0.05$, 0.01) increased the number of sectional crossings and rearing. Considering the social interaction test, *A. ascalonicum* significantly ($p<0.05$) increased the number of interactions. Peak anti-anxiety effects were mostly observed at the dose of 100 mg/kg.

Conclusion: The aerial part hydroethanolic extract of *Allium ascalonicum* possesses anxiolytic properties.

Keywords: *Allium ascalonicum*, Liliaceae, anxiolytic activity, medicinal plants, traditional medicine.

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/71/158

Brassicaceae: nutrient analysis and investigation of tolerability in people with Crohn's disease in a New Zealand study

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ABSTRACT

Background: Nutrition is an important environmental factor influencing symptoms of Crohn's disease, one of the two main expressions of inflammatory bowel disease. Varieties of Brassicaceae supply valuable nutrients. They are often avoided by people with Crohn's disease because of the adverse effects they are perceived to have on symptoms. The purpose of this study was to review the nutritional content of commonly eaten forms of Brassicaceae and identify from selected Brassicaceae those that exacerbate, ameliorate or make no difference to the symptoms of people with Crohn's Disease.

Methods: In this study commonly eaten Brassicaceae were identified and analysed for major nutrients, vitamins, minerals, phytochemicals and FODMAPs. An investigation on the tolerability of ten forms of Brassicaceae on people with Crohn's disease was also conducted. This was based on the responses of adult subjects in the 'Genes and Diet in Inflammatory Bowel Disease Study' based in Auckland, New Zealand.

Results: The nutrient analysis of the Brassicaceae showed their important contribution of fibre, vitamins, minerals, and phytochemicals, especially glucosinolates. Our study revealed that over 70% of respondents found that the consumption of broccoli, Chinese greens and rocket (arugula) made no difference to their Crohn's disease ($p=0.0001$).

Conclusions: Brassicaceae contain key nutrients which contribute significantly to a person's health through their fibre, vitamin, mineral and phytochemical content. Many people with Crohn's Disease can tolerate different forms of Brassicaceae. By identifying the particular varieties that can be consumed by people with Crohn's disease and encouraging them to eat them, their nutrition, immune status and anti-inflammatory and anti-cancer factors will be enhanced.

Key words: Brassicaceae: Key nutrients: Tolerability: Crohn's Disease
Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/70/156

Agaricus blazei Murill - immunomodulatory properties and health benefits

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ABSTRACT

The *Agaricus blazei* Murill (AbM), also known as *Agaricus brasiliensis L.* due to its origin in Brazilian rain forest, is an edible mushroom of the *Basidiomycetes* family, which also comprises medicinal mushrooms such as *Hericium erinaceus* and *Grifola frondosa*. AbM has been used in traditional medicine locally and also recently as a health food worldwide. Since it has been found to possess immunomodulatory properties, its biological and health-related effects, as well as its isolated active ingredients e.g. beta-glucans, have been examined by scientists. Other investigations have been performed with mixed mushroom products, such as AndoSan™, which contains mostly AbM, but also the two other mushrooms above. AbM-related benefits reviewed here include effects against cancer, infections, inflammation, allergy/ asthma and diabetes. Effects of AndoSan™ and other AbM-based extracts have been compared in a bacterial sepsis model.

Keywords: *Agaricus blazei*, AndoSan™, allergy, asthma, cancer, infection, inflammation, immunomodulation.

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Flavocoxid (Limbrel®) manages osteoarthritis through modification of multiple inflammatory pathways: a review

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ABSTRACT

Limbrel (flavocoxid) is marketed as an FDA-regulated medical food for the clinical dietary management of osteoarthritis (OA) to be used under physician supervision. Flavocoxid is composed of a >90% mixture of baicalin and catechin and represents a non-targeted anti- inflammatory which works differently than non-steroidal anti-inflammatory drugs (NSAIDs) that bind to and only inhibit the *cyclooxygenase* moieties of COX-1 and COX-2. Flavocoxid binds to and weakly modulates the *peroxidase* activity of the COX enzymes permitting low level expression of prostaglandins (PGs), prostacyclin (PGI_2) and thromboxane (TxA_2). In addition, flavocoxid weakly inhibits phospholipase A2 (PLA_2) and 5-lipoxygenase (5-LOX) as well as increases I□Bα and prevents nuclear factor kappa B (NF□B) activation/induction of inflammatory genes such as tumor necrosis factor-alpha (TNFα), interleukin-1β (IL-1 β), IL-6, COX-2, inducible nitric oxide synthase (iNOS) and 5-LOX. In clinical studies, flavocoxid shows equivalent efficacy to naproxen with statistically fewer renal (edema) and upper gastrointestinal (GI) side effects, does not affect platelet function and bleeding times, does not change international normalized ratio (INR) in warfarinized patients, is well-tolerated in patients with previous NSAID-induced GI side effects, and decreases or eliminates the use of gastroprotective medications in patients who previously required them to tolerate NSAIDs. With its broad, non-targeted and multiple weak activities which result in fewer side effects compared to NSAIDs, flavocoxid represents a different way managing OA by working on the underlying and multiple causes of cartilage degradation as well as joint inflammation.

Keywords: Flavocoxid, Limbrel, osteoarthritis, inflammatory pathways, and medical foods

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Antioxidant and antimicrobial activity of lecithin free egg yolk protein preparation hydrolysates obtained with digestive enzymes

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ABSTRACT

Several biological activities have now been associated with egg protein- derived peptides, including antihypertensive, antimicrobial, immunomodulatory, anticancer and antioxidant activities, highlighting the importance of these biopeptides in human health, and disease prevention and treatment. Special attention has been given to peptides with antioxidant and antimicrobial activities as a new source of natural preservatives in food industry. In this study, the antioxidant properties of the egg-yolk protein by-product (YP) hydrolysates were evaluated based on their radical scavenging capacity (DPPH), Fe^{2+}chelating effect and ferric reducing power (FRAP). Furthermore, antimicrobial properties of obtained hydrolysates against Bacillus species were studied. The degrees (DHs) of hydrolysis for 4h hydrolysates were: 19.1%, 13.5% and 13.0%, for pepsin, chymotrypsin and trypsin, respectively. Pepsin was the most effective in producing the free amino groups (1410.3 µmolGly/g). The RP-HPLC profiles of the protein hydrolysates showed differences in the hydrophobicity of the generated peptides.

Trypsin hydrolysate obtained after 4h reaction demonstrated the strongest DPPH free radical scavenging activity (0.85 µmol $Trolox_{eq}$/mg). Trypsin and chymotrypsin hydrolysates obtained after 4h reaction exhibited 4 times higher ferric reducing capacity than those treated by pepsin. The hydrolysis products obtained from YP exhibited significant chelating activity. The 4h trypsin hydrolysate exhibited weak antimicrobial activity against *B. subtilis B3; B. cereus B512; B. cereus B 3p and B. laterosporum B6.*

Keywords: Antioxidative activity, DPPH, peptides, hydrolysis, egg-yolk protein

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Effect of grape seed extract on postprandial oxidative status and metabolic responses in men and women with the metabolic syndrome - randomized, cross-over, placebo-controlled study

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ABSTRACT

Objective: This investigation was undertaken to determine whether a grape seed extract (GSE) that is rich in mono-, oligo- and poly- meric polyphenols would modify postprandial oxidative stress and inflammation in individuals with the metabolic syndrome (MetS).

Background: MetS is known to be associated with impaired glucose tolerance and poor glycemic control. Consumption of a meal high in readily available carbohydrates and fat causes postprandial increases in glycemia and lipidemia and markers of oxidative stress, inflammation and insulin resistance.

Materials/methods: After an overnight fast, twelve subjects with MetS (5 men and 7 women) consumed a breakfast meal high in fat and carbohydrate in a cross-over design. A GSE (300 mg) or placebo capsule was administrated 1 hr before the meal (-1 hr). Changes in plasma insulin, glucose, oxidative stress and inflammatory markers were measured hourly for 6 hr.

Results: Plasma hydrophilic oxygen radical absorbance capacity (ORAC) measured as the positive incremental area under the curve (-1 to 5 hr) was significantly increased when the meal was preceded by GSE compared with placebo ($P<0.05$). Meal-induced increases in oxidized LDL were attenuated with GSE ($P<0.05$). Plasma glucose concentrations (area under the curve from -1 to 5 hr) were also significantly lower when the meal was preceded by GSE ($P<0.05$) while the insulin concentrations remained unchanged ($P>0.05$). No changes in inflammatory markers were evident.

Conclusion: These data suggest that GSE enhances postprandial plasma antioxidant status and reduces the glycemic response to a meal, high in fat and carbohydrate in subjects with the MetS.

Key words: Polyphenols, Oxidative stress, Inflammation, ORAC, Oxidized LDL

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Content validity and reliability of a food frequency questionnaire to measure eicosapentaenoic acid and docosahexaenoic acid intakes in young adults: A pilot study

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ABSTRACT

Background: The food environment is rapidly changing with regard to omega-3 fatty acids. Research is hindered by the lack of a tool specifically designed to measure intakes of long-chain omega-3 fatty acids in US populations. The purpose of this pilot study was to assess the content validity and reliability of a novel 14-item food frequency questionnaire (FFQ) designed to measure contemporary sources of eicosapentaenoic aid (EPA) and docosahexaenoic acid (DHA).

Methods: During May of 2009, college students (n = 165) completed the FFQ and provided feedback. Forty-five completed the questionnaire a second time allowing for the evaluation of test-retest reliability**.**

Results: None of the students reported consuming a food naturally rich in EPA and DHA that was not included in the FFQ. Overall instrument reliability (n = 54) was strong ($\rho = 0.86$, $p < 0.001$) and the reliability for each of the non-functional food items ranged from moderate to strong ($\rho = 0.48$ to 0.86, $p < 0.001$). Correlation coefficients for each of the functional food items were low and/or non-significant. Uncertainty regarding omega-3 functional foods was listed as a reason by eight of the twelve who felt one or more of the questions were difficult to answer.

Conclusions: Overall instrument reliability was strong and content validity was good. Nonetheless, participant feedback, and the decreased test-retest coefficients for the omega-3 functional foods, suggests unfamiliarity may be problematic when measuring intakes from these food sources.

Keywords: Functional foods, n-3 fatty acids, dietary assessment, seafood, eicosapentaenoic acid, docosahexaenoic acid

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Metabolic correction for attention deficit/hyperactivity disorder: A biochemical-physiological therapeutic approach

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ABSTRACT

Objective: This investigation was undertaken to determine the reference values of specific biochemical markers that have been have been associated with behavior typical of ADHD in a group of patients before and after metabolic correction.

Background: Attention deficit hyperactivity disorder (ADHD) affects approximately two million American children, and this condition has grown to become the most commonly diagnosed behavioral disorder of childhood. According to the National Institute of Mental Health (NIMH), the cause of the condition, once called hyperkinesis, is not known.

The cause of ADHD is generally acknowledged to be multifactorial, involving both biological and environmental influence. Molecular, genetic, and pharmacological studies suggest the involvement of the neurotransmitter systems in the pathogenesis of ADHD. Polymorphic variants in several genes involved in regulation of dopamine have been identified, and related neurotransmitter pathways alterations are reported to be associated with the disease.

Nutritional deficiencies, including deficiencies in fatty acids (EPA, DHA), the amino acid methionine, and the trace minerals zinc and selenium, have been shown to influence neuronal function and produce defects in neuronal plasticity, as well as impact behavior in children with attention deficit hyperactivity disorder.

Materials/Methods: This study was based on data extracted from our patient history database covering a period of over ten years. We performed laboratory tests in 116 patients 2.7-25 years old with a diagnosis of ADHD. Sixty-six percent (66%) of patients were males. Patients were followed from 3 month to 3 years. We compared the distributions of fatty acids, essential metals, and the levels of metabolic stress factors with established reference ranges before and after interventions. In addition, we analyzed the association between toxic metal concentrations and the levels of essential metals.

Results: This study was based on data extracted from our patient history database covering a period of over ten years. We performed laboratory tests in 116 patients 2.7-25 years old with a diagnosis of ADHD. Sixty-six percent (66%) of patients were males. Patients were followed from 3 month to 3 years. We compared the distributions of fatty acids, essential metals, and the levels of metabolic stress factors with established reference ranges before and after interventions. In addition, we analyzed the association between toxic metal concentrations and the levels of essential metals. According to these data, the metabolic correction of ADHD by supplementation with minerals,

vitamins, essential fatty acids, and amino acids can ameliorate ADHD symptoms. Eighty percent (80%) of children who were treated from several weeks to 1-2 years, demonstrated improvement of metabolic stress level, measured by pyrroles. For these patients the levels of EPA were increased and the omega-6/omega-3 ratio was improved.

Conclusion: In the studied population it was demonstrated that metabolic correction of biochemical disturbances using essential fatty acids, amino acids, and minerals can improve fatty acid profiles and metabolic stress levels. These disturbances or variations from reference values have been associated with behavior typical of ADHD. Further studies need to be conducted with integrative metabolic correction therapy to determine its value in the management of ADHD.

Key words: Attention deficit hyperactivity disorder, metabolic correction, fatty acid composition, essential metals, toxic metals, pyrroles, vitamins and minerals.

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Impact of dietary intervention with a functional food supplement to combat anemia - the blood iron metabolic disorder among the coffee plantation laborers

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ABSTRACT

Objective: To assess the nutritional status and other nutrition related problems of the workers. To design, implement and evaluate the impact of dietary intervention for the nutritional metabolic disorder which is directly related to productivity.

Background: Indian economy greatly relies on agriculture. Agriculture is set to play a more dynamic role in the economy. The present study focuses on the nutritional status with special reference to the blood iron profile of manual coffee plantation laborers belonging to Kodaikannal, Tamil Nadu, India. The outcome of this study on the dietary intervention, based on nutritional picture of coffee plantation laborers, will have a nationwide application because of the simplified, stable coffee plantation operations throughout India.

Method: Experiments were carried out in three phases. In the first phase, the personal background of the laborers was assessed. In the second phase, the nutritional and health status of the laborers, through dietary survey comprising 24 Hour Food Recall record and weighment of cooked food consumed for three consecutive days, clinical and biochemical profile were studied. The serum iron was measured with the total iron binding capacity, from which the transferrin saturation was calculated. In the third phase, dietary intervention was implemented with a nutrient rich nutraceutical food supplement - *spirulina* incorporated soup. The supplementation was extended for a period of 120 days. The subjects were grouped into control and the experimental group. The control group was given plain soup and the experimental group was administered with soup incorporated with *spirulina*. The impact of intervention on the biochemical and nutritional profile of the laborers was reassessed in similar working conditions.

Results: A deficit of 0.1 mg to 0.3 mg of iron intake per kg body weight in the male and female laborers was observed when compared to their RDA The clinical pictures reveal that 94 percent suffered from anemia, 56 percent showed anemic signs of spooning of nails (koilonychyia), 36 percent of the subjects had glossitis (mouth ulcer), 16 percent suffered from bleeding gums, 4 percent had cheilosis (ulceration of tongue) and 28 percent had angular stomatitis. The average hemoglobin level was 8.6 ± 1.12g/dl for men and 8.1±1.01g/dl for women which are 28 and 37 percent less than normal respectively. Dietary intervention of 5g of *spirulina* in 150 ml of soup had significantly improved the blood iron profile. Among the male laborers, 10 percent who suffered from ***severe*** anemia with 7.9 $g.dl^{-1}$ hemoglobin before intervention were shifted to ***moderate*** levels of 9.4 $g.dl^{-1}$, 30 percent who

suffered from *mild* anemia were shifted to ***normal*** ones and among 60 percent of male laborers who were moderately anemic, 50 percent reverted to ***normalcy***.

Conclusion: In the present study it was observed that the habitual dietary intake showed deficiency in consumption of iron rich foods and the clinical picture revealed the signs and symptoms of anemia The blood iron profile - Hemoglobin (Hb), Serum Iron, Transferrin Saturation, Serum Ferritin, Total Iron Binding Capacity (TIBC) and Unsaturated Iron Binding Capacity (UIBC) were greatly influenced by dietary intervention with the functional food *Spirulina* incorporated soup The blood hemoglobin content increased by 21 percent *i.e* from 10.9 to 13.3g.dl^{-1}. Serum iron, serum ferritin and transferrin levels showed a consistent and progressive rise while TIBC and UIBC reduced resulting in a positive iron balance.

Keywords: Dietary intervention, functional food, *Spirulina*, hemoglobin, anemia

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Angiotensin-converting enzyme inhibitory effects of dairy- and soy-derived peptides in pre-hypertensive overweight men and women

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ABSTRACT

Background: Hypertension is considered the most prevalent cardiovascular disorder and a significant public health problem. A functional food that could potentially impede progression into a hypertensive state in pre-hypertensive individuals is of significant interest to clinicians and consumers. *In vitro* and animal studies suggest the presence of potential ACE inhibitory dairy- and soy-derived peptides. Very few human-based research studies have been conducted to investigate the blood pressure lowering and/or ACE-inhibitory effects of whey and soy protein hydrolysates in humans. This pilot study tested the acute effects of 20g doses of whey and soy hydrolysates in pre-hypertensive, overweight men and postmenopausal women on serum ACE activity and blood pressure.

Findings: Using a randomized crossover design, four initial subjects received five treatments (unhydrolyzed casein, whey protein isolate, whey protein hydrolysate, soy protein isolate, soy protein hydrolysate) at different testing visits separated by three-day washout periods. Blood pressure and blood draws to measure ACE activity were taken at thirty-minute intervals following treatment consumption. Both the soy protein and whey protein hydrolysates had notable *in vitro* ACE-inhibitory activity, both before and after heat treatment. No differences were observed among the protein treatments for either ACE activity or systolic blood pressure.

Conclusions: The results of this pilot study support a discrepancy between *in vitro* and human- based *in vivo* ACE-inhibitory acute effects of whey and soy protein hydrolysates, underscoring the need for further research to better understand potential explanations for these findings.

Key Words: ACE (Angiotensin-converting enzyme), Casein, Soy, Whey, Protein, Blood pressure, Dairy, Bioactive, Peptides

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Anti-cancer activities of *Ganoderma lucidum*: active ingredients and pathways

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ABSTRACT

Ganoderma lucidum, commonly referred to as Lingzhi, has been used in Asia for health promotion for centuries. The anti-cancer effects of *G. lucidum* have been demonstrated in both *in vitro* and *in vivo* studies. In addition, the observed anti-cancer activities of Ganoderma have prompted its usage by cancer patients alongside chemotherapy.

The main two bioactive components of *G. lucidum* can be broadly grouped into triterpenes and polysaccharides. Despite triterpenes and polysaccharides being widely known as the major active ingredients, the different biological pathways by which they exert their anti-cancer effect remain poorly defined. Therefore, understanding the mechanisms of action may lead to more widespread use of Ganoderma as an anti-cancer agent.

The aim of this paper is to summarise the various bioactive mechanisms that have been proposed for the anti-cancer properties of triterpenes and polysaccharides extracted from *G. lucidum*. A literature search of published papers on NCBI with keywords “Ganoderma” and “cancer” was performed. Among those, studies which specifically examined the anti-cancer activities of Ganoderma triterpenes and polysaccharides were selected to be included in this paper.

We have found five potential mechanisms which are associated with the anti-cancer activities of Ganoderma triterpenes and three potential mechanisms for Ganoderma polysaccharides. In addition, *G. lucidum* has been used in combination with known anti-cancer agents to improve the anti-cancer efficacies. This suggests Ganoderma’s bioactive pathways may compliment that of anti-cancer agents. In this paper we present several potential anti-cancer mechanisms of Ganoderma triterpenes and polysaccharides which can be used for the development of Ganoderma as an anti-cancer agent.

Keywords: *Ganoderma lucidum*, cancer, bioactive pathways, triterpene, polysaccharide

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Activation of the intrinsic-apoptotic pathway in LNCaP prostate cancer cells by genistein- topotecan combination treatments

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ABSTRACT

Background: Prostate cancer is the second most common cancer in American men. The development of alternative preventative and/or treatment options utilizing a combination of phytochemicals and chemotherapeutic drugs could be an attractive alternative compared to conventional carcinoma treatments. Genistein isoflavone is the primary dietary phytochemical found in soy and has demonstrated anti-tumor activities in LNCaP prostate cancer cells. Topotecan Hydrochloride (Hycamtin) is an FDA-approved chemotherapy for secondary treatment of lung, ovarian and cervical cancers. The purpose of this study was to detail the potential activation of the intrinsic apoptotic pathway in LNCaP prostate cancer cells through genistein-topotecan combination treatments.

Methods: LNCaP cells were cultured in complete RPMI medium in a monolayer (70-80% confluency) at 37ºC and 5% CO_2. Treatment consisted of single and combination groups of genistein and topotecan for 24 hours. The treated cells were assayed for i) growth inhibition through trypan blue exclusion assay and microphotography , ii) classification of cellular death through acridine/ ethidium bromide fluorescent staining, and iii) activation of the intrinsic apoptotic pathway through Jc-1: mitochondrial membrane potential assay, cytochrome c release and Bcl-2 protein expression.

Results: The overall data indicated that genistein-topotecan combination was significantly more efficacious in reducing the prostate carcinoma's viability compared to the single treatment options. In all treatment groups, cell death occurred primarily through the activation of the intrinsic apoptotic pathway.

Conclusion: The combination of topotecan and genistein has the potential to lead to treatment options with equal therapeutic efficiency as traditional chemo- and radiation therapies, but lower cell cytotoxicity and fewer side effects in patients.

Key words: topotecan; genistein; intrinsic apoptotic cell death

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Effect of 1-O-Alcylglycerols from sea hydrobionts on the metabolic status of rats with alimentary dyslipidemia

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ABSTRACT

Objective: Sea hydrobionts are a rich source of biologically active lipid compounds. Search for new biologically active substances to determine their pharmacological effectiveness is of current interest.

Background: In recent interest held pharmaceuticals from marine hydrobionts containing 1- *O*-alkyl-diacylglycerol (ADG). Significant amounts of ADG found in the tissues of some marine organisms of Pacific ocean - squid *Berryteuthis magister* (up to 50% in the lipids of the liver), crab *Paralithodes camtschatica* (10% lipids of the hepatopancreas). This makes it possible to use these aquatic animals as new sources of dietary supplements. In rats with alimentary dyslipidemia (DLP) examined the effect of nature 1-*O*-alkyl-glycerol (AG) on the metabolism of lipids, the state of the hepatobiliary, antioxidant systems and hematological parameters of blood.

Method: Alimentary model DLP caused high-fat diet of beef fat and cholesterol. Were injected AG in rats with DLP a dose of the 0.4 g/kg for 30 days. 1-*O*-alkyl-glycerol were obtained by hydrolysis of the lipids of the liver ADG squid *Berryteuthis magister*. Biochemical parameters of lipid and carbohydrate metabolism, and liver enzymes measured in blood serum. Investigated the total antioxidant activity (TAA) of blood plasma, the activity of catalase in erythrocytes, glutathione reductase (GR) and glutathione peroxidase (GP) activity, glutathione (GSH) lever. The content of initial and final products of lipid peroxidation – hydroperoxides of lipids (HPL), malondialdehydes (MDA) in the blood were investigated. Determination of hematological parameters is carried out on «Abacus» (USA). Statistical significance of differences was calculated by Student's t-test.

Results: Introduction AG resulted in a reduction in triglycerides in the blood serum of rats by 24.2% compared with rats with DLP ($p < 0.05$), increase in HDL-C by 63% ($p < 0.001$). There was an increase in blood glucose concentration by 21.3% ($p < 0.001$), and lactate dehydrogenase (LDG) activity by 30% ($p < 0.05$), ALT – 24% ($p < 0.001$) compared with rats with DLP. After use AG in rats showed an increase in the activity of catalase, reduction of lipid hydroperoxides in plasma. Showed normalization of the TAA and the trend to reduce the concentration of MDA. In the glutathione-redox system under the influence of AG increased activity GR, GP, GSH levels. After use AG an increase in the total number of red blood cells in the blood by 40% ($p < 0,001$), total hemoglobin by 38% ($p < 0.001$), platelet count by 30% ($p < 0.001$), lymphocytes - 43% ($p < 0.001$), blood clotting time increased by 57%.

Conclusion: The study showed that the use of AG causes increased protective functions - hematopoietic, immune-stimulating and antioxidant. These data suggest the widespread use of AG from lipid liver squid *Berryteuthis magister* in rehabilitation practice of various pathologies.

Keywords: natural 1-O-alkyl-lglycerols, dislipidemia, metabolic status

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The influence of obesity in patients with prostate cancer - Review of the literature

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ABSTRACT

Recent studies have demonstrated an association between higher body mass index and increased aggressiveness in prostate cancer.

The present narrative review, based on a search of Medline® and Embase® databases from October 1982 to October 2012, explores the relationship between higher body mass index and localized prostate cancer. In particular, the current epidemiological and mechanistic evidence for interactions between obesity and prostate cancer are discussed.

Obesity is associated with alterations in androgen levels, decreased sex hormone binding globulin and increased estrogen levels, insulin resistance, hyperglycemia, alterations in plasma lipoprotein levels particularly raised triglycerides and reduced high density lipoprotein, decreased levels of adiponectin, and increased levels of circulating insulin-growth factor- 1, leptin and dietary saturated fats. Obese men have more aggressive prostate cancer with a greater percentage prostate involvement, increased tumor volume and higher-grade disease, enlarged prostates, high prostate-specific antigen levels, increased risk of having positive margins and recurrence.

Moreover, there is strong evidence of the beneficial effects of functional foods for the treatment of obesity. Additionally, an increasing number of studies support that obesity-induced inflammation plays an important role in the development of obesity-related pathologies. Despite, the beneficial role of nutriment in prostate cancer control, the use of functional foods in prostate cancer is not recommended for lack of large epidemiological studies.

This data supports the hypothesis that obese men have more aggressive prostate cancers and that the obesity is a modifiable risk factor of prostate cancer.

Key Words: prostate cancer, metabolic syndrome, obesity, high BMI, risk factor, diet, functional foods.

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Functional foods for weight management: Dietary Fiber – a systematic review

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ABSTRACT

It has been estimated that more than 1.5 billion adults are overweight or obese worldwide [1], rendering obesity a global epidemic [2]. Obesity is associated with significant morbidity, including type 2 diabetes, cardiovascular disease, osteoarthritis and some cancers [3]. Thus, obesity is clearly a medical issue, its costs impacting heavily on health care systems in both developed and developing nations [4]. The combined impact of transmissible and chronic disease in the third world is particularly devastating to the very health care systems with fewest resources [5].

Because obesity has been identified as a major health issue, treating obesity is an important goal. However, weight loss management has proven notoriously difficult. It is well documented that reduced energy intake and increased energy expenditure may reduce body weight in the short term, but obesity relapse is the long term is anticipated [6]. In a study of overweight or obese US adults who weighed ≥ 10% less than their maximum body weight the year prior to the survey (n=1310), 33.5% regained > 5% during that year [7].

Despite its somewhat unimpressive success rate, "lifestyle" weight management remains the first line intervention for obesity treatment [8]. Lifestyle weight management can be defined as interventions based on energy restriction (weight loss diet); increased energy output (exercise); and/or behavioral change (cognitive or behavior therapy). Functional foods have been explored as a tool for enhancing lifestyle weight management.

Functional foods evaluated for their efficacy as obesity interventions can be divided into two broad categories: 1) foods which suppress appetite and increase satiety; and 2) foods which enhance thermogenesis. The present review will focus on those foods thought to act by increasing satiety and suppressing appetite.

Key words: Obesity, weight loss, systematic review, dietary fiber

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Benzotropolone moiety in theaflavins is responsible for inhibiting peptide- transport and activating AMP-activated protein kinase in Caco-2 cells

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ABSTRACT

Objective: In the small intestine, peptide transporter 1 (PEPT1) plays a role in the transport of di- and tri-peptides. Recently, we found that theaflavins (TFs), dimeric catechins, inhibited the transport of di-peptides across Caco-2 monolayers by suppressing the expression of PEPT1 through AMP-activated protein kinase (AMPK) activation. In this study, we investigated the structural requirement of theaflavins for the effect, and the mechanism(s) underling theaflavin-induced AMPK activation.

Methods: Theaflavin-3'-*O*-gallate (TF3'G) was used for this study, since it possessed the most potent inhibition power for peptide-transport among theaflavins. Absorption ability was measured with Caco-2 cell monolayers treated with or without 20 □M sample (TF3'G or its related compounds) in an Ussing Chamber. The amount of Gly-Sar (a model of PEPT1- transporing peptide) transport at fixed time-points to 60 min was determined by fluorescent naphthalene-2,3-dicarboxaldehyde-derivatized assay (Ex/Em: 405 nm/460 nm). The apparent permeability coefficient (P_{app}) was used to evaluate the permeability. Expression of PEPT1 protein in Caco-2 cells treated with or without 20 □M TF3'G in the presence or absence of inhibitor (10 μM compound C as AMPK inhibitor or 25 μM STO-609 as CaMKK inhibitor) was evaluated by Western blot.

Results: The P_{app} value of Gly-Sar significantly ($P < 0.05$) decreased in 20 μM purprogallin- treated Caco-2 cells as well as in TF3'G-treated cells, together with the reduction of PEPT1 expression, while their monomeric catechins did not show any P_{app} reduction. In TF3'G- treated Caco-2 cells, the recovery of the reduced PEPT1 expression was found by 10 μM compound C, but not STO-609.

Conclusion: The study demonstrated that the benzotropolone moiety in theaflavins was a crucial structural requirement for exerting the inhibition of intestinal peptide-transport, and the suppression of PEPT1 expression by theaflavins would be caused by activating LKB1/AMPK pathway, but not CaMKK/AMPK pathway.

Keywords: Theaflavin-3'-□-gallate, Peptide transport, PEPT1, Benzotropolone, AMP- activated protein kinase, Calmodulin-dependent protein kinase kinase

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A five patient's case study on the influence of two different probiotics on individual intestinal microbiota

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ABSTRACT

Background: The composition and activities of indigenous intestinal microbiota are of paramount importance to human immunity, nutrition, and pathological processes, and hence, the health of the individual. It is well established that the intestine is an important site for local immunity. It is known that the effect of probiotics increases beneficial microbiota and improves chronic conditions such as atopic diseases, irritable bowel disease, and obesity. However, as there are so many probiotics, it is unknown which probiotics might have more of an impact upon intestinal microbiota.

Objective: To understand how two different types of probiotics influence human intestinal microbiota, we analyzed human fecal microbiota after taking each of the probiotics.

Methods: Five outpatients from Yoko Clinic (1 male and 4 females; aged between 34–46 years old) were enrolled in this study. None of the subjects had cancer or any active inflammatory diseases. The five patients took *Lactobacillus buchneri* (SU) for 4 weeks, no probiotics the following week, and mixed probiotics (NS) which are *Lactobacillus plantarum* (NS-5), *Lactobacillus rhamnosus* (NS-11), *Lactobacillus delbruekii* (NS-12), *Lactobacillus helveticus* (NS-8), *Lactobacillus fermentum* (NS-9) for the following 4 weeks. Fecal samples were collected before and after the outpatients took each of the two probiotics, and were then analyzed using a kit from Techno Suruga Laboratory Co., Ltd. The analysis of the microbiota was performed by targeting bacterial 16S rRNA genes with a terminal restriction fragment length polymorphism analysis program (Nagashima method).

Results: Three patients of the five patients decreased the percentage of beneficial bacteria (*Lactobacillales*, *Bifidobacteria)* after taking SU (13.7 ± 7.1% to 4.0 ± 3.5%), whereas the remaining two patients showed an increased percentage of beneficial bacteria (16.8 ± 3.4% to 30.4 ± 4.6%). After taking NS, the three patients who decreased the percentage of beneficial bacteria after taking SU increased their beneficial bacteria (4.0 ± 3.5% to 8.0 ± 2.1%), whereas the two patients who increased beneficial bacteria after taking SU showed a decreased percentage of beneficial bacteria (30.4 ± 4.6% to 16.4 ± 7.4%).

Conclusion: This study demonstrated that the two probiotics had different influences. Probiotics should be selected not only for their quality but also for compatibility with each intestinal bacterial flora.

Key words: probiotics, intestine, microbiota

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Processed coffee alleviates DSS-induced colitis in mice

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ABSTRACT

Background: Coffee is one of the most widely consumed beverages in the world and it has been demonstrated that it has important therapeutic activities not only because of its caffeine content but also owing to the presence of other biologically active small molecules such as chlorogenic acid, trigonelline and cyclopentadiones. However, chlorogenic acid is degraded into catechol, pyrogallol and hydroxyhydroquinone, which are thought to induce irritation of the gastric mucosa. To reduce the content of irritant compounds processing methods have been developed prior to roasting the coffee beans.

Objectives: The aim of this study was to study the anti-inflammatory and gastro-protective effects of processed coffee (Idee-Kaffee) on in LPS-treated human primary monocytes and in a murine model of colon inflammation (IBD model).

Results: In this study we have analyzed the effects on inflammatory events in cultured cells and in mice drinking a commercially available processed coffee. The processed coffee inhibited lipopolysaccharide (LPS)-induced proinflammatory cytokines such as interleukin (IL)-1, tumor necrosis factor (TNF), IL-6 and IL-8, and other inflammatory mediators such as prostaglandin (PG)E_2 and 8-isoprostane in cultured human primary monocytes. Oral administration of dissolved processed coffee, i.e., in its usual beverage form, improved greatly the adverse macroscopic and histological features of dextran sodium sulfate (DSS)- induced colitis in mice in a dose-dependent manner. Processed coffee not only largely prevented DSS-induced colitis but also dramatically suppressed *in vivo* NF-B and STAT3 activities through inhibition of IB and STAT3 phosphorylation. Furthermore, this soluble coffee bean extract reduced the expression of proinflammatory cytokines TNF, IL-11, and IL-6 and the expression of cyclooxygenase (COX)-2 in colonic tissues.

Conclusions: This work identified processed coffee as an anti-inflammatory beverage with the capacity to reduce substantially DSS-induced colitis as well as the colitis-associated cellular inflammatory events.

Keywords: coffee, Inflammatory Bowel Disease, NF-B, STAT3, cytokines

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Bioactive form of resveratrol in glioblastoma cells and its safety for normal brain cells

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ABSTRACT

Background: Resveratrol, a plant polyphenol existing in grapes and many other natural foods, possesses a wide range of biological activities including cancer prevention. It has been recognized that resveratrol is intracellularly biotransformed to different metabolites, but no direct evidence has been available to ascertain its bioactive form because of the difficulty to maintain resveratrol unmetabolized in vivo or in vitro. It would be therefore worthwhile to elucidate the potential therapeutic implications of resveratrol metabolism using a reliable resveratrol-sensitive cancer cells.

Objective: To identify the real biological form of trans-resveratrol and to evaluate the safety of the effective anticancer dose of resveratrol for the normal brain cells.

Methods: The samples were prepared from the condition media and cell lysates of human glioblastoma U251 cells, and were purified by solid phase extraction (SPE). The samples were subjected to high performance liquid chromatography (HPLC) and liquid chromatography/tandem mass spectrometry (LC/MS) analysis. According to the metabolite(s), *trans*-resveratrol was biotransformed *in vitro* by the method described elsewhere, and the resulting solution was used to treat U251 cells. Meanwhile, the responses of U251 and primarily cultured rat normal brain cells (glial cells and neurons) to 100μM *trans*-resveratrol were evaluated by multiple experimental methods.

Results: The results revealed that resveratrol monosulfate was the major metabolite in U251 cells. About half fraction of resveratrol monosulfate was prepared *in vitro* and this *trans*-resveratrol and resveratrol monosulfate mixture showed little inhibitory effect on U251 cells. It is also found that rat primary brain cells (PBCs) not only resist 100μM but also tolerate as high as 200μM resveratrol treatment.

Conclusions: Our study thus demonstrated that *trans*-resveratrol was the bioactive form in glioblastoma cells and, therefore, the biotransforming activity of *trans*-resveratrol would be reversely correlated with the chemosensitivity of the treated cells. The findings from PBCs suggest that an effective anti-glioblastoma dose of resveratrol may not exert side-effect on normal brain cells, providing a strong evidence for practical use of resveratrol in the management of human brain malignancies.

Key words: Resveratrol, glioblastoma, drug metabolism

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Inhibition of SIRT1 transcription in resveratrol-differentiated medulloblastoma cells

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ABSTRACT

Backgrounds: Medulloblastoma (MB) is the commonest brain malignancy in childhood with poor prognosis, because of its rapid aggressive growth and frequent occurrence. The current chemotherapeutic regimens for medulloblastoma patients involve a combination of lomustine, cisplatin, carboplatin, vincristine or cyclophosphamide, which have distinct short- and long-term side-effects. It is therefore in urgent need to explore safer and more effective adjuvant approach(s). Resveratrol, a polyphenol rich in numerous plants, has multiple biological activities including anticancer effects. Our previous data confirmed that resveratrol inhibited proliferation and induced differentiation and apoptosis of medulloblastoma cells. SIRT1 is a deacetylase of class III HDACs and the supposed molecular effecter of resveratrol. SIRT1 involves in aging prevention and cancer formation in a cell-context specific manner. Nevertheless, the datum concerning the role(s) of SIRT1 in formation and prognosis of medulloblastoma is still missing.

Objective: The present study aimed to address the expression patterna of SIRT1 in medulloblastoma tissues and non-cancerous counterparts and to explore whether resveratrol exerts its anti-medulloblastoma effects via regulating SIRT1 expression and bioactivity.

Methods: The expression of SIRT1 in medulloblastoma and non-cancerous counterparts was elucidated by immunohistochemical ataining (IHC). To clarify the function of SIRT1 in medulloblastomas, SIRT1 expression in UW228-3 medulloblastoma cells were suppressed by RNA interference (RNAi). The influence of resveratrol in SIRT1 expressions in UW228-3 cells was analyzed by reverse transcription-polymerase chain reaction (RT-PCR), immunocytochemistry (ICC) and Western blotting (WB). The catalytic activity of deacetylase SIRT1 was examined by measuring the acetylation of the main substrate p53.

Results: IHC staining revealed that SIRT1 was expressed in 64.17% of MB tissues, which was higher than that in noncancerous cerebellum tissues (14.29%). The frequencies of SIRT1 expression in the nodular MB (22.22%) with better prognosis is lower than that in anaplastic MB (79.07%) and classic MB (60.29 %; $P<0.05$). The proliferation of UW228-3 cells was remarkably suppressed after being transfected with SIRT1 siRNA, accompanied with extensive cell death. The results of RT-PCR and WB showed that after 48 hours 100 M resveratrol treatment, SIRT1 expression in UW228-3 cells was down-regulated at both transcriptional and translational levels. However, resveratrol has no effect on the deacetylase activity of SIRT1.

Conclusion: The above findings suggested that SIRT1 expression is corrected with the formation and prognosis of

human MB. Resveratrol influences SIRT1 functioning in human MB cells through inhibiting SIRT1 expression rather than modulating its acetylation activity.

Keywords: resveratrol, SIRT1, RNA interference, deacetylase, medulloblastoma

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Active hexose correlated compound extends the lifespan and increases the thermotolerance of nematodes

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ABSTRACT

Background: Active hexose correlated compound (AHCC) is the extract from cultured mycelia of *Lentinula edodes*, a species of *Basidiomycetes* mushroom. AHCC contains various polysaccharides, including partially acylated □-1,4-glucan, which is one of its major constituents. The application of AHCC has been markedly increased in complementary and alternative medicine as a functional food because AHCC improved the prognosis of postoperative hepatocellular carcinoma patients. AHCC has anti-inflammatory and antioxidant effects, such as the suppression of nitric oxide production in hepatocytes. AHCC might affect resistance to environmental stress, which is assumed to play a pivotal role in the longevity of many organisms.

Objective: To investigate the effect of AHCC on longevity, we measured the lifespan of the nematode *Caenorhabditis elegans*, a model animal that is widely used to assess longevity. We also examined the effect of AHCC on resistance to heat stress, *i.e.*, thermotolerance.

Methods: The lifespan of *C. elegans* animals grown on media in the absence or presence of AHCC at 20°C was evaluated. Thermotolerance assays were performed at 35°C, the restrictive temperature of the animals. The effects of AHCC on lifespan and thermotolerance were analyzed with longevity mutants. Expression levels of stress-related genes, including heat shock genes, were measured by strand-specific reverse transcription-polymerase chain reaction after heat shock.

Results: Wild-type *C. elegans* animals exhibited a longer mean lifespan by up to 10% in the presence of AHCC in the growth media than animals in the absence of AHCC. Furthermore, AHCC markedly increased thermotolerance at 35°C. Epistasis analyses showed that lifespan extension by AHCC at least partly required two longevity-promoting transcription factors: DAF-16 (*C. elegans* homolog of FOXO) and HSF-1 (*C. elegans* homolog of heat shock transcription factor 1). After heat shock, AHCC activated the transcription of the heat shock genes, which are the targets of HSF-1. Similarly, the expression of hsf-1 mRNA was elevated following AHCC treatment. Recently, natural antisense transcripts were shown to regulate mRNA stability at the posttranscriptional level. In nematodes, AHCC increased the natural antisense transcript of the *hsf-1* gene.

Conclusion: AHCC conferred lifespan extension and thermotolerance to *C. elegans*. Our analyses suggest that the

beneficial effects of AHCC on longevity are involved in the activation of at least two transcription factors, DAF-16 and HSF-1, most likely through an antisense transcript-mediated mechanism.

Keywords: longevity, heat stress resistance, HSF, FOXO, heat shock gene

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Interactive effects of 1, 25-dihydroxyvitamin D3 and soy protein extract (SPE) on oral cancer growth in vitro: evidence for potential functional relationships

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ABSTRACT

Background: Previous studies have found specific soy isoflavones (Genistein, Daidzein, Glycitein) demonstrate anti-tumor properties against several cancer types, including oral cancer. Few studies have evaluated whole soy extract, containing a combination of these isoflavones and other bioreactive compounds, which may function synergistically and more effectively against oral cancers. Preliminary work by this group has now demonstrated whole soy protein extract (SPE) inhibits oral cancer cell growth specifically and selectively, through independent cell- cycle and apoptotic pathways. However, more recent evidence now suggests that ingestion of vitamin D_3, either in dietary foods or supplements may potentiate the activity of soy components and their anti-tumor effects.

Objective: The primary goal of this study was to investigate the interactive and inter-connected effects of 1, 25-dihydroxyvitamin D_3 administration with the anti-proliferative effects of whole soy protein extract (SPE) on oral cancer and normal cell lines *in vitro*.

Methods: Three oral squamous cell carcinoma cell lines (SCC15, SCC25, and CAL27) were treated with 1, 25-dihydroxy Vitamin D_3 at physiological concentrations (10-125 nmol). Cell growth was then compared with cell treatment using soy protein extract (SPE) within the normal physiologic range (0 - 10 □□/L). Interactive effects were then evaluated using co-administration of SPE and 1, 25-dihydroxy Vitamin D_3. Quantitative RT-PCR was performed at various time points to determine any changes in mRNA expression for key cell cycle and apoptotic signaling pathway regulators, including *p53*, *c-myc*, *ornithine decarboxylase (ODC)*, *caspase-2*, *caspase- 8*, and *bax*.

Results: Administration of 1, 25-dihydroxy Vitamin D_3 induced distinct dose-dependent, growth-inhibitory effects in all three oral cancer cell lines examined. These inhibitory effects were comparable to the overall range of growth inhibition induced by SPE. However, the combined effects of co-administration were far greater, suggesting the presence of synergistic relationships between these components. In addition, these results indicate that either treatment alone appeared to modulate mRNA expression of oral cancer cell-cycle promoters *c-myc* and *ODC*, as well as the *caspase*-dependent apoptosis pathway, while only 1, 25-dihydroxy Vitamin D_3 administration appeared to influence the *bax* pathway.

Conclusion: These results suggest that co-administration with 1, 25-dihydroxy Vitamin D_3 and SPE may enhance their anti-tumor effects. This study may help to explain, in part, why balanced diets rich in fruits, vegetables, and soy protein, are associated with protection against development and progression of oral cancers, although further study is needed to develop specific public health recommendations for oral cancer treatment and prevention.

Key words: vitamin D, soy extract, whole soy protein, oral cancer, growth inhibition.

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Breast cancer prevention with *Morinda citrifolia* (noni) at the initiation stage

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ABSTRACT

Background: It has been reported that noni has multiple health benefits for over 2000 years. In this study, the cancer preventive effects of Tahitian noni® juice (TNJ) at the initiation stage on DMBA-induced mammary tumorigenesis in female SD rats was investigated.

Objective: We took advantage of the DMBA-induced mammary carcinogenic model to study the preventive effects of TNJ at the initiation stage of mammary carcinogenesis in female SD rats by using clinical observation, pathological examination, and ^{32}P-postlabeling assay.

Methods: One hundred and sixty female SD rats were divided into eight groups with 20 rats in each group. Three doses of TNJ or placebo was given to the animals at the age of 35 days until the end of the experiment. When the animals were 55 days old, 25 mg/kg DMBA was fed to the animals in the DMBA group, placebo, and TNJ groups. The 20 rats were kept at age-matched controls. Palpable tumors were examined twice a week after DMBA administration in each group by an experienced professional. The size of tumor was measured by a graduated caliper. A piece of tumor, vascularization area, and mammary glands in the thoracic and abdomen areas of each rat were dissected respectively and fixed in 10% neutral buffered formalin for light microscope examination. The DMBA-DNA adduct formation in mammary tissues was detected by 32P-postlabeling assay.

Results: The tumor latency in TNJ groups was delayed about 60-90 days when compared with positive controls. The number of palpable tumors per group was significantly reduced by 73%, 72% and 80% in 3%, 5%, and 10% TNJ groups respectively when compared with positive controls at the end of 330 days after DMBA administration. The number of palpable tumors in the placebo groups was slightly reduced in the early stage, but much less than that in the TNJ groups. The multiplicity and malignancy of lesions were significantly reduced and the survival rate of animals in the TNJ groups was significantly increased compared with positive controls at different time points. Histological examination showed that the malignancy of lesions in TNJ groups did not show a significant change when compared with that in positive and placebo groups.

Conclusion: In conclusion, this is the first study which indicates that TNJ possesses a cancer preventive effect at the initiation stage of chemical carcinogenesis induced by DMBA in female SD rates.

Key words: *Morinda citrifolia,* Tahitian noni® juice, breast cancer, cancer prevention

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Dietary omega-3 fatty acids and locomotor activity in an animal model of attention deficit hyperactivity disorder (ADHD)

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ABSTRACT

Background: Attention deficit hyperactivity disorder (ADHD) is the most frequent behavioral disorder of childhood and is characterized by hyperactivity, attention problems and impulsivity. Pharmacological and behavioral therapies have been shown to be effective. In addition, the role of dietary compounds in the etiology and possibly the treatment of ADHD has attracted increasing attention. For example, the lack of dietary essential fatty acids has been suggested to be associated with symptoms of ADHD in humans.

Objective: To investigate the effects of omega-3 polyunsaturated fatty acids (n-3 PUFAs) on locomotor activity in the spontaneously hypertensive rat (SHR) which has been proposed as an animal model of ADHD.

Methods: Two groups of randomly assigned spontaneously hypertensive rats were fed with either n-3 PUFA-deficient or n-3 PUFA-enriched food (based on AIN93G) for six weeks and this was continued during the phase of behavioral testing. Locomotor activity was subsequently assessed using an open field test.

Results: The results showed a marked difference in locomotor activity between the two groups of SHRs. In comparison with rats fed with n-3 deficient food, the animals on an n-3 enriched diet showed a statistically significant decrease in motor activity as assessed by the distance traveled.

Conclusions: The present study demonstrates a marked reduction in locomotor activity following an n-3 PUFA-enriched diet in SHRs, i.e. the dietary enrichment with n-3 PUFAs reduced the motor activity in an established animal model of ADHD. Dietary n-3 PUFAs may therefore play a role in the pathophysiology of ADHD. **Key words:** omega-3 polyunsaturated fatty acids, attention deficit hyperactivity disorder, ADHD, animal model, spontaneously hypertensive rat, SHR, motor activity

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Inhibitory effect of a formulated extract from multiple citrus peels on LPS-induced inflammation in RAW 246.7 macrophages

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ABSTRACT

Background: Formulated Citrus Peel Extract (GL) made from the peels of six citrus fruits available in Japan, namely *navel oranges, citrus hassaku, citrus limon, citrus natsudaidai, citrus miyauchi and satsuma*, was initially developed as a cosmetic product to protect skin from UV irradiation. Anecdotal evidences of anti-cancer property of GL have been reported by consumers based on the cases such as topical application for melanoma, and oral ingestion for prostate, lung and liver cancers. Those anecdotal reports stimulated us to investigate anti-tumorigenesis activity of GL. In the previous study, we reported that the topical application of GL inhibited DMBA/TPA-induced skin tumor formation by decreasing inflammatory gene parameters.

Objective: In this study, we mainly investigated the effect of GL on translocation of NF-kB together with production of nitric-oxide and TNF-α induced by LPS in RAW 264.7 cells. **Results:** This investigation showed that GL decreased the release of TNF-α and nitric oxide from macrophage RAW264.7 cells stimulated by LPS in a dose-dependent manner. In addition, GL suppressed the expression of iNOS and nuclear translocation of NF-kB in RAW264.7 cells, inhibited the degradation of IκB-α, and scavenged hydroxyl radicals (DMPO/OH adduct) *in vitro*.

Conclusions: Our findings suggest that GL suppresses the inflammation *in vitro*, and exerts chemopreventive activity through the inhibition of production of TNF-α and iNOS proteins due to the inhibition of nuclear translocation of NF-kB and oxidative stress. GL appears to be a novel functional natural product capable of preventing inflammation and inflammation-associated tumorigenesis.

Keywords: GL, Citrus peel extract, anti-inflammation, Nitric oxide, iNOS, NF-kB, TNF-α

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Biography of biophenols: past, present and future

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ABSTRACT

Background: The term "biophenols" was first coined by Romeo and Uccella in 1996 to denote bioactive phenols in olives replacing the more common and less chemically accurate term "polyphenols". "Biophenols" has started gaining popularity beyond olive chemistry and currently used by researchers to refer to plant phenols in general. Biophenols constitute the largest group of secondary plant metabolites with ubiquitous presence in plants and wide spectrum of biological activities. During the last three decades, biophenols have seized scientific attention, lured industry and attracted consumers' interest due to their antioxidative potential in preservation of food and maintaining human health. For the first time, a definition for "biophenols" has been proposed to present a more precise and comprehensive umbrella term to encompass all phenolic compounds of botanical origin. In this article, the author is tracing the landmarks of the history of biophenol research; profiling contemporary research directions; highlighting research controversies and uncertainties; and presenting an outlook of the biophenols future research.

Keywords: polyphenols, chemistry, pharmacology, biological activities, antioxidant

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Cost-effectiveness analysis for the treatment of chronic kidney disease with low-protein diet

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ABSTRACT

Background: Several clinical studies have shown that a low protein diet in patients with Chronic Kidney Disease (CKD), delays and prevents the natural progression of the end stage renal disease (ESRD) and the necessary treatment of renal dialysis. Studies to investigate the effects of the low protein diets in preventing severe kidney failure are few for Italy. The aim of this study is to estimate the cost-effectiveness of a low protein diet treatment compared with no dietary treatment in patients with CKD 4-5 after 2, 3, 5 and 10 years.

Methods: A Markov model simulating was developed to estimate costs and QALYs associated with low protein treatment and no treatment for patients with CKD 4-5. The prevalence of patients with CKD 4-5 refers to a population aged ≥40 years old was 0.3% estimated by a study of Gambaro et al. on the 2010. The transition probability was estimated on data from seven studies identified by a Cochrane review to determine the efficacy of low protein diets in delaying the need to start maintenance dialysis. The Quality Adjusted Life Years (QALYs) scores used were estimated with the Time Trade Off by a study of Gorodetskaya et al. in 2005. The costs of dialysis have been estimated by a study of Censis (2009) and amounted to approximately €34,071.7 per patient per year. The costs of a low- protein diet refer to contributions of €1,440 per patient per year made by Lazio Region for patients that use a low-protein diet.

Main Results / Conclusion: The treatment with a low-protein diet is more effective in terms of QALYs: the difference is always in favour of dietary treatment from a 0.09 after the first two years, 0.17 after three years, 0.37 after five years and up to a differential of 1 year after the first 10 years of treatment. In terms of cost-effectiveness, the dietary treatment is always dominant in all the intervals considered. The dominance is due to the fact that the treatment is more effective in terms of QALYs and at the same time is less expensive. The results of these simulations indicate that the treatment of patients with CKD with a low protein diet is cost effective relative to no treatment in an Italian setting.

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Producing micron- and nano- size formulations for functional foods applications

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ABSTRACT

Background: Nutrient deficiencies affect the health and wellness of large populations around the world. For example, the majority suffer from vitamin, essential fatty acid (such as omega-3), dietary fiber, and other important ingredient deficiencies due to their limited supply in the human food chain. Current trends in the nutraceutics industry to place these substances in higher, more- efficiently dispersed quantities in our food have become critically essential to their business plans. Nutrients in the form of small solids or droplets improve bioavailability. However, there remain numerous barriers to successful implementation of cost effective manufacturing processes. These challenges are addressed in the work presented here with particular focus on stability, bioavailability, and consumer acceptance. The goal is to develop large scale manufacturing systems that implement efficient platform technologies, with their respective operational maps, to produce functional food formulations, with particle sizes of these specially formulated nutraceutical ingredients in the micron-and nano-range.

Objective: Demonstrating that stable micron- and nano-size emulsions, liposomes, and aqueous suspensions of functional food formulations can be produced using both “top down” and “bottom up” methods is our main objective. Addressing the challenges associated with the incorporation of these ingredients into large scale manufacturing systems, mainly mechanical stability and related shelf-life issues, is also a focus. That is, to develop proper processing protocols providing improved quality foods enriched with ingredients that are in limited supply in our food chain; to enhance human health and wellness world-wide.

Methods: The formulations considered here typical of those used for increasing bioavailability of the infused, specially formulated ingredients with anti-cancer, anti-aging, and in-general wellness properties, lowering fat content and enhancing the shelf-life stability. Included are (a) an oil-in-water (fish oil/omega-3) emulsion, (b) liposome chaperones to vitamin C, and (c) aqueous suspensions (curcumin crystals, lutein/carotenoids, and fiber in soy milk). The production techniques include both “top-down” particle size reduction and “bottom-up” formation of crystals/precipitates via solubility adjustments. Both techniques are based on high shear processing of multiple liquid feeds. Using an impinging jet system, micro-mixing scales less than 100 nm were obtained.

Results: (a) All nano-emulsion types, single, double and larger, either as oil-in-water and water- in-oil, can effectively be produced from various formulations using “top-down” methods. Illustrated here are single, oil-in-water systems; concentrations of 12-14 wt. % fish oil/omega-3 were mixed with water containing food grade

surfactants. The high shear processing produced stable, submicron particles; with median particle sizes of 119-163 nm, no particles larger than 1 micron, and the “fish” odor was suppressed. Pertinent discussions related to the other types are also given as suggested path forward approaches for the development of nutrient enriched functional foods. This includes water-in-oil formulations for reduced fat content and the delivery of multiple species via double and triple emulsions, as compared to liposome configurations.

(b) Although liposomes may be used to encapsulate both hydrophobic and hydrophilic substances, we selected liposomal vitamin C as our initial proof-of-concept system since it is absorbed into the body over four times more easily than its non-encapsulated form. After top down processing, the median size was 200 nm, compared to a median size of about 5 microns obtained by traditional self-assembly protocols. (b) Aqueous suspensions of micron- and nano- size formulations were also accomplished. The top down size reduction technique was used for processing soy bean fibers and lutein and the bottom-up method used for curcumin crystals. The fibers initially had a median size of 150 microns and a bi-modal distribution was obtained after processing; 99% of the particles were smaller than 15 microns with median sizes at 10 microns and the larger peak at about 200 nm. The curcumin submicron particles were formed via anti- solvent crystallization; with stable particles in the range of 300-500 nm.

Conclusions: Our study demonstrates that stable micron- and nano-size emulsions, liposomes, and aqueous suspensions can be produced using both “top down” and “bottom up” methods. The formulation properties, in terms of particle size and stability, strongly depend on the processing parameters used in terms of energy input and temperature history. The energy requirements of the “bottom up” methods may be substantially lower than those of “top down” methods. Although some of the processes presented here have been scaled up to commercial levels, more work is needed in terms of fully assessing the bioavailability of the produced formulations and optimizing the processes to minimize cost.

Key words: nano-emulsion, nano-suspension, high-shear processing, crystallization, curcumin, fish oil, liposomal vitamins: C and E, lutein, nutraceuticals, omega-3, soybean fiber.

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Nutritional Proteomics: Investigating molecular mechanisms underlying the health beneficial effect of functional foods

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ABSTRACT

Objective: We introduce a new technical and conceptual term "nutritional proteomics" by identifying and quantifying the proteins and their changes in a certain organ or tissue dependent on the food intake by utilizing a mass spectrometry-based proteomics technique.

Purpose: Food intake is essentially important for every life on earth to sustain the physical as well as mental functions. The outcome of food intake will be manifested in the health state and its dysfunction. The molecular information about the protein expression change caused by diets will assist us to understand the significance of functional foods. We wish to develop nutritional proteomics to promote a new area in functional food studies for a better understanding of the role of functional foods in health and disease.

Methods: We chose two classes of food ingredients to show the feasibility of nutritional proteomics, omega-3 polyunsaturated fatty acids and omega-6 polyunsaturated fatty acids both of which are involved in the inflammation/anti-inflammation axis. Each class of the polyunsaturated fatty acids was mixed in mouse chow respectively. The liver tissue of mice fed with omega-3 diet or omega-3 diet was analyzed by the state-of-the-art shotgun proteomics using nano-HPLC-ESI-MS/MS. The data were analyzed by the number of differentially expressed proteins that were guaranteed by 1% false discovery rate for protein identification and by the statistical significance of variance evaluated by p-value in two-tailed distribution analysis better than 0.05 (n=4). The differential pattern of protein expression was characterized with Gene Ontology designation.

Results: The data analysis of the shotgun nutritional proteomics identified 2,810 proteins that are validated with 1% FDR. Among these 2,810 proteins, 125 were characterized with statistical significance of variance ($p<0.05$; n=4) between the omega-3 diet and the omega-6 diet by two- tailed distribution analysis. The results illustrate that the dietary influence of omega-3 and omega-6 on protein expression is eminent with the proteins directly responsible for catalytic activity in the "Molecular Function" category, totaling 192 proteins, of Gene Ontology designation. In a similar analysis with regard to the "Cellular Localization" category, protein expression changed the most in the sub-categories of "Cytoplasm", "Membrane", "Nucleus", and "Mitochondrion", totaling 221 proteins. The same analysis with regard to "Biological Process" considering the top four categories, *i.e.,* "Metabolic process", "Regulation of biological (process)", "Response to stimulus", and "Transport" also indicated significant alteration of 182 proteins. These results illustrate a robust influence of

dietary elements, omega-3 or omega-6 polyunsaturated fatty acids, on the protein expression in mouse liver.

Conclusions: Application of nutritional proteomics to the dietary effect of omega-3 polyunsaturated fatty acids compared to that of omega-6 on mouse liver revealed; 1) significant number of proteins are altered between the two diets dependent on the classes of polyunsaturated fatty acids, omega-3 or omega-6, in the diet. The change of protein expression is likely to carry the molecular information that we could possibly decipher, leading to a better understanding of the role of omega-3 polyunsaturated fatty acids in inflammatory/anti-inflammatory process. The results corroborate the concept and utility of nutritional proteomics that should be developed as a part of functional food studies with regard to other dietary types.

Keywords: Nutritional proteomics, functional foods, mass spectrometry, genome database, cellular signaling, omega-3 and omega-6 polyunsaturated fatty acids

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Astaxanthin as a Medical Food

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ABSTRACT

Astaxanthin is a red pigment that belongs to the carotenoid family like β-carotene. And it's found in seafood such as crustaceans: shrimp and crabs and fish: salmon and sea bream. Recently, astaxanthin has been reported to have antioxidant activity up to 100 times more potent than that of vitamin E against lipid peroxidation and about 40 times more potent than that of β-carotene on singlet oxygen quenching. Astaxanthin does not show any pro-oxidant activity and its main sight of action is on/in the cell membrane. Various important benefits to date have suggested for human health such as immunomodulation, anti-stress, anti-inflammation, LDL cholesterol oxidation suppression, enhanced skin health, improved semen quality, attenuating eye fatigue, sport performance and endurance, limiting exercised induced muscle damage, suppressing the development of life-style related diseases such as obesity, atherosclerosis, diabetes, hyperlipidemia and hypertension. Nowadays, the research and demand for natural astaxanthin in human health application are explosively growing worldwide. Especially, the clinicians use the astaxanthin extracted from the microalgae, *Haematotoccus pluvialis*, as an add-on supplementation for the patients who are unsatisfied with the current medications or who can't receive any medications because of their serious symptom. For example, the treatment enhances their daily activity levels or QOL in heart failure or benign prostatic hypertrophy/lower urinary tract symptom patients. Other studies and trials are under way on chronic diseases such as non- alcoholic steatohepatitis, diabetes and CVD. We may call astaxanthin "a medical food" in the near future.

Keywords: astaxanthin, medical food, *Haematococcus*, add-on supplementation

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Effect of a dietary supplement containing kurozu (a Japanese traditional health drink) concentrate on several obesity-related parameters in obese Japanese adults: a randomized, double-blind, placebo-controlled trial

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ABSTRACT

Objective: This study was undertaken to examine the Kurozu concentrate (KC) based dietary supplement on several obesity-related parameters in obese Japanese male and female adults.

Background: Kurozu, which is a specific type of rice vinegar produced by fermentation of unpolished brown rice, has long been used as a traditional health food and folk medicine in Japan. A recent animal study and our preliminary human study suggest that the KC supplement has potential for use in the management of obesity.

Materials and Methods: A 12-week, randomized, double-blind, placebo-controlled trial was conducted involving 48 Japanese adult subjects (28 males and 20 females) with obesity. Subjects were either assigned to the group consuming the KC supplement for 12 weeks (870mg/day; 480 mg/day as KC) (n=24; 14 males and 10 females) or the placebo group (n=24; 14 males and 10 females). All test participants were assessed using several obesity-related parameters, including body weight, BMI, waist circumference, and abdominal fat computed tomography (CT) sections. These measurements took place at baseline and at week 12.

Results: At week 12, a significant decrease in body weight ($P<0.043$) and nearly significant decreased values of BMI ($P=0.052$) were observed in the KC group compared to the placebo group. The reduction in waist circumference at week 12 within the KC group was not significantly greater than the placebo group. Examination of abdominal CT sections around the navel indicated that, although most of the values of the total fat area, subcutaneous fat area, and visceral fat area for both of the placebo and KC groups significantly increased during the 12- week intervention, the magnitude of increase in the total fat area for all subjects and that of the total fat area, subcutaneous fat area, and visceral fat area for females on one or more of three CT sections were significantly lower in the KC group than the placebo group ($P<0.05$).

Conclusion: Although the results are not definitive, KC supplementation may have potential for improving some obesity-related parameters in obese subjects, particularly females.

Key words: Kurozu concentrate (KC), KC-based dietary supplement (KC supplement), abdominal obesity-related parameters, body mass index (BMI), computed tomography (CT), abdominal fat

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Cancer-specific therapeutic potential of resveratrol: metabolic approach against hallmarks of cancer

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ABSTRACT

Cancer hallmarks include evading apoptosis, limitless replicative potential, sustained angiogenesis, tissue invasion and metastasis. Cancer cells undergo metabolic reprogramming and inevitably take advantage of glycolysis to meet the increased metabolic demand: rapid energy generation and macromolecular synthesis. Resveratrol, a polyphenolic phytoalexin, is known to exhibit pleiotropic anti-cancer effects most of which are linked to metabolic reprogramming in cancer cells. This review summarizes various anti-cancer effects of resveratrol in the context of cancer hallmarks in relation to metabolic reprogramming.

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/44/99

Intravenous ascorbic acid protocol for cancer patients: scientific rationale, pharmacology, and clinical experience

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ABSTRACT

Background: Ascorbic acid (vitamin C, ascorbate) has been shown to protect cells against various types of oxidant injury at physiologically relevant concentrations. Vitamin C has been suggested as having both a preventative and therapeutic role in a number of pathologies when administered at much higher-than-recommended dietary allowance levels**.** This article reviews the scientific rational for intravenous vitamin C as a potential treatment for cancer.

Many mechanisms of action for ascorbate efficacy against cancer have been proposed over the years. Cancer patients are often deficient in vitamin C and require large doses to replenish depleted stores. It has been demonstrated *in vitro* and in animal studies that vitamin C is preferentially toxic to tumor cells at millimolar concentrations; moreover, pharmacokinetic data suggest that these concentrations are clinically achievable when ascorbate is administered intravenously. Data suggests that ascorbate may serve as a biological response modifier, affecting inflammation and angiogenesis as well as improving immune function parameters.

While Phase II clinical trials using ascorbate in cancer therapy are under way, vitamin C is not subject to the regulations that synthetic drugs are and therefore has been used clinically for decades to treat cancer patients. This clinical experience suggests the therapy is safe and may be effective in some instances. Attached to this article is the Riordan IVC Protocol, which details an intravenous vitamin C protocol that can be safely administered to cancer patients.

Keywords: Cancer, inflammation, C-reactive protein, inflammatory cytokines, high-dose vitamin C

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The Potential Anti *Helicobacter pylori* and antioxidant effects of Artemisia Judaica

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ABSTRACT

Artemisia judaica (*AJ)* is one of the common species of the genus *Artemisia* that grows in Saudi Arabia desert and Sinai, Egypt where animals graze on it. It is widely used in traditional medicine and by Bedouins there. *(AJ)* has anthelmintic, antibacterial, antiinflammatory, analgesic and antipyretic effects. The present study aimed to (1) elucidates the antibacterial action of *AJ* against *H. pylori* and different other bacterial species (2) delineate the potential antibacterial mechanism of action of *AJ* in comparison with tetracycline and cefotaxime (3) measure the trolox equivalent antioxidant capacity (TEAC) of the AJ water extract. Preparation of the *(AJ)* extracts was done by three different methods two of them are usually performed by population in Middle East by boiling of the shade-dried herb in water as tea (decoction), or soaked in tap water for over night (infusion), other method was done by concentrating the aqueous extract of *Artemisia judaica* under vacuum. The results of this study revealed that *(AJ)* has neither antibacterial effects either against H. pylori nor any other bacterial species**.** On the other hand the extract of AJ prepared by any of the above mentioned methods shows significant ($p<0.005$) antioxidant action as compared with blank and related to trolox antioxidant capacity.

Key words: *Artemisia judaica, Helicobacter pylori,* antioxidant capacity

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Chemoprevention of HBV-related hepatocellular carcinoma by the combined product of resveratrol and silymarin in transgenic mice

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ABSTRACT

Background: Patients with chronic hepatitis B virus (HBV) infection are at a high risk to develop hepatocellular carcinoma (HCC). Recently, metabolic syndrome has been found to carry a risk for HCC development. Considering the limitation of chemotherapeutic drugs for HCCs, the development of chemopreventive agents for high risk chronic HBV carriers is urgently demanded. In this study, we used combined silymarin and resveratrol extract which have been shown to exhibit biologic effects on activating peroxisome proliferator activated receptors (PPAR) and inhibiting mTOR signaling in a transgenic mice model harboring HBV viral oncoproteins.

Methods: The transgenic mice model harboring HBx and pre-S2 mutant constructs which develop HCC was adopted. First, we *in vitro* tested the ideal combination dosages of the silymarin and resveratrol product, and then we fed the natural product to the transgenic mice. The chemopreventive effects on preventing the development of HCC were evaluated.

Results: MTT assay showed an enhanced effect of the combined silymarin and resveratrol product on the reduction of cell proliferation in two hepatoma cell lines, Huh-7 and Hep G2. *In vitro* reporter assay and Western blot analyses revealed that the combined product could activate PPAR/PGC-1 signaling and inhibit mTOR expression. *In vivo,* the combined products could significantly ameliorate fatty liver and reduce HCCs in transgenic mice harboring HBV oncoproteins.

Conclusions: The combined silymarin and resveratrol product exhibits a synergistic effect on the reduction of HCC development in transgenic mice model and may represent a potential agent for the prevention of HCC in high risk chronic HBV carriers.

Key words: HBV, HCC, Transgenic mice, Chemoprevention

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Intake of Mung Bean Protein Isolate Reduces Plasma Triglyceride Level in Rats

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ABSTRACT

Background: Mung bean is well known as a starch source, but the physiological effects of mung bean protein have received little attention. In this study, we isolated mung bean protein from de-starched mung bean solutions, and investigated its influence on lipid metabolism.

Objective: The aim of this study is to clarify the influence of the lipid metabolism by consumption of mung bean protein isolate (MPI)

Methods: Diets containing either mung bean protein isolate (MPI) or casein were fed to normal rats for 28 days.

Results: Both groups ate the same amount of food, but the plasma triglyceride level, relative liver weight and liver lipid contents (cholesterol and triglyceride pool) in the MPI group were significantly lower than in the casein group. In the MPI group, the expression of sterol regulatory-element binding factor 1 (SREBF1) mRNA in the liver was significantly different when compared with the casein group. The significantly lower levels of insulin and free fatty acids in the MPI- fed rats may be due to the regulation of genes related to lipid metabolism in the liver.

Conclusions: These results suggest that MPI may improve the plasma lipid profile by normalizing insulin sensitivity.

Keywords: mung bean, *Vigna radiata* L., 8S globulin, triglyceride, β-conglycinin, 7S globulin, insulin sensitivity, SREBF1

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Molecular mechanism of intracellular lipid accumulation: Suppressive effect of Pycnogenol^{R} in liver cells

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ABSTRACT

Cells are physiologically ready to accumulate lipids such as triacylglycerides in the cytoplasm. Five classes of perilipin (PLIN) family proteins are known to be involved in the process of intracellular lipid accumulation. PLIN2 is expressed ubiquitously including adipocytes, hepatocytes and macrophages. Over-expression of PLIN2 is demonstrated in the lesions of fatty liver diseases and atherosclerosis. Suppression of PLIN2 expression prevents from developing these pathological conditions in animal models, suggesting that PLIN2 could be a therapeutic target molecule for excessive intracellular lipid accumulation which leads to various metabolic derangements. The PLIN2 gene promoter has two important *cis*-acting elements in close proximity:AP-1 element which mediates inflammatory signals and PPRE which mediates free fatty acid effect. In NMuLi mouse liver cells, FFA such as oleic acid requires both functional AP-1 and PPRE simultaneously to stimulate the promoter activity, indicating the presence of intimate interaction of inflammatory and metabolic signals on this gene. Pycnogenol^{R}, French maritime pine bark extracts, suppressed the oleic acid-induced PLIN2 expression and lipid accumulation in NMuLi cells. We found that Pycnogenol^{R} did not suppress the PLIN2 promoter activity or AP-1 binding to DNA. Instead, Pycnogenol^{R} facilitates the PLIN2 mRNA degradation, leading to suppression of lipid accumulation. This effect seems to be independent of antioxidant effect of Pycnogenol^{R}. We raise the idea that PLIN2 is a putative target molecule for prevention of pathological condition induced by excessive lipid accumulation, and this class of natural compounds could be putative therapeutic modalities.

Key words: Pycnogenol^{R}, lipid droplet, perilipin, fatty liver disease

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A randomized, controlled trial to assess short-term black pepper consumption on 24-hour energy expenditure and substrate utilization

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ABSTRACT

Background: Thermogenic ingredients may play a role in weight management. *In vitro* and rodent work suggests that components of black pepper may impact energy expenditure, and in humans, other TPRV1 agonists e.g. capsaicin, augment EE.

Objectives: To determine the impact of BP on 24-hour EE, respiratory quotient, and biochemical markers of metabolism and satiety, a randomized, controlled, cross-over study of black pepper (0.5mg/meal) versus no pepper control was conducted in post-menopausal women. Subjects spent two 24-hour periods in a whole room indirect calorimeter.

Results: Post-meal glucose, insulin, gut peptides and catecholamines were measured. Energy expenditure, respiratory quotient, or biochemical markers assessed did not differ significantly between the black pepper and no pepper control study days.

Conclusions: Our findings do not support a role for black pepper in modulating energy expenditure in overweight postmenopausal women. Future work targeting alternative populations, administering black pepper in the fasted state, or in combination with other spices, may reveal the thermogenic effect of this spice.

Trial registration: This trial was registered at clinicaltrials.gov (NCT01729143).

Key words: Black pepper, piperine, energy expenditure, metabolic chamber

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Verification of anti-fatigue effect of anserine by angle fatigue indicator based on median frequency changes of electromyograms

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Keywords: anserine, muscle fatigue, electromyogram, median frequency power, MDF angle

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Modulation of protein quality control systems as novel mechanisms underlying functionality of food phytochemicals

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ABSTRACT

Background: Phytochemicals are secondary metabolites of plants that are produced for their defense against environmental stresses, such as polyphenols, which are considered to play a major role in protection against ultraviolet (UV) light-induced oxidative damage, as well as anti-fungal and anti-microbial activities. In addition, there is a great body of evidence showing that phytochemicals exhibit a wide array of physiological activities in humans. Accumulated data show that the bioavailability of most, if not all, phytochemicals is quite poor and their substantial biotransformation after ingestion has also been noted. Thus, they are characterized as non-nutritive xenobiotics in animals, and the question of why phytochemicals, which are produced for plant self-defense, have beneficial effects in humans is quite intriguing. Meanwhile, stress-induced denaturing of cellular proteins greatly affects their tertiary structure and critically disrupts their biological functions, occasionally leading to aggregation for the onset of some pathology. Many recent studies have indicated that protein quality control (PQC) systems play key roles in counteracting 'proteo-stress', which is comprised of several processes, including protein refolding by heat shock proteins (HSPs) and degradation of abnormal proteins by the ubiquitin-proteasome system as well as autophagy.

Objective: Phytochemicals are xenobiotics, thus their biochemical interactions with animal proteins are considered to occur in a non-specific manner, which raises the possibility that some phytochemicals cause proteo-stress for activating PQC systems. Because their status is thought to be a critical determinant of homeostasis, the physiological functions of phytochemicals may be partially mediated through those unique systems. The present study was thus undertaken to address this possibility.

Methods and Results: We focused on zerumbone (ZER), an electrophilic sesquiterpene present in *Zingiber zerumbet* Smith (shampoo ginger). This agent has been reported to exhibit various bioactivities, including anti-inflammation and cancer prevention[1,2]. Treatment of Hepa1c1c7 mouse hepatoma cells with ZER resulted in marked up-regulation of multiple HSPs, such as HSP40 and HSP70. Furthermore, oral administration to the nematode *Caenorhabditis elegans* and SD rats increased the expressions of some HSPs[3]. Interestingly, ZER also increased proteasome activity in Hepa1c1c7 cells, which was accompanied with up-regulation of 5, a major proteasome functional protein. In addition, the agent notably up-regulated the expressions of several pro-autophagic markers, including p62 and microtubule-associated protein 1 light-chain 3 (LC3)-II[4]. Experiments with biotin-labeled ZER as well as a specific antibody against ZER-adduct proteins revealed that it binds numerous cellular proteins in a non-specific manner. Along a similar line, incubation with ZER led to formations of p62-conjugated proteins and aggresomes. Together, these results suggest that ZER causes proteo-stress for

potentiating the integrity of PQC systems. In support of this notion, ZER-bound proteins have been suggested to be partially recognized by HSP90, leading to dissociation of heat shok factor 1 (HSF1) from HSP90 for inducing multiple HSP genes. Next we speculated that mild chemical stress by ZER may exert beneficial effects, since ZER-bound proteins were time-dependently degraded, suggesting that defense capacity was amplified to a great level as compared with the non-treated condition. As expected, ZER conferred thermoresistance to *Caenorhabditis elegans* (*C. elegans*) and suppressed the proteo-toxicity of 4-hydroxy-2-nonenal, a potent electrophile produced through a lipid peroxidation process, in a p62-dependent manner. We then screened a number of nutrients and phytochemicals for their HSP70 inducibility, and found that certain phytochemicals, such as curcumin, phenethyl isothiocyanate, ursolic acid, and lycopene, were significantly active, whereas most nutrients were virtually inactive. These results may be associated with the fact that phytochemicals, but not nutrients, are foreign chemicals to animals, as noted above.

Conclusion: Up-regulation of antioxidant and xenobiotics-metabolizing enzymes has been reported to be an adaptive response in animals exposed to phytochemicals. Our present results imply that the process also increases the capacity to counteract proteo-stresses through activation of PQC systems. This putative phenomenon, representing the concept of hormesis[5], may be associated with mechanisms underlying the physiological functions of phytochemicals. Therefore, chronic ingestion of this class of chemicals may result in 'chemical training', in which self-defense systems are continuously activated for adaptation to phytochemical-driven stresses.

Key words: heat shock proteins, ubiquitin-proteasome system, autophagy, *C. elegans*

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Anti-inflammatory, anthropometric and lipomodulatory effects Dyglomera® (aqueous extract of *Dichrostachys glomerata*) in obese patients with metabolic syndrome

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Running Title: Anti metabolic syndrome effects of Dyglomera®

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ABSTRACT

Background: Increased visceral fat, dyslipidemia and increased markers of inflammation and coagulation are cardiovascular risk factors commonly encountered in obese people with metabolic syndrome. Previous studies have shown that ground *Dichrostachys glomerata* (DG), a spice used in Western Cameroon, can have beneficial effects on inflammation and various other cardiovascular disease risk factors. The purpose of the present study was to evaluate the effects of Dyglomera®, an aqueous extract of DG (standardized to NLT 10% polyphenols) on certain anthropometric, biochemical (including pro-inflammatory and pro-thrombotic states) and hemodynamic parameters in obese patients with metabolic syndrome.

Methods: The study was an 8-week randomized, double-blind, placebo-controlled trial involving 116 males and 202 females aged between 24 and 58 years. Participants were randomly divided into two groups: treatment and placebo. Capsules containing the active treatment (200 mg Dyglomera®) or placebo (200 mg maize powder) were administered 30–60 minutes before lunch and dinner throughout the study period. Various biochemical (namely, blood glucose, lipid profile, pro-inflammatory and pro-thrombotic markers), anthropometric and hemodynamic parameters were measured at baseline and after 4 and 8 weeks of treatment.

Results: At the end of the study, the Dyglomera® group showed statistically significant differences in all 16 parameters compared to baseline values. Changes in BMI and waist circumference were accompanied by changes in biochemical parameters, with the exception of adiponectin levels which were not correlated to waist circumference and PAI-1 values. The results confirm the hypothesis that Dyglomera®, the aqueous extract of DG, has anti- inflammatory properties, and is effective in reducing cardiovascular disease risk factors associated with metabolic syndrome in obese human subjects.

Key words: *Dichrostachys glomerata* extract, inflammation, obesity, metabolic syndrome

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Krill protein hydrolysate reduces plasma triacylglycerol level with concurrent increase in plasma bile acid level and hepatic fatty acid catabolism in high-fat fed mice

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ABSTRACT

Background: Krill powder, consisting of both lipids and proteins, has been reported to modulate hepatic lipid catabolism in animals. Fish protein hydrolysate diets have also been reported to affect lipid metabolism and to elevate bile acid (BA) level in plasma. BA interacts with a number of nuclear receptors and thus affects a variety of signaling pathways, including very low density lipoprotein (VLDL) secretion. The aim of the present study was to investigate whether a krill protein hydrolysate (KPH) could affect lipid and BA metabolism in mice.

Method: C57BL/6 mice were fed a high-fat (21%, w/w) diet containing 20% crude protein (w/w) as casein (control group) or KPH for 6 weeks. Lipids and fatty acid composition were measured from plasma, enzyme activity and gene expression were analyzed from liver samples, and BA was measured from plasma.

Results: The effect of dietary treatment with KPH resulted in reduced levels of plasma triacylglycerols (TAG) and non-esterified fatty acids (NEFAs). The KPH treated mice had also a marked increased plasma BA concentration. The increased plasma BA level was associated with induction of genes related to membrane canalicular exporter proteins (*Abcc2*, *Abcb4*) and to BA exporters to blood (*Abcc3* and *Abcc4*). Of note, we observed a 2-fold increased nuclear farnesoid X receptor (*Fxr*) mRNA levels in the liver of mice fed KPH. We also observed increased activity of the nuclear peroxiosme proliferator-activated receptor alpha (PPARα) target gene carnitine plamitoyltransferase 2 (CPT-2).

Conclusion: The KPH diet showed to influence lipid and BA metabolism in high-fat fed mice. Moreover, increased mitochondrial fatty acid oxidation and elevation of BA concentration may regulate the plasma level of TAGs and NEFAs.

Key words: Krill protein hydrolysate, triacylglycerol, fatty acids, TNFα

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An extract from date seeds stimulates endogenous insulin secretion in streptozotocin-induced type I diabetic rats

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ABSTRACT

Background: The efficacy of an extract from date seeds has been tested successfully on the glycemic control of type I diabetes mellitus in rats. A suggestion that date seed extract could stimulate certain cells to differentiate into insulin-secreting cells has been proposed. In order to investigate such a possibility, this study was conducted to measure C-peptide levels in the serum of type 1 diabetic rats treated with date seed extract.

Methods: Two hundred rats were divided into 4 groups. Group I served as the control. Group II was given daily ingestions of 10 ml of date seed extract. Groups III and IV were made diabetic by streptozotocin injection and were given daily subcutaneous injections of 3 IU/day of insulin for 8 weeks. Group IV received, in addition, daily ingestions of 10 ml of seed extract. At the end of experiment, blood samples were collected from each rat, and blood glucose and serum C- peptide levels were measured.

Results: No significant differences in the means of blood glucose and serum C-peptide levels were observed between groups I (control group) and II (date seed extract-treated control group). Group IV (date seed extract-insulin-treated diabetic group) showed a statistically significant reduction in the mean blood glucose level compared to Group III (insulin-treated diabetic group). The mean serum C-peptide level was significantly higher in group IV compared to group III.

Conclusion: Biochemical results suggested an increase in endogenous insulin secretion in the case of type 1 diabetic rats treated with date seed extract, which might be the cause of its hypoglycemic effect.

Keywords: Date seed extract; type 1 diabetes; serum C-peptide

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Antioxidant and anti-inflammatory activities of loquat (*Eriobotrya japonica*) tea

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ABSTRACT

Background: Fresh loquat leaves contain several kinds of flavonoids and have been reported to have preventive effects against some human diseases such as diabetes, coughs and ulcers,. Recently, fresh loquat leaves in Japan were processed to a beverage, called loquat tea, after the fresh leaves are roasted at 350□C for 30 minutes. However, the scientific evidence supporting the functions of these processed leaves is still minimal.

Objective: The aim of this study is to investigate the antioxidant and anti-inflammatory activities of roasted loquat tea extract (LTE) *in vitro* and in culture cells.

Methods: Bioactive fractions of LTE were separated by column chromatograph. Antioxidant activities were determined by DPPH and ROS assay. Pro-inflammatory mediators cyclooxygenase-2 (COX-2) and prostaglandin E_2 (PGE_2) were determined by Western blot and ELISA assay, respectively. Chemical quantification and characterization were analyzed by HPLC, FR-IR, and NMR. Phenolic content was measured by Folin-Ciocalteu assay.

Results: The results showed that loquat tea extract (LTE) possessed stronger DPPH scavenging activity than fresh. Cellular data revealed that LTE inhibited the production of reactive oxygen species (ROS), and further suppressed the production of COX-2 and PGE_2 in lipopolysaccharide (LPS)-activated RAW 264.7 cells. Chemical quantification and characterization data indicated that LTE contained new bioactive phenolic components that were produced from the roasting processes of fresh loquat leaves.

Conclusions: Loquat tea made from roasted loquat leaves contained new bioactive phenolic compounds that contribute to its antioxidant and anti-inflammatory activities.

Keywords: Loquat tea, Antioxidant activity, Anti-inflammatory activity, Chemical characterization

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Squalene: a multi-task link in the crossroads of cancer and aging

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ABSTRACT

Since its discovery in the beginning of the XXth century, squalene has been recognized as an important link in metabolic pathways. More recently, it has been further recognized as an intermediate step in the biosynthesis of cholesterol. Its well known antioxidant capability, together with its ability to protect skin, improve the immune system, and modulate the lipid profile, confer a high potential to this natural substance, which is spread all across the body structure, though mainly in the epithelial tissues, and in particular the skin sebum. This review will focus mainly on its major properties, which are related to anticancer properties, the maintenance of the oxidation/antioxidation balance, and its antiaging capabilities. Although the substance was originally obtained from shark liver oil, it is currently possible to obtain useful amounts from vegetable sources like extra virgin olive oil, therefore avoiding the dependence on capturing the aforementioned animal species. Recognized as one of the key components of the Mediterranean dietary style, squalene is necessary to adequately manage oxygen and its derivatives in every cell of the body.

Key words: aging, antioxidants, cancer, cholesterol, diet, olive oil, squalene

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Characterization and functional properties of new everbearing strawberry (*Fragaria x ananasa* Duch.) cultivar, 'Summertiara' berries

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ABSTRACT

Background: In recent years, a new everbearing strawberry cultivar, 'Summertiara' was cultivated to supply the strawberries in pre-harvest season from July to October in Japan. For highly research and development of processing of this cultivar, 'Summertiara' berries, the objective of this study was to characterize these berries, with relation to chemical parameters, total phenols, total flavonoids, total vitamin C, and total anthocyanins, and was to investigate the solubility and the stability of anthocyanins from the berries. Moreover, the functional properties such as antioxidative activity, active oxygen species scavenging activity, and antihypertensive activity were also evaluated.

Methods: Chemical analysis, colour measurement, and sensory evaluation of new everbearing strawberry cultivar, 'Summertiara' berries were performed. Next, the solubility of anthocyanins from the berries and stability of these against pH, temperature, and an incandescent lighting were investigated. Moreover, functional properties of the extracts prepared from berries were elucidated using 5 different methods.

Results: The contents of water, proteins, lipids, carbohydrates, and ash were the same as those of other cultivar berries. The sugar-acid ratio in the berries was low; these were acidulous. By sensory evaluation, the main factors were vivid red colour, aroma, and acidity. The berries were rich in phenols, flavonoids, vitamin C, and anthocyanins. The anthocyanins of the berries became unstable by heat treatment and light exposures such as visible rays. On the other hand, the extracts prepared from the berries showed the functionalities such as antioxidant activity, active oxygen species scavenging activities, and antihypertensive activity.

Conclusions: The strawberry cultivar, 'Summertiara' berries were the most suitable for processing ingredient of strawberry-derived products with superior health promoting functionalities.

Keywords: Summertiara, everbearing strawberry cultivar, characterization, sensory evaluation, color and storage, functional property

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Neurodegenerative and fatiguing illnesses, infections and mitochondrial dysfunction: use of natural supplements to improve mitochondrial function

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ABSTRACT

Background: Many chronic diseases and illnesses are associated with one or more chronic infections, dysfunction of mitochondria and reduced production of ATP. This results in fatigue and other symptoms that occur in most if not all chronic conditions and diseases.

Methods: This is a review of the published literature on chronic infections in neurodegenerative diseases and fatiguing illnesses that are also typified by mitochondrial dysfunction. This contribution also reviews the use of natural supplements to enhance mitochondrial function and reduce the effects of chronic infections to improve overall function in various chronic illnesses.

Results: Mitochondrial function can be enhanced by the use of various natural supplements, notably Lipid Replacement Therapy (LRT) using glyerolphospholipids and other mitochondrial supplements. In various chronic illnesses that are characterized by the presence of chronic infections, such as intracellular bacteria (*Mycoplasma, Borrelia, Chlamydia* and other infections) and viruses, LRT has proven useful in multiple clinical trials. For example, in clinical studies on chronic fatigue syndrome, fibromyalgia syndrome and other chronic fatiguing illnesses where a large majority of patients have chronic infections, LRT significantly reduced fatigue by 35-43% in different clinical trials and increased mitochondrial function. In clinical trials on patients with multiple intracellular bacterial infections and intractable fatigue LRT plus other mitochondrial supplements significantly decreased fatigue and improved mood and cognition.

Conclusions: LRT formulations designed to improve mitochondrial function appear to be useful as non-toxic dietary supplements for reducing fatigue and restoring mitochondrial and other cellular membrane functions in patients with chronic illnesses and multiple chronic infections.

Key words: Neurodegenerative and fatiguing illnesses, infections and mitochondrial dysfunction, ATP, Lipid Replacement Therapy (LRT)

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Nonculturable forms of bacteria in lyophilized probiotic preparations

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ABSTRACT

Background: Nonculturable cells are formed under stress. These viable but nonculturable (VBNC) cells retain the ability to revert to active growth and division when conditions become favorable, or after treatment with resuscitating factors. Information about the possible presence of VBNC in bacterial lyophilized probiotic preparations, foodstuffs, live vaccines, etc., indicates that human as well as animal intestines are a significant area for research.

Methods: Samples were stored for different periods of time (up to 30 years) according to the manufacturers' manuals. Total counts were conducted using the Goryaev-Thoma counting chamber and actual viability was assessed by luminescence microscopy after staining with Live/Dead® (Baclight™). CFU/ml counts were made using solid or semisolid media. Viable cells that lacked the ability to form colonies were considered VBNC.

Results: We studied 11 batches of commercial probiotics (Russia) from different sources, con- taining lyophilized E. coli, lactobacilli, or bifidobacteria, in ampoules or vials. In E. coli prepara- tions, depending on storage periods, the amounts of VBNC varied from 4.1% (3 years) to 99.7% (30 years) and showed different total viability (52.2 – 91.3%), as well as the percentage of VBNC cells. A different sample that had been expired for 11 years was 79.5% NC. It is also noteworthy that the 5-dose vials, 4 years past expiration, from yet another source, showed a higher amount of VBNC cells (85.5%). Two different batches that had been expired for three years contained 4.1 and 21.3% VBNC cells. 4 of the 5-dose vials of lyophilized lactobacilli were not expired and contained 58.8 – 80.4% VBNC cells. Total viability varied from 92.9 to 100%, and there was an unmistakable positive correlation between total viability and culturability. The last batch, which had expired 6 years earlier, has 23.7% viable cells and about 98% VBNC. Non- expired bifidobacterial samples contained 70.7 and 95.5% of viable cells and were 50 and 100% culturable.

Conclusion: We demonstrated the presence of VBNC cells in lyophilized probiotic preparations that contained live bacteria. Probiotics stored past their expiration date may retain a high potential medical effect because they contained high numbers of viable cells. VBNC cells in studied preparations may have the potential to return to an actively growing state.

Keywords: nonculturable forms of bacteria, probiotics

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Stabilization of a functional refreshment from mango nectar and yacon *(Smallanthus sonchifolius)* through spray drying encapsulation

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ABSTRACT

Background: Yacon syrup (YS) may be implemented as a functional sweetener because of its concentration of fructooligosaccharides (FOS), which are sugars that are resistant to enzymatic hydrolysis in the human digestive tract. Additionally, health benefits related to the consumption of FOS have been reported, such as preventing constipation and reducing blood sugar and lipid levels in diabetic patients. Yacon is a tuber from the South American Andes region, and its nutraceutical effects have been researched.

Objective: The effect of YS as sweetener in a Mango Nectar (MN) stabilized through SD (which is?) and encapsulated with maltodextrin and Arabic gum (AG) was evaluated as a natural and alternative beverage for diabetic patients.

Methods: A sequential experimental design was used. First, mangoes were characterized into three ripening stages, evaluating pH, TSS, WC, WA, and TTA of each stage. Then, four formulations of MN with YS with concentrations of 33.3, 66.6, and 99.9% yacon-to-juice ratio were evaluated according to the quantity of TSS, which were analyzed over the acceptance of untrained judges. Later on, the formulation with the best acceptance was chosen and evaluated based on the performance of the encapsulation of components through SD using maltodextrin and AG with a 30% concentration and tricalcium phosphate (TP) with a 0.15% concentration. Lastly, the encapsulation process with maltodextrin with a 30% concentration was analyzed at temperatures of 100, 105, 110, and 130°C over the rehydration, evaluating WA, TSS, and Vitamin C.

Results: The mango with 12°Brix was selected for the formulation. The YS addition to MN generated significant differences ($p<0.001$) in the flavor because of the concentration with the addition of a 33.3% enhancing the flavor. As a result, the 33.3% concentration was selected for further testing. The final stage showed significant differences in the performance of the process of WA, TTA, TSS, and Vitamin C. Similar results were obtained regarding these components after the rehydration of the MN five days after storage. The retrieval of Vitamin C was not affected by the temperature, suggesting a favorable encapsulation.

Conclusion: The YS represents a potential nutraceutical sweetener, which may be used with concentrations around 33.3% over Tommy MN. The process of encapsulation through SD generates a product that is stable in storage and easily reconstructed.

Key words: fructooligosaccharides, inulin, micro-encapsulation, spray drying, yacon

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Dioscorea dumetorum-fed rats exhibited decreased body weight, blood glucose, and insulin in STZ-induced diabetes

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ABSTRACT

Background: Preventive measures that could slow down the rising incidences of diabetes mellitus are essential. The use of neglected local foods, which have effects on this chronic disease beyond basic nutrition as dietary controls, is desirable.

Objective: The effect of *Dioscorea dumetorum* (Kunth) Pax *(Dioscoreaceae)* feed on satiety, weight, blood glucose, and insulin levels were investigated in streptozotocin-induced diabetic rats.

Methods: Twenty adult male rats in four groups of five were used for the experiment. Three groups – *D. dumetorum,* glibenclamide, and standard pellet-fed rats were induced with diabetes by i.p. administration of 50mg kg^{-1} streptozotocin, while the fouth group (?) served as a non- diabetic control. *D. dumetorum* was fed at 15g daily for ten days before induction, and after induction, feeding continued. Glibenclamide was orally administered 5mg kg^{-1} daily. Both the untreated and non-diabetic rats were kept on standard rat pellets. Feed intake, weight, and blood glucose concentration were monitored daily, while insulin level was measured on day two and day six after inductions.

Results: Average feed intake for non-diabetic rats was 15g for *D. dumetorum* per day, which dropped to 10.3g after induction of diabetes. Weight of normal non-diabetic rats consistently increased (142.61 ± 4.37g – 169.43 ± 8.61g) for the duration (17 days) of the experiment. The *D. dumetorum*-fed rats showed weight reduction of 5.4%, glibenclamide 4.0%, and untreated diabetic 6.15%. Non-diabetic rats blood glucose levels ranged between 70 to 100mg dL^{-1}. Streptozotocin (STZ) (i.p.) administration increased blood glucose levels from 370% to 626% in the rats. *D. dumetorum*-fed rats showed reduced ($p<0.05$) blood glucose levels of 22.6%. Glibenclamide had 5.5% reduction ($p<0.05$). Insulin was absent in *D. dumetorum*-fed rats, whereas 0.95ng ml^{-1} of insulin was detected in glibenclamide-administered rats. These quantities were lower ($p<0.001$) than 1.40ng ml^{-1} in the non-diabetic rats.

Conclusion: This study revealed that *D. dumetorum* tuber caused decreased hunger, weight reduction, and displayed hypoglycemic property in diabetic rats, even after heat treatment. Its probable mechanism of anti-hyperglycemic activity might not be through increased insulin secretion.

Key words: *D. dumetorum*, streptozotocin-induced diabetes, weight, blood glucose, insulin.

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Supplementation of selenium-enriched yeast attenuates age-dependent transcriptional changes of heart in mitochondrial DNA mutator mice

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ABSTRACT

Background: Age is a major risk factor in developing heart diseases and has been associated with profound transcriptional changes in mammalian tissues. Low tissue selenium has recently been linked to several age-related diseases, including cardiovascular disease. This study investigated the global effects of age and dietary supplementation of selenium on heart transcriptional profiles in POLG mutator mice.

Methods: Heart transcription profiles from young (2-month-old) and old (13-month-old) animals fed either a control diet or a diet supplemented with 1.0 mg selenium from selenium- enriched yeast (SP)/kg diet were obtained and validated using microarray and real-time RT- PCR techniques.

Results: Aging led to significant transcriptional changes, where the expression of 1942 genes in old animals was changed by a fold change larger than 2.0, when compared to young animals. Age-regulated genes are associated with cardiovascular system development, immune and inflammatory response, and cellular oxidative stress response. Multiple genes linked with cardiomyocyte apoptosis, hypertrophy, and cardiac fibrosis, such as Myh7, Lcn2, Spp1, and Serpine1, were significantly up-regulated in old animals. SP supplementation also caused significant transcriptional changes in the heart, especially in old mice where many age-dependent transcriptional changes were totally or partially reversed by SP. Upstream regulator analysis further indicated that genes for Foxo1 and Foxo3, two transcriptional regulators involved in the regulation of cardiac muscle remodeling, were significantly activated by SP, suggesting that Foxo-mediated transcriptional activities play important roles in the anti-aging properties of SP.

Conclusions: Results of this study indicate that SP supplementation attenuated age-related transcriptional changes in the heart of old POLG mice, which implies a potential clinical application of dietary selenium in preventing decline of cardiac function in old animals.

Key words: Aging, heart, gene expression, selenium

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In vivo anti-carcinogenic property of a formulated citrus peel extract

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ABSTRACT

Background: Cancer is one of the two leading fatal diseases humans face. Synthesized drugs available for cancer intervention have many limitations in applications and effectiveness and are often associated with serious of side effects, which can further damage the patients' quality of life. Recently, the development of natural-product-based and therapeutically sound anti-cancer agents have gained popularity in the fields of functional and medical foods, which may exhibit advantages of minimal toxicity and multiple active molecular components. Citrus peel or its extract has been reported to have potent pharmacological activities and health benefits because of abundant flavonoids present in citrus fruits, particularly in the peels.

Results: The results of these studies demonstrated the efficacy of Gold Lotion (GL), an extract of multiple varieties of citrus peels that contains abundant flavonoids, including a high percentage of polymethoxylflavones (PMFs), which can protect against skin cancer, colon cancer, and prostate cancer in mice. These results are clearly promising and warrant a human trial with GL in future studies.

Summary: Briefly, these data have demonstrated that GL is efficacious in preventing and treating cancer in several model systems. This review summarizes the results of currently available data regarding the *in vivo* anti-cancer activity of GL, and identifies opportunities for subsequent human clinical trials to assess preventive and therapeutic effects in the near future.

Keywords: gold lotion, citrus peel extracts, skin cancer, colon cancer, prostate cancer

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/21/54

Proanthocyanidins from the American Cranberry (Vaccinium macrocarpon) Induce Cell Cycle Alterations in DU145 Human Prostate Cancer Cells in Vitro by Affecting the Expression of Cell Cycle-Associated Proteins

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ABSTRACT

Background: Prostate cancer is one of the most common cancers in the world. There are genetic and environmental factors that can potentially impact the development and progression of many types of cancer, including prostate cancer. As a consequence of environmental factors, such as diet having a potential effect on the development of prostate cancer, considerable interest in the possible health benefits associated with the inclusion and consumption of certain foods in the diet exists.

Context and purpose of this study: This study describes the effects of a proanthocyanidin- enriched fraction (PACs) isolated from the American cranberry (*Vaccinium macrocarpon*) on the behaviour of androgen-refractory (insensitive) DU145 human prostate cancer cells *in vitro*.

Results: Following treatment of DU145 human prostate cancer cells with 25 µg/mL of PACs for six hours, PACs significantly decreased the cellular viability of DU145 cells. PACs treatment (25 µg/mL for 6 hours) of DU145 cells increased the proportion of cells in the G2-M phase of the cell cycle and decreased the proportion of cells in the G1 phase of the cell cycle. These alterations were associated with changes in cell cycle regulatory proteins and other cell cycle associated proteins. PACs increased the expression of cyclin E, cyclin D1, CDK2 and CDK4, and decreased the expression of cyclin A and cyclin B1. The protein expression level of p27 increased, and the protein expression levels of $p16^{INK4a}$, p21, and pRBp107 decreased in response to PACs treatment. The protein expression level of pRBp130 was unchanged in response to PACs treatment.

Conclusions: These findings demonstrate that proanthocyanidins from the American cranberry can affect the behaviour of human prostate cancer cells *in vitro* and further support the potential health benefits associated with cranberries.

Keywords: Prostate cancer, proanthocyanidin-enriched fraction (PACs), American cranberry (*Vaccinium macrocarpon*)

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Inhibition of atherosclerotic plaque formation in ApoE-deficient mice by dietary supplementation with *Lactobacillus casei*

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ABSTRACT

Background: Elevated serum cholesterol in humans is generally a risk factor correlated with the development of atherosclerosis (AS). *Lactobacillus casei* has been demonstrated to have the potential to reduce human serum cholesterol levels. The purpose of this study was to evaluate the anti-atherosclerotic effect of *Lactobacillus casei* (Strain Shirota) in apoE-deficient mice.

Methods: A total of 60 male ApoE-deficient mice of 4 weeks age, were randomly divided into 4 groups of 15 each group and matched for body weight. Four groups of apoE-deficient mice consumed one of the following diet: AIN-93G purified diet (n=15); AIN-93G purified diet with *Lactobacillus casei* (Strain Shirota; 0.5 mL of 10^8 cfu/mL**,** n=15); AIN-93G purified diet with *Lactobacillus casei* (Strain Shirota; 0.5 mL of 10^{10} cfu/mL**,** n=15); AIN-93G purified diet with *Lactobacillus casei* (Strain Shirota; 0.5 mL of 10^{12} cfu/mL**,** n=15).

Results: After 16 weeks intervention, the areas of atherosclerotic plaques in the aortic sinus were determined. Plaques were much more severe in control group than in *lactobacillus casei*-treated groups ($P < 0.05$). The plaque area of aortic sinus in mice fed *lactobacillus casei* with 0.5 mL of 10^8, 10^{10}, or 10^{12} cfu/mL was 44.61%, 56.01%, 82.58% less compared with control group, respectively. Compared with control group, total cholesterol accumulation in aortas and livers showed a significant reduction in mice fed with *lactobacillus casei* ($P < 0.05$). Addition of *lactobacillus casei* also ameliorated serum lipid profile by decreasing total serum cholesterol and increasing HDL cholesterol concentration.

Conclusions: *lactobacillus casei* significantly improved lipid profile and reduced cholesterol accumulation in liver and aorta, leading the inhibition of the formation of atherosclerotic lesion.

Keywords: *lactobacillus casei*, atherosclerosis, apoE-deficient mice,cholesterol

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/19/48

Hepatotropic, antioxidant and antitoxic action of amaranth oil

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ABSTRACT

Background: It is our opinion that amaranth seed oil's properties merit further study due to their high quantity of squalene. Squalene has been shown to have antitoxic, antioxidant, and hepatotropic properties. The liver is one of the most important organs in the human body, and as a filtering organ, it is subjected to many toxic compounds and free radicals. Thus, protecting the liver with an antioxidant and antitoxic compound could offer significant benefits.

Objective: In the present study we have evaluated the antitoxic, antioxidant, and hepatotropic (hepatoprotective) effects of amaranth oil acquired via a patented pressing method. Rats were treated with amaranth oil, a comparative compound, or a control compound and then subjected to various toxic, oxidizing, and other compounds in order to examine amaranth oil's effects.

Results: Amaranth oil was found to have a positive and dose-dependent effect both *in vivo* and *in vitro*. Amaranth oil's hepatoprotective activity was confirmed by both biological and morphological examination. This study suggests that amaranth oil acts to prevent and reduce CT damage in liver tissue. This was especially the case in doses of 300 mg/kg, proved both by normalization of hepatic ferments-markers indexes and morphological examinations.

Conclusion: The amaranth oil acquired via a patented pressing method possesses antitoxic and antioxidant activity. In this connection, the amaranth oil can be recommended for prophylaxis of toxic and drug-induced liver lesions and as a component of the functional food and dietetics of various diseases.

Keywords: antioxidant activity, free-radical oxidation, hypoxia, erythrocytes hemolysis, squalene, amaranth oil, hepatoprotector, hexenalum sleep, toxic hepatitis

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Enhanced Antibacterial Activity of MGO™ Manuka Honey complexed with α– cyclodextrin (Manuka Honey with CycloPower™)

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Running Title: Manuka honey complexed with -cyclodextrin

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ABSTRACT

Background: Manuka honey is recognized for it's health-promoting properties and it's use in medicine is well documented. However, the actions of Manuka honey are limited by rapid digestion and the inactivation of bioactive components such as methylglyoxal. Cyclodextrins are naturally occurring glucose rings that improve stability and bioactivity of products. This study investigates the tolerability and bioactivity of -cyclodextrin-complexed Manuka honey called Manuka Honey with CycloPower ™.

Methods: The antibacterial properties of Manuka honey complexed with -cyclodextrin (Manuka honey with Cyclopower™) were compared to uncomplexed Manuka honey against a range of common organisms using standard measurements of minimum inhibitory (MIC) and bactericidal (MBC) concentrations. Time course growth measurements were determined using a sublethal concentration of 2% w (honey solids)/v and measuring the area under the growth curve.

Results: In tube MIC assays, Manuka honey completely inhibited *Staphylococcus aureus* (MSSA and MRSA), *Streptococcus pyogenes*, *Helicobacter pylori* and *Moraxella catarrhalis* at concentrations of 10% w/v or less, with MIC values decreasing as the methylglyoxal content of the honeys increased from 100 to 550 mg/kg. MIC values at a given methlyglyoxal level were also decreased for *S. pyogenes, M. catarrhalis* and *H. pylori* by complexing the Manuka honey with -cyclodextrin. *Pseudomonas aeruginosa* was not inhibited by any of the Manuka honey or Cyclopower treatments at the concentrations tested (2-10% w/v). Manuka honey with Cyclopower™ had an increased bacteriostatic action against *S. aureus,* MRSA and *P. aeruginosa* compared with Manuka honey.

Conclusions: This study concludes that Manuka honey is an effective antibacterial agent that can be enhanced by complexing with -cyclodextrin.

Keywords: Manuka honey, methylglyoxal, -cyclodextrin, antimicrobial

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A comparison of the gene expression profiles and pathway network analyses after treatment of Prostate cancer cell lines with different *Ganoderma lucidum* based extracts

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ABSTRACT

Background: *Ganoderma lucidum* is a type of fungus commonly consumed in Asia for the promotion of health and longevity. The observed biological activity of *G. lucidum* includes anti-cancer and anti-inflammatory effects which may be useful in the treatment and prevention of cancer and other chronic diseases. *G. lucidum* grows under conditions which range from tropical to temperate and has a different physiology depending on the geographical region in which it is grown. For this reason, the health benefits may vary depending on the form of *G. lucidum* and the environmental conditions to which it was exposed. This led us to investigate the effect of wildly grown *G. lucidum,* from the Himalayan region versus other commercially available *G. lucidum* products, on two human cancer cell lines.

Methods: Extraction of the bioactive components found in *G. lucidum* is essential, as the fungus is tough and indigestible. Four different Ganoderma extracts were prepared. Thereafter, the extracts were tested on two human prostate cancer cell lines, and the IC_{50}s were determined. This was followed by the use of Affymetrix GeneChip® PrimeView™ Human Gene Expression Arrays to identify the changes in gene expression due to the treatment of prostate cancer cell lines (PC3 and DU145) with Ganoderma extracts. Several key genes identified with Affymetrix analysis were validated using RT-PCR.

Results and Discussion: We found that all the Ganoderma extracts showed growth inhibition in the cancer cell lines tested. Using Affymetrix microarray analysis, we identified four main biologically active pathways: cell cycle control/apoptosis, cell-cell adhesion, DNA repair, and inflammatory /immune response, where activity was influenced by the Ganoderma extracts used. Using RT-PCR, we tested ten genes associated with all four pathways. The RT-PCR results supported our findings in the Affymetrix analysis, i.e. that *G. lucidum* extracts have an anti-inflammatory and cell cycle effect and therefore may have long term health benefits. These effects were specific to the extract tested.

Key Words*: Ganoderma lucidum,* PC3, DU145, gene expression, Affymetrix, pathways, RT-PCR

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In vitro regulation of enzymes of the renin-angiotensin-aldosterone system by isoquercitrin, phloridzin and their long chain fatty acid derivatives

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ABSTRACT

Background: Hypertension is a crucial risk factor for development of cardiovascular and neurological diseases. Flavonoids exhibit a wide range of biological effects and have had increased interest as a dietary approach for the prevention or possible treatment of hypertension. However, continuous efforts have been made to structurally modify natural flavonoids with the hope of improving their biological activities. One of the methods used for the possible enhancement of flavonoid efficacy is enzymatic esterification of flavonoids with fatty acids.

Objective: The current study is designed to investigate the antihypertensive activity of isoquercitrin (quercetin-3-*O*-glucoside, Q3G) and phloridzin (PZ) in comparison to their twelve long chain fatty acid derivatives via enzymatic inhibition of renin angiotensin aldosterone system (RAAS) enzymes.

Methods: The novel flavonoid esters were synthesized by the acylation of isoquercitrin and phloridzin with long chain unsaturated and saturated fatty acids (C_{18}–C_{22}). These acylated products were then tested for their *in vitro* angiotensin converting enzyme (ACE), renin and aldosterone synthase activities.

Results: The linoleic and α-linolenic acid esters of PZ were the strongest (IC_{50} 69.9-70.9 µM) while Q3G and PZ (IC_{50} >200 µM) were the weakest renin inhibitors *in vitro* ($p \leq 0.05$). The eicosapentaenoic acid ester of PZ (IC_{50} 16.0 µM) was the strongest inhibitor of ACE, while PZ (IC_{50} 124.0 µM) was the weakest inhibitor ($p \leq 0.05$) among all tested compounds. However, all investigated compounds had low (5.0-11.9%) or no effect on aldosterone synthase inhibition ($p \leq 0.05$). The parent compound Q3G and the eicosapentaenoic acid ester of PZ emerged as the strongest ACE inhibitors.

Conclusions: The structural modification of Q3G and PZ significantly improved their antihypertensive activities. The potential use of PZ derivatives as natural health products to treat hypertension needs to be further evaluated.

Keywords: hypertension, phloridzin, isoquercitrin, flavonoids, ACE, renin, RAAS, acylation, fatty acids

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Comparison of nitrogen bioaccessibility from salmon and whey protein hydrolysates using a human gastrointestinal model (TIM-1)

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ABSTRACT

Background: The TIM-1 system is a computer-controlled multi-compartmental dynamic model that closely simulates *in vivo* gastrointestinal tract digestion in humans. During digestion, the compounds released from meal matrix by gastric and intestinal secretions (enzymes) are progressively absorbed through semipermeable membranes depending on their molecular weight. These absorbed (dialysed) compounds are considered as bioaccessible, which means that they can be theoretically absorbed by the small intestine in the body.

Methods: Salmon protein hydrolysate (SPH), whey protein hydrolysates extensively (WPH- High) or weakly (WPH-Low) hydrolysed, non-hydrolysed whey protein isolate (WPI) and mixtures of WPI:SPH (90:10, 80:20) were digested in TIM-1 using the conditions for a fast gastrointestinal transit that simulate the digestion of a liquid meal in human adults. During digestion (2 hours), samples were collected in intestinal compartments (duodenum, jejunum, and ileum) and in both jejunal and ileal dialysates to determine their nitrogen content. All the products were compared in terms of kinetics of nitrogen absorption through the semipermeable membranes (bioaccessible nitrogen) and nitrogen distribution throughout the intestinal compartments at the end of the 2 hour digestion.

Results: After a 2 h-digestion in TIM-1, SPH was the protein substrate from which the highest amount of nitrogen (67.0%) becomes available for the small intestine absorption. WPH-High had the second highest amount (56.0%) of bioaccessible nitrogen while this amount decreased to 38.5–42.2% for the other protein substrates. The high nitrogen bioaccessibility of SPH is consistent with its richness in low molecular weight peptides (50% < 1000 Da).

Conclusions: The results of this study indicate that SPH provides a higher proportion of bioaccessible nitrogen to a healthy adult compared to all forms of whey proteins, including extensively hydrolysed whey protein hydrolysate. The substitution of non-hydrolysed WPI by small amounts of SPH (10–20%) improved slightly its nitrogen bioaccessibility, making the mixture particularly suitable for applications such as medical foods that require rapid protein uptake and where the use of extensively hydrolysed whey protein is unfeasible due to its undesirable organoleptic properties.

Keywords: Salmon protein hydrolysate, Whey protein, Nitrogen bioaccessibility, TIM-1

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^{14}C-Psilocin tissue distribution in pregnant rats after intravenous administration

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ABSTRACT

Background: Many species of hallucinogenic mushrooms have been found in the genus *Psilocybe*. The main psychoactive chemicals of *Psilocybe* mushrooms are psilocin and its phosphoryloxy derivative, psilocybin. In addition to its psychedelic effects, psilocybin is an effective agent to lift the mood of depressed patients with terminal cancers.

Objective: To study the dispositional kinetics of ^{14}C-psilocin in pregnant rats after intravenous injection, to calculate tissue dose surrogates *i.e*., tissue ^{14}C concentration and area under the concentration-time curve using the experimental data, to quantify trans-placental passage of psilocin and/or its metabolites, and to identify new psilocin metabolite(s) in rat urine.

Methods: A group of 15 pregnant Wistar rats weighing between 0.30-0.36 kg was used in the study. Each rat was given a single dose of 7.5 mg/kg ^{14}C-psilocin *i.v.* Three rats were randomly selected and sacrificed at 0.5, 1.0, 2.0, 4.0, and 8.0 hr post-dosing. The maternal and fetal tissues were quickly removed and the radioactivity in these tissues determined by liquid scintillation counting.
In a separate study, urine samples were collected from 6 male Wistar rats after administering
15 mg/kg of unlabeled psilocin *i.p*. The urine samples were collected and extracted by chloroform-methanol (9:1 v/v) and analyzed using a gas chromatograph/mass spectrometer.

Results: ^{14}C-Psilocin crossed the placental barrier of pregnant rats readily after *i.v.* administration; maternal tissue ^{14}C concentrations were found to be much higher than those in fetal tissues. The areas under the curve for maternal tissues also were much higher than the fetal tissues. In general, maternal tissues could be divided into the fast eliminating organ group, which included the brain (elimination half-life <13 hr) and the slow eliminating organ group, which included all fetal tissues (elimination half-life >13 hr). A new psilocin metabolite tentatively identified as dihydroxyindoleacetic acid was found in the urine.

Conclusion: Our study showed that psilocin readily crossed the placental and blood-brain barriers of pregnant rats. Because psilocin was eliminated slowly from the fetal tissues of rats, human consumption of magic mushrooms should be avoided during pregnancy.

Key words: magic mushrooms, psilocin, placental barrier, pregnant rats

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/9/26

N-alkylamides: from plant to brain

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ABSTRACT

Background: Plant *N*-alkylamides (NAAs) are bio-active compounds with a broad functional spectrum. In order to reach their pharmacodynamic targets, they have to overcome several barriers of the body in the absorption phase. The permeability kinetics of spilanthol (a diene NAA) and pellitorine (a triene NAA) across these barriers (*i.e.* skin, oral/gut mucosa, blood- brain barrier) were investigated.

Methods: The skin and oral mucosa permeability were investigated using human skin and pig mucosa in an *ex vivo in vitro* Franz diffusion cell set-up. The gut absorption characteristics were examined using the *in vitro* Caco-2 cell monolayer test system. The initial blood-brain barrier transport kinetics were investigated in an *in vivo* mice model using multiple time regression and efflux experiments. Quantification of both NAAs was conducted using HPLC-UV and bio- analytical UPLC-MS methods.

Results: We demonstrated that spilanthol and pellitorine are able to penetrate the skin after topical administration. It is likely that spilanthol and pellitorine can pass the endothelial gut as they easily pass the Caco-2 cells in the monolayer model. It has been shown that spilanthol also crosses the oral mucosa as well as the blood-brain barrier.

Conclusion: It was demonstrated that NAAs pass various physiological barriers *i.e.* the skin, oral and gut mucosa, and after having reached the systemic circulation, also the blood-brain barrier. As such, NAAs are cosmenutriceuticals which can be active in the brain.

Key words: Plant *N*-alkylamides, pharmacokinetics, mucosa/skin, blood-brain barrier (BBB), cosmenutriceuticals

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Polyunsaturated fatty acids in the treatment of attention deficit hyperactivity disorder

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ABSTRACT

Background: Attention deficit/hyperactivity disorder (ADHD) is one of the most common behavioral disorders in children. Insufficient dietary intake of long-chain polyunsaturated fatty acids (LC-PUFAs) has been suggested to have an impact on the development of symptoms of ADHD in children. Individuals with ADHD have been demonstrated to have significantly reduced blood concentrations of PUFAs and, in particular, reduced levels of omega-3 (n-3) PUFAs. These findings suggest that PUFA supplementation may reduce the attention and behavior problems associated with ADHD.

Objective: To provide an overview of the efficacy of dietary LC-PUFA supplementation in the treatment of ADHD.

Methods: Literature published up until December 2013 on the effects of n-3 PUFA supplementation on ADHD symptoms was obtained using a PubMed search and critically reviewed.

Results: Dietary PUFA supplementation appears to have beneficial effects on ADHD symptoms although these effects are small. The clinical relevance of these observations remains to be determined.

Conclusion: There is only limited support for the efficacy of PUFA supplementation for the core symptoms of ADHD. Given the small effect sizes regarding PUFA supplementation, it may not be a sufficient therapy for a majority of patients with ADHD.

Keywords: diet, nutrition, polyunsaturated fatty acid, PUFA, attention deficit/hyperactivity disorder, ADHD

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“Weak direct” and “Strong indirect” interactions are the mode of action of food factors

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Summary

Age-dependent and lifestyle related diseases such as metabolic syndromes have become a social problem worldwide. Since these disorders are closely related to dietary lifestyle, the old saying “foods are medicine” is now being re-evaluated. Thus, dietary protection against these diseases is attracting much attention. As research into functional foods advances, a book of knowledge is being accumulated on the active ingredients, termed “food factors”, present in food resources. Identifying such molecules usually follows the conventional methodology used for finding drug candidates from natural resources. The question has arisen as to whether the mode of action of food factors as molecules is the same as that of drugs. In this article, the functional properties of food factors and drugs are comparatively reviewed and the characteristic features of food factor function is discussed, based on the idea of “weak direct” and “strong indirect” actions of food factors to their receptors.

Keywords: Food factor; Functional models; Weak direct interaction; Strong indirect interaction; Ligand-receptor interaction

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Efficacy and safety of *Citrus sudachi* peel in obese adults: A randomized, double-blind, pilot study

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ABSTRACT

Objective: This study was undertaken to explore the efficacy and safety of *Citrus sudachi* peel for metabolic risk factors in obese male and female adults.

Background: *Citrus sudachi* Hort. ex Shirai (Rutaceae), called “sudachi”, is a small, round, green citrus fruit that is mainly cultivated in Tokushima Prefecture in Japan. Our group reported that *Citrus sudachi* peel powder improved glucose tolerance and dyslipidemia in Zucher-fatty rats and reduced hyperglycemia and hypertriglyceridemia in GK diabetic rats.

Materials and Methods: We conducted a randomized, double-blind, placebo-controlled trial in 40 participants with abdominal obesity and metabolic risk factors including hypertension, impaired glucose tolerance and elevated triglyceride levels. Participants were randomized to receive either tablets that contained 1.3 g dried *Citrus sudachi* peel powder or placebo tablets for 12 weeks. The sudachi peel group included 14 males and 5 females with a mean age of 54.5 years, and the placebo group included 18 males and 2 females with a mean age of 51.9 years.

Results: Physical status including body weight, waist circumference and blood pressure and laboratory markers including metabolic parameters were not different at any observation point between the two groups. However, among participants with serum triglyceride levels of more than 120 mg/dl, body weight, waist circumference and serum triglyceride levels were significantly decreased at several observation points after the start of treatment in the sudachi peel group but not in the placebo group. No serious adverse events were observed in the sudachi peel group.

Conclusions: *Citrus sudachi* peel has the potential effect to safely improve abdominal obesity and lower serum levels of TG in obese individuals with hypertriglyceridemia. A large-scale randomized, double-blind clinical study targeting subjects with both abdominal obesity and high TG levels is needed to confirm the metabolic effects of

Citrus sudachi peel.

Trial registration: UMIN Clinical Trials Registry (UMIN-CTR) UMIN000002682. Accession number of the Ethics Committee for Clinical Trials of Food in Tokushima University Hospital is F5.

Key words: health functional food, anti-obesity, triglyceride

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The effects of dietary omega-3 polyunsaturated fatty acid supplementation on attention and impulsivity in an animal model of attention deficit/hyperactivity disorder (ADHD)

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ABSTRACT

Background: Attention deficit/hyperactivity disorder (ADHD) is one of the commonest psychiatric disorders in children and adolescents. The main symptoms of ADHD are hyperactivity, inattention and impulsivity. Both etiology and neurobiological basis of ADHD are unknown. In this context, long-chain polyunsaturated fatty acids (LC-PUFAs), especially omega-3 (n-3) PUFAs, have become a focus of interest. The symptoms of ADHD have been suggested to be associated with a deficiency of n-3 PUFAs. In addition, the impact of a supply of dietary n-3 PUFAs in the treatment of ADHD has frequently been discussed.

Objective: The aim of the present study was to examine the influence of n-3 PUFA supplementation on attention and impulsivity in the spontaneously hypertensive rat (SHR) which has been proposed to be a valid genetic animal model of ADHD.

Methods: Seven-week-old male SHRs were randomly divided into two groups of 15 rats and fed one of two experimental diets (n-3 PUFA-enriched or n-3 PUFA-deficient) prior to and during behavioral testing. Attention and impulsivity were assessed using a three-choice- serial-reaction-time-task (3CSRTT) which is based on the five-choice-serial-reaction-time- task. The experiment was performed with three-month-old rats.

Results: Our findings demonstrate a marked difference between groups regarding impulsivity but not attention. The n-3 PUFA-enriched diet significantly reduced impulsivity in SHRs compared with rats fed with the n-3 PUFA-deficient diet.

Conclusion: The present data show a decrease in impulsivity following a dietary n-3 PUFA supplementation, but no changes in attention. A possible explanation for these results is that the attention displayed by SHR may not be linked to n-3 PUFA supply. It is important to note that inattention and impulsiveness are two of the main symptoms of ADHD. Our results regarding dietary n-3 PUFA supply may support the positive findings in human studies demonstrating that n-3 PUFA administration can improve the cognitive or behavioral symptoms in children with ADHD.

Key words: omega-3 polyunsaturated fatty acid, animal model, spontaneously hypertensive rat, attention, impulsivity, attention deficit/hyperactivity disorder

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Probiotics as regulators of inflammation: A review

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ABSTRACT

A substantial and increasing body of clinical evidence supports the role of specific strains and mixtures of probiotics in the prevention and treatment of certain diseases. Several general mechanisms of action have been proposed, including supporting repair of hyperpermeable epithelial barriers, interfering with infection by pathogens, and restoring a healthful balance of commensal microbes to affect metabolism. Emerging evidence supports an additional role of probiotics as important modulators of immune system responses, including inflammation, at mucosal surfaces. In particular, by preventing or repairing 'leaky' epithelial barriers, probiotics can indirectly affect the inflammatory response by negating the source of pro-inflammatory stimuli associated with low-grade endotoxemia. They also enhance production of short chain fatty acids with anti-inflammatory properties (e.g. butyrate) as well as increase synthesis of antimicrobial peptides that influence inflammation resolution pathways in the mucosa. Furthermore, probiotics and some of their secreted metabolic products can act as ligands for innate immune system receptors, directly influencing key pro-inflammatory pathways. They also stimulate the differentiation and activity of important immune cells (e.g., dendritic cells, T cells), and subsequently increase production of important regulatory cytokines, including interleukin-10 (IL-10) and transforming growth factor-beta (TGF-□□. Finally, there are limited but increasing animal studies and clinical trials demonstrating probiotics do affect common biomarkers of inflammation, including C-reactive protein, as well as signs and symptoms of the associated diseases suggesting they can have therapeutic benefit in the treatment of chronic inflammatory disease.

Keywords: probiotics, inflammation, endotoxemia, epithelial, cytokines, immune, butyrate, antimicrobial peptides

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Turmeric and Chinese goldthread synergistically inhibit prostate cancer cell proliferation and NF-kB signaling

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ABSTRACT

Background: Pre-clinical studies using bioactive compounds from botanicals appear to offer some protection against cancer. Research using single bioactives contributes greatly to our understanding of their mechanism of action, but *in vitro* studies demand concentrations that are higher than achievable in humans (µM). However, maintaining these bioactives in the presence of other compounds originally derived from the food or extract of origin may synergistically lower the bioactive dose so translatability becomes feasible. The objective of this study was to determine if bio-efficacy of phytonutrients can be enhanced when used in combination even at doses that are ineffective for any compound when used in isolation.

Methods: The anti-proliferative and molecular effects of herbs (turmeric and Chinese goldthread) and their bioactives (curcumin and *ar*-turmerone, berberine and coptisine, respectively) were determined in isolation and in combination. Using CWR22Rv1 and HEK293 cells, cell proliferation (as assessed by the MTT assay) and NF-κB promoter activity (using a luciferase reporter construct) were evaluated and synergy of action was assessed by the Chou- Talalay method utilizing CompuSyn® software.

Results: Turmeric and Chinese goldthread act synergistically (combination index<1) when inhibiting cell proliferation with all cell lines tested. The synergy of action of combinations of companion bioactives from the same herb (i.e., curcumin/*ar*-turmerone and berberine/coptisine) and bioactives from different herbs (i.e., curcumin/berberine) help to explain why turmeric and Chinese goldthread are more effective than their major bioactives in isolation. At the molecule level, curcumin+*ar*-turmerone and curcumin+coptisine synergistically attenuated TNFα- stimulated NF-κB promoter activity. Even compounds with poor efficacy become more biologically active in the presence of companion compounds. Importantly, the effects of combining any two bioactives or herbal extracts were highly synergistic at concentrations approaching physiological significance (nanomolar).

Conclusions: These results suggest that bioactives in combination (as plant extracts or isolated compounds) are highly synergistic at the cellular and molecular level at physiologically relevant concentrations. These data help to explain why complex mixtures of botanicals may be more efficacious than their bioactives in isolation.

Keywords: Synergy; Chou-Talalay; turmeric; Chinese goldthread; curcumin; berberine; *ar*- turmerone; coptisine; prostate cancer; NF-κB

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/1/2

Effects of clear kefir on biomolecular aspects of glycemic status of type 2 diabetes mellitus (T2DM) patients in Bandung, West Java [study on human blood glucose, c peptide and insulin]

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ABSTRACT

Background: Diabetes Mellitus (DM) triggers an excessive reaction of free-radicals. It increases reactive oxygen species and reduces antioxidants status as well as the β cell damage. Clear kefir was used for DM therapies, however it limited biomolecular exploration of its bioactive roles. Research aimed to investigate the effects of clear kefir on the biomolecular nature of the glycemic status of T2DM in Bandung.

Methods: The randomized pretest-posttest control group was conducted by 106 T2DM patients. Research was done in several hospitals in Bandung and Cimahi, West Java from 2012–2013. Samples were divided randomly into three groups: (1) T2DM with HbA_{1c} < 7 was fed a standard diet, supplemented with 200 ml/day of clear kefir, (2) T2DM with HbA_{1c} > 7 fed standard diet and supplemented 200 ml/day by clear kefir, (3) T2DM with HbA_{1c} was fed a standard diet as a control group. Dose response was obtained from a preeliminary vivo study, and then converted to human dosage by year 2011. Intervention was effectively done for 30 days. HbA_{1c} was measured by HPLC. Fasting blood glucose (FBG) and Postprandial blood glucose levels (PBG) were measured by enzymes levels. C Peptide and insulin were measured by Elisa. Data was analyzed by a statictics programme by significance p<0,05. Study was approved by ethic committee.

Results: HbA_{1c} was significantly reduced in delta level (p<0.01) and FBG (p<0.015) among kefir groups. PBG was not significantly reduced among groups. C-Peptide was significantly increased in delta level, except in control group (p<0.014). Insulin was reduced significantly, except in control group (p<0.003).

Conclusions: Supplementation of clear kefir reduced blood glucose levels (HbA_{1c}, FBG, PBG) and increased c-peptide. Clear kefir's biomolecular mechanisms and chemistry characterization is a challenge for future studies.

Keywords: Diabetes melitus, hyperglicemia, clear kefir, insulin, c peptide

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Evidence-based modeling of mode-of-action for functional ingredients influencing Alzheimer's disease through neurotrophin pathway

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ABSTRACT

Background*:* Brain-derived neurotrophic factor (BDNF) is the most widely expressed member of the neurotrophin family in the human brain and is crucially involved in the development of neural circuits, modulation of synaptic plasticity, and regulation of cognitive functions, including learning and memory. Many studies have shown the association of altered BDNF levels with neurodegenerative and neuropsychiatric disorders. However, BDNF is not able to cross the blood-brain barrier and, thus, its delivery to the nervous system is a challenge. Therefore, functional diets with the ability to induce production of BDNF in the brain may offer an alternative route. The objective of this study was three-fold: first, to find out diets that are causally linked to the agonistic activity of BDNF in the neurotrophin signaling pathway; second and mainly, to investigate mode-of-action of these functional diets through systems-based mechanistic modeling in the context of Alzheimer's disease; and third, to demonstrate the proof-of-concept application of systems biology methods, that are well established in the pharmaceutical sector, to the emerging field of functional food.

Methods: In the first step, two cause-and-effect models of BDNF signaling in two states, i.e. normal state and Alzheimer's disease state, were constructed using published knowledge in scientific literature and pathway databases. A "differential model analysis" between the two states was performed by which mechanistic mode-of-action of BDNF in neurotrophin signaling pathway could be explained with a high molecular resolution in both normal and disease states. The BDNF mode-of-action model was further validated using the "biomarker- guided validation" approach. In the second step, scientific evidence on the effect of various functional diets on BDNF levels and BDNF-related biological processes or outcomes was harvested from biomedical literature using a disease-specific semantic search. This information was then added to the mechanistic model of BDNF mode-of-action and used to substantiate the mode-of-action model.

Results: The differential model analysis resulted in a mechanistic mode-of-action model for

the effector BDNF signaling pathway through NTRK receptors (Neurotrophic tyrosine kinase receptor type 2) in neurons. The model revealed an amyloid-mediated neurotrophin switch mechanism by which the amyloid-beta protein competitively blocks BDNF-NTRK2 downstream signaling under Alzheimer's conditions, thereby "switching" the entire pathway from its normal state with neuroprotective effect to the disease state with a strong push towards neuron apoptosis. This hypothetical switch mechanism was validated by expressed biomarkers as well as empirical data obtained from experimentation of BDNF mimetics in animal models. Several functional diets were found in the literature that showed agonistic effects on the effector BDNF pathway. These effects are exerted through increased levels of BDNF and subsequently, activating the BDNF survival pathway, which leads to similar

observations that have been made with BDNF mimetics in animal models.

Conclusions: To our knowledge, this is the first study to investigate mode-of-action of functional foods using systems-based modeling approaches. Moreover, such models can answer the question how functional diets can possibly act at the molecular level and interfere with the disease mechanism. Using scientific evidence supporting such models, there is a possibility to introduce new functional formulations by combining functional ingredients of these diets.

Keywords: evidence-based modeling, mode-of-action, functional ingredient, BDNF, Alzheimer's disease

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Characterization and specificity of probiotics to prevent *salmonella* infection in mice

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ABSTRACT

Background: Probiotic strains of bacteria can prevent *Salmonella* from causing disease by preventing the pathogen from colonizing the intestines. Two strains of probiotics, *Lactobacillus acidophilius* and *Pediococcus spp,* that were obtained from poultry fecal samples have been shown to be efficacious in poultry. The objective of this study was to determine if these strains of probiotics could prevent salmonellosis in a mouse model.

Methods: First, both strains of probiotics were evaluated for *in vitro* efficacy to inhibit the growth of and interfere with virulence gene regulation in *Salmonella enterica*. For *in vivo* efficacy, mice was used which models Typhoid illness. Mice were divided into 2 groups: Control and treatment, *Lactobacillus* and *Pediococcus* (LP; 10^8 Log CFU). Two experiments were conducted. In the first experiment, the mice were treated with *LP* in water for the first two days of the experiment and challenged with *Salmonella* at day three. In the second experiment, the *LP* treatment was given in the water for 10 days and challenge was performed on day 11. In both experiments, at day 20 post-challenge, all mice were sacrificed, intestinal tracts and organs removed and cultured for *Salmonella*.

Results: The probiotic strains inhibited the growth of *Salmonella* and down-regulation of virulence genes was noted, but dependent on the strain of *Salmonella* being evaluated. For the *in vivo* experiment, the probiotics did not afford the mice protection from infection and increasing the length of time the probiotics were administered did not improve the efficacy of the probiotics.

Conclusions: It appears that these strains of probiotic bacteria are effective against *Salmonella in vitro.* However, these isolates did not afford protection from *Salmonella* infection to mice which may be due to host specifity as these isolates were obtained from poultry.

Keywords: *Salmonella,* Probiotic, *Lactobacillus, Pediococcus,* Mice

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Gluten-free and casein-free diets in the treatment of autism

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ABSTRACT

Background: Autism is a complex psychiatric disorder characterized by three core symptoms, i.e. impairments in social interaction, restricted patterns of behavior and impairments in communication. In the framework of the "opioid excess theory", the disorder symptoms are compared to the behavioral effects of opiates. Based on this, a possible nutritional basis of autism has been proposed, hypothesizing that certain food proteins such as gluten and casein can be transformed to opioid peptides during digestion. These peptides might eventually be able to enter the blood stream and act upon the central nervous system. As a consequence, a diet low in such proteins has been hypothesized to ameliorate the behavioral symptoms of autistic children.

Objective: The scope of this review was to analyze the effects of gluten-free and casein-free (GFCF) diets on children with autism, as well as to provide information concerning additional aspects related to the GFCF diet in autism.

Methods: A literature search was conducted including scientific publications up until December 2013. Search results were screened for any kind of GFCF dietary intervention as well as surveys dealing with GFCF as a treatment for autism.

Results: A review of survey data shows that up to 25 % of parents of affected children report on current use of a GFCF diet. The majority of identified studies evaluating GFCF diet outcomes failed to meet basic methodological standards of interventional science. Comparison of study results did not show any clear-cut results, with a substantial proportion of studies failing to show any positive dietary effect. The results of more sophisticated trials were far from equivocal and the studies differed by many methodological aspects. Some variables such as information source and trial duration seemed to affect outcome.
Conclusions: Evidence for the effectiveness of the GFCF diet in the treatment of autism is sparse. Rigorous scientific evaluations partly failed to confirm therapeutic effects of the GFCF diet. These and other negative results related to the opioid excess theory weaken the underlying rationale for GFCF diet use. Nevertheless, more sophisticated investigations should be conducted in order to identify possible benefits and harms of such a dietary approach.

Key words: gluten-free and casein-free diet, opioid excess theory, autism, autistic spectrum disorder, therapeutic effects, evidence base, prevalence of use

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In-vitro screening of acetylcholinesterase inhibitory activity of extracts from Palestinian indigenous flora in relation to the treatment of Alzheimer's disease

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ABSTRACT

Background: Cholinesterase inhibitory therapy serves as a strategy for the treatment of Alzheimer's disease (AD). Several acetylcholinesterase inhibitors (AChEIs) are used for the symptomatic treatment of AD. These compounds have been reported to have adverse effects, including gastrointestinal disturbances.

This study was therefore partly aimed at investigating *in vitro* possible AChEIs in herbal medicines traditionally used in Palestine to treat cognitive disorders, and to point out the role of these plants as potential sources for development of newly potent and safe natural therapeutic agents of AD. Assay of AChE activity plays an important role *in vitro* characterization of drugs including potential treatments for AD. The most widely used method, is based on Ellman's method. The reactant used in this method shows chemical reactivity with oxime antidots and thiol leading to false positive reactions. A new alternative assay could be of high interest.

Methods: The effect on AChE activity of 92 extracts of 47 medicinal plants were evaluated using a new micro-well plate AChE activity (NA-FB) and Ellman's assays. In addition, antioxidant activity using DPPH was determined.

Results: The main advantages of the new method (NA-FB) is that the colorimetric change is better observable visually allowing spectrophotometric as well as colorimetric assay, and does not show any chemical reactivity with thiol. 67.4% and 37% of extracts inhibited AChE by $\geq$50% using the NA-FB and Ellman's assays, respectively. Using NA-FB assay, 84 extracts interacted reversibly with the enzyme, of which *Mentha spicata* (94.8%), *Foeniculum vulgare* (89.81), and *Oxalis pes-caprae* (89.21) were most potent, and 8 showed irreversible inhibition of which leaves of *Lupinus pilosus* (92.02%) were most active. Antioxidant activity was demonstrated by 73 extracts *Majorana* syriaca (IC_{50} 0.21mg/ml), and *Rosmarinus officinalis* (0.38) were the most active.

Conclusions: NA-FB assay has shown to be simple, accurate, sensitive, spectrophotometric and colorimetric, and superior to Ellman's, and therefore can be used efficiently for qualitative and quantitative studies of AChEI activities of extracts. Palestinian flora have shown to be a rich source for, new and promising agents (AChEIs) for the treatment of AD Further studies are needed to isolate and identify the active compounds responsible for AChEI activities.

Keywords: Alzheimer's disease, ACh, medicinal plants, *β*-naphthyl acetate, micro-well plate AChE activity Assay (NA-FB)

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Safety test of a supplement, 5-aminolevulinic acid phosphate with sodium ferrous citrate, in diabetic patients treated with oral hypoglycemic agents

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ABSTRACT

Objective: This study aimed to examine the safety of 5-aminolevulinic acid phosphate (5-ALA) with sodium ferrous citrate (SFC) in diabetic patients treated with one or more oral hypoglycemic agents (OHAs).

Background: Recent intervention studies performed in the USA and Japan have shown that a nutritional supplement of 5-ALA with SFC efficiently reduced blood glucose levels in pre-diabetic population without any adverse events. Thus, it was anticipated that 5-ALA with SFC may potentially be taken as a beneficial supplement by diabetic patients who were being treated with OHA therapy. Nevertheless, it is important to examine its safety and efficacy in diabetic population.

Methods: This study was a prospective single-blinded, randomized, placebo-controlled and parallel-group comparison study. Medically treated diabetic patients between the ages of 30 and 75 were recruited from the Tokyo metropolitan area of Japan and 45 subjects were selected after screening. These subjects were randomly assigned to three groups: daily intake of 15mg 5-ALA, 50mg 5-ALA, and a placebo (n=15, respectively). The supplement or placebo was administered for 12 weeks followed by a four week washout period. The primary endpoint was safety and occurrence of hypoglycemic attack, while the secondary endpoint was changes of fasting blood glucose (FBG) and hemoglobin A1c (HbA1c).

Results: Adverse events related to 5-ALA with SFC were not observed in all the groups. Abnormalities in blood and urine tests were not observed either. Significant decrease in FBG was not detected in all the groups. However, there was a small but significant decrease in HbA1c at 4 and 8 week in the 15 mg 5-ALA group. Significant decrease in HbA1c was not observed in the 50 mg 5-ALA group, although a tendency to decrease after 4 weeks was apparent.

Conclusion: 5-ALA with SFC is a safe and potentially beneficial supplement if taken by diabetic patients treated with OHAs.

Trial registration: UMIN 000008038

Key words: type 2 diabetes, 5-aminolevulinic acid (5-ALA), sodium ferrous citrate (SFC), oral hypoglycemic agent (OHA), hemoglobin A1c (HbA1c), fasting blood glucose (FBG)

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Uses of *Justicia spicigera* in medicine and as a source of pigments

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ABSTRACT

Justicia spicigera (muicle) is a plant that has been used from the pre-Hispanic era to contemporary times in Mexico. It has been used in the traditional medicine for healing diseases such as dysentery, diabetes, leukemia, and anemia, just to mention some human disorders. It has been used for obtaining indigo dye after making extraction with water to be used for coloring of baskets, crafts, and clothes. The pigments, as a powder, have been studied for use for coloring foods. The dyeing characteristics of the *J. spicigera* pigments have antioxidant properties due to the flavonoids content. Since this plant has been used for making infusions to people for curing some physical disorders, today *J. spicigera* is being studied to take advance of its dyeing and antioxidant properties to be used in the food and pharmaceutical industries.

Key words: *Justicia spicigera* (muicle), antioxidants, traditional medicine, pigments for foods, indigo, phytochemicals

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Effects of fisetin on mouse lipid metabolism in vitro and in vivo

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ABSTRACT

Objective: The aim of this study was to investigate the anti-obesity effects of the polyphenol fisetin in 3T3-L1 preadipocytes and C57BL/6 female mice that were fed a high-fat diet (HFD).

Background: Polyphenols, such as sakuranetin, hesperetin, tea catechin, and quercetin, reportedly regulate adipocyte differentiation in 3T3-L1 cells. Furthermore, green tea, apple, and molokheiya polyphenols exhibit anti-obesity activities in HFD-treated obese rats or mice. Fisetin is abundant in plants, fruits, and vegetables and exhibits multiple biological activities, such as the inhibition of prostate cancer growth, neuroprotection, and protection against osteoporosis. In addition, fisetin regulates obesity by targeting mammalian target of rapamycin complex 1 signaling, which is a central mediator of lipid biosynthesis.

Materials and methods: (1) *in vitro* experiments; we investigated the effects of fisetin on intracellular lipid accumulation and glycerol-3-phosphate activity during the differentiation of 3T3-L1 cells. We monitored expression of adipogenetic related-genes in 3T3-L1 cells by real-time polymerase-chain-reaction. (2) *in vivo* experiments; we examined the effects of fisetin on anti-obesity activities in C57BL/6 female mice that were fed an HFD.

Results: Fisetin inhibited intracellular lipid accumulation and glycerol-3-phosphate activity during the differentiation of 3T3-L1 cells in a dose-dependent manner (50-75 □M). In addition, real-time polymerase-chain-reaction revealed that this compound suppressed the expression of peroxisome proliferator-activated receptor γ (PPARγ), adipocyte protein 2, and perilipin mRNAs in 3T3-L1 cells. In contrast, anti-obesity activities, such as reduction of body weight and fat tissue, and improvements in obesity-related blood biochemical parameters and fatty liver, were not observed in HFD-induced mice treated with fisetin (20 mg/kg body weight) by intraperitoneal injections twice per week for 8 weeks.

Conclusions: Fisetin exerted anti-adipogenic activities by inhibiting the expression of PPARγ mRNA in 3T3-L1 preadipocytes. However, fisetin (20 mg/kg body weight) did not affect HFD-induced obesity. Our findings indicated that fisetin could be used as an effective remedy in the treatment of the symptoms of obesity.

Keywords: Fisetin, MC3T3-L1 cells, Fatty accumulation, PPARγ, Obesity, Anti-obesity activity

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Evaluation of flaxseed effects on non-alcoholic fatty liver disease (NAFLD) in rabbits submitted to a hypercholesterolemic diet

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ABSTRACT

Background: The aim of the present study is to evaluate the role of flaxseed in non-alcoholic fatty liver disease, as well as on the lipid profile in rabbits submitted to hypercholesterolemic diet.

Subject and Methods: 32 male rabbits, weighing approximately 1.5kg and averaging four months of age, were distributed into three groups. Group 1 received standard food plus 0.5% of cholesterol from dried egg, during 8 weeks. Group 2 obtained the same diet in the first 4 weeks, and 8mg/kg of ground flaxseed was added in the remaining weeks. Lastly, group 3 was fed with the previous group's increased diet throughout the entire period. In the follow-up, the animals were euthanized, and liver blades were prepared to evaluate the histopathologic study. The evaluation score of NAFLD (ESN), as well as plasma levels of total cholesterol, LDL- cholesterol, HDL-cholesterol, triglycerides and body weight, were all determined.

Results: Increased levels of total cholesterol were obtained in both groups, with the smallest variation found in G3 (p=0.002). This variation was also found when the levels of LDL- cholesterol were assessed (p=0.001). There was a reduction of triglyceride levels at the end of the study in G3 (p=0.008). A variation was noticed between the ESN groups, but the induced reduction was not statistically significant.

Conclusion: Further studies are necessary, in order to elucidate the effects of flaxseed in NAFLD as well as in diseases that have risk factors for the development of the disease.

Keywords: non-alcoholic fatty liver disease, flaxseed, experimental study, functional food

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Bioactive proteins against pathogenic and spoilage bacteria

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ABSTRACT

Background: It is likely that both human nutrition and the nutrition of livestock are benefited by the presence of bioactive proteins within their respective diet regimes. Bioactive proteins have been defined as specific protein fragments that positively impact bodily functions or conditions and may, ultimately, influence overall human health. The ingestion of bioactive proteins may have an effect on the major body systems—namely, the cardiovascular, digestive, immune and nervous systems. According to their functional properties, bioactive proteins may be classified as antimicrobial, antithrombotic, antihypertensive, opioid, immune-modulatory, mineral binding and anti-oxidative. There are many examples of biologically active food proteins and active peptides that can be obtained from various food protein sources. They have a physiological significance beyond the pure nutritional requirements; in other wordsthey have the acquisition of nitrogen for normal growth and maintenance.

Objective: This study aims to specify and characterize the extent and mode of action of bioactive proteins in their native form, (glycinin, glycinin basic sub-unit and β-conglycinin) against specific main pathogens (*Listeria monocytogenes*, *Escherichia coli* O157:H7 and *Salmonella enterica serovar Enteritidis*). We will be using standard media while identifying the main constituents responsible for this action.

Methods: Glycinin, basic sub-unit and β-conglycinin were isolated from soybean protein and tested for their antimicrobial action against pathogenic and spoilage bacteria, They were thencompared to the properties of penicillin. Methylated soybean protein and also methylated chickpea protein (MSP and MCP), with isoelectric points around pI 8, were prepared by esterifying. 83 % of their free carboxyl groups and their interactions with Gram positive and Gram negative bacteria were examined.

Results: The three divisions of cationic proteins exhibited antibacterial activities equivalent to or higher than the activity of penicillin, with the basic sub-unit exhibiting the highest activity, followed by glycinin.; β-conglycinin exhibited the lowest level of activity with a MIC of 50, 100 and 1000 µg/mL, respectively. The $IC_{50\%}$ values of the basic subunit, glycinin and β-conglycinin, against *Listeria monocytogenes,* were 15, 16 and 695 µg/mL; against *Bacillus subtilis* the values were 17, 20, and 612 µg/mL; and against *Salmonella Enteritidis* the values were 18, 21 and 526 µg/mL, respectively. Transmission electron microscopy images of *L. monocytogenes* and *S. Enteritidis* exhibited an increase in cell size and a separation of the cell wall from the cell membrane when treated with glycinin or basic sub-unit. The scanning electron microscopy of *B. subtilis* indicated signs of an irregular, wrinkled outer surface as well as the fragmentation, adhesion, and aggregation of damaged cells or cellular debris when treated with glycinin or the basic subunits; however not with penicillin. The proliferation of *L. monocytogenes*, *S. Enteritidis* and *Escherichia coli* O157:H7-when artificially inoculated in raw milk ,stored at 4 or 25 °C) was significantly ($P<0{\cdot}05$) reduced by the glycinin sub-unit and nisin (0·5% w/v); but they were only slightly reduced by β-conglycinin and

moderately reduced by lysozyme. The two substances (MSP and MCP) exhibited a concentration-dependent inhibitory action against two of the studied bacteria with a minimum inhibitory concentration of approximately 100 µg/mL. The supplementation of raw milk with esterified legume proteins (MSP and MCP) has significantly ($p < 0.05$) reduced the levels of TBC, PBC and PSC in raw milk stored at a temperature of 4 °C. This potentially will delaythe onset of spoilage of by four days.

Conclusion: Both glycinin and the basic sub-unit have a more swift antimicrobial action than that of penicillin. Basic sub-units exhibited the highest efficiency at killing bacterial cells, followed by glycinin, penicillin and β-conglycinin- with the lowest effect; while the bacteria most susceptible to the antimicrobial agents were shown to be *L. monocytogenes*, followed by *B. Subtilis* and *S. Enteritidis*- with the lowest susceptibility. The antibacterial action of glycinin was similar to the effects exerted by nisin, and was much more effective than lysozyme. The modified legume proteins have general antibacterial properties against both spoilage and pathogenic bacteria in raw milk preserved under refrigeration or at room temperature.

Keywords: bioactive proteins, pathogenic and spoilage bacteria

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The effect of industrial processing of salmon oil on its ability to reduce serum concentrations of oxidized low-density lipoprotein- β2-glycoprotein-I complex in a mouse model

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ABSTRACT

Background: Circulating serum levels of oxidized low-density lipoprotein, β2-glycoprotein I complex (oxLDL-GP), have been previously correlated with adverse cardiovascular events and have been shown to be reduced by consumption of enzymatically liberated extra virgin salmon oil (EVSO). This mouse study measured the changes in the oxLDL-GP lowering effect when consuming EVSO with varying levels of EPA+DHA (eicosapentenoic acid and docosahexenoic acid) as well as when consuming EVSO that was subjected to various processing treatments commonly carried out during fish oil production.

Methods: Sprague Dawley mice were fed a diet containing eight different EVSO's incorporated into a normal diet at the Human Equivalent Dose (HED) of 1000 mg for 8 weeks. Serum was collected at the start and at the end of the trial and the oxLDL-GP concentrations were measured using an ELISA assay. Statistical analysis of the results was carried out using a 1-tail, paired Student t-Test.

Results: In order to lower circulatory oxLDL-GP levels, the mice had to consume a minimum of 80 mg per day HED of EPA+DHA. Heat treatment of the EVSO did not affect this bioactivity but hydrolysis with acid or base and re-esterification to the triglyceride form or significant oxidation (rancidity) rendered the oil inactive on this important cardio-vascular disease (CVD) biomarker.

Conclusions: This result shows that harsh processing conditions on fish oils can lead to the destruction of biological efficacy in spite of increasing the concentration of typical fish oil bioactive constituents such as EPA+DHA. It also lends support to the developing nutrition theory that eating highly-refined, processed or concentrated-ingredient supplements derived from functional foods may not be able to reproduce their full nutritive and health-benefiting effects.

Keywords: Oxidized-LDL; processing; Salmon; Oil; omega-3; rancidity

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/157/411

Flavonol-enriched fraction from *Vaccinium macrocarpon* fruit inhibits matrix metalloproteinase-2, matrix metalloproteinase-9 and urokinase-type plasminogen activator expression in human prostate cancer cells *in vitro*

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ABSTRACT

Background: Prostate cancer, amongst other cancer types has a genetic and environmental component, which can contribute to prostate cancer development and progression. *Vaccinum macrocarpon* (American cranberry) is a botanical that contains several phytochemicals which have been suggested to play a role in preventing cardiovascular disease, cancer, and urinary tract infections as well as in the maintenance of oral health.

Context and purpose of this study: This investigation evaluated the effects of a flavonol- enriched fraction (FL) from the American cranberry (*Vaccinium macrocarpon*) containing quercetin and myricetin glycosides on matrix metalloproteinase (MMP) and urokinase-type plasminogen activator (uPA) activities and their associated regulatory proteins in DU145 human prostate cancer cells *in vitro.*

Results: A flavonol-enriched fraction (FL) was prepared from *Vaccinium macrocarpon* berries and the effect of this fraction on prostate cancer cell behaviour was assessed using biochemical and molecular approaches including cytotoxicity assays and Western blot analysis to determine protein expression. Cranberry FL decreased cellular viability of DU145 cells at a concentration of 25 ug/ml by 20% after 6 hours of treatment. Further investigations determined that associated with this cytotoxicity, cranberry FL decreases matrix metalloproteinase (MMP) (specifically MMP-2 and MMP-9) activity and urokinase plasminogen activator (uPA) activity through effects on specific temporal MMP regulators and uPA regulators and by affecting either the phosphorylation status and/or expression of specific MAP kinase, PI-3 kinase, NF-kB and AP-1 pathway associated proteins.

Conclusion: This study demonstrates, for the first time, the ability of *Vaccinium macrocarpon* flavonols to modulate cellular pathways associated with migration, invasion, and proliferation, suggesting that cranberry (*Vaccinium macrocarpon*) is a viable candidate for further research as a natural product that may protect against certain cancers.

Key Words: *Vaccinium macrocarpon*, matrix metalloproteinases, urokinase, anti-cancer activity

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Rose hip *(Rosa canina L)*: A functional food perspective

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ABSTRACT

Rose hip (*Rosa canina L*.) is the pseudo-fruit of the rose plant, which is widely known as a valuable source of polyphenols and vitamin C. Both *in vivo* and *in vitro* studies have demonstrated that this fruit exhibits anti-inflammatory, antioxidant, and antiobesogenic activities. The health benefits of Rose hip (RH) have been attributed to its wide range of bioactive compounds including the anti-inflammatory galactolipid: (2S)-1,2-di-O-[(9Z,12Z,15Z)-octadeca-9,12,15-trienoyl]-3-O- β-D-galactopyranosyl glycerol (GOPO), vitamin C, phenolics, lycopene, lutein, zeaxanthin, and other carotenoids. As cyclooxygenase inhibitors, RH compounds may reduce the risk of cancer, heart disease, and various inflammatory conditions. The aim of this review is to present an overview of the functional, medical, and physiological properties of RH.

Keywords: *Rosa canina,* Rose hip, antioxidant, anti-inflammatory, GOPO, lycopene, and vitamin C

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Nrf2 activation as a future target of therapy for chronic diseases

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ABSTRACT

Chronic inflammation integrally related to oxidative stress has been increasingly recognized as a contributing factor in various chronic diseases such as neurodegenerative diseases, pulmonary diseases, metabolic syndrome, and cardiovascular diseases as well as premature aging. Thus, inhibiting this vicious circle has the potential to delay, prevent progression, and treat those diseases. However, adverse effects of current anti-inflammatory drugs and the failure of exogenous antioxidant encourage scientists to develop new therapeutic alternatives.

The nuclear factor E2-related factor 2 (Nrf2) is the transcription factor that is responsible for the expression of antioxidant response element (ARE)-regulated genes and have been described as having many therapeutic effects. In this review, we have discussed the role of oxidative stress in various chronic diseases. Furthermore, we have also explored various novel ways to activate Nrf2 either directly or indirectly, which may have therapeutic potential in attenuating oxidative stress, inflammation and mitochondrial dysfunction that contributes to chronic diseases.

Keywords: Oxidative stress, Mitochondria, Inflammation, Nrf2, Nutrition, Chronic diseases

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Formulation and characterization of novel functional beverages with antioxidant and anti-acetylcholinesterase activities

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ABSTRACT

Background: Nowadays, there is increased consumer demand for high-antioxidant foods. Drinking high-antioxidant beverages may help to protect against aging, Alzheimer's disease, and other chronic diseases. Grapes and some plants including *Phyllanthus emblica*, *Terminalia chebula*, *Kaempferia parviflora*, *Centella asiatica*, *Nelumbo nucifera*, *Rauvolfia serpentina*, *Ginkgo biloba*, *Crocus sativus*, *Clitoria ternatea* and others are well-known to possess antioxidant, neuroprotective and other health-promoting activities. Thus, it is possible to use these plants for the development of new functional beverages.

Methods: Ten formulations of beverages were produced. The 5 non-alcoholic beverages contained dried medicinal plants, fresh grapes and others and are as follows: beverage B1: 10.2% *K. parviflora* rhizomes, 5.1% brown sugar and 84.7% water; beverage B2: 0.45% *Ardisia polycephala* leaves, 0.45% *C. asiatica* leaves, 0.36% *C. ternatea* flowers, 0.45% *C. sativus* pollens, 0.45% *G. biloba* leaves, 0.45% *Melodorum fruticosum* flowers, 0.90% *N. nucifera* petals, 0.45% *Nymphaea lotus* petals, 5.43% crystalline sugar and 90.58% water; beverage B3: 0.62% *A. polycephala* fruits, 0.35% *C. ternatea* flowers, 0.44% *G. biloba* leaves, 2.64% *K. parviflora* rhizomes, 1.76% *P. emblica* fruits, 0.88% *T. chebula* fruits, 5.28% brown sugar and 88.03% water; beverage B4: 0.51% *Acorus calamus* stems, 0.68% *C. ternatea* flowers, 4.23% *K. parviflora* rhizomes, 0.85% *N. nucifera* petals, 0.85% *N. lotus* petals, 0.85% *M. fruticosum* flowers, 0.34% *R. serpentina* roots, 0.34% *U. gambir*, 1.69% *Zingiber officinale* rhizomes, 5.08% brown sugar and 84.60% water; beverage B5: 53.09% fresh grapes, 2.65% brown sugar and 44.25% water. After heating, filtering, and cooling, these beverages were put in sterile bottles. One part of each beverage was stored at 4□C for 23 weeks before analyzing, but the other two parts were used to prepare the alcoholic beverage of each formulation. Grapes were mixed with the beverages B1, B2, B3, B4 and B5 in the ratio of 60:40 to prepare alcoholic beverages W1, W2, W3, W4 and W5, respectively. Two different fermentation conditions (fermentation with or without pieces of sliced medicinal plant residue, PMPR) were compared. After fermenting, racking and aging, all alcoholic beverages, as well as all non-alcoholic beverages, were analyzed for some phytochemical properties.

Results: Grape fermented with PMPR had higher anti-acetylcholinesterase and antioxidant activities, and total phenolics, flavonoids and tannins, compared to the others. Among all non- alcoholic beverages, the beverage B3 contained the highest anti-acetylcholinesterase (22.78% inhibition at 1:10,000 dilution) and antioxidant activities (reducing capacity, 4.22 mmol Fe(II)/100 mL), total phenolics, flavonoids, and tannins (494.44 mg gallic acid equivalents) (GAE)), 383.22 mg catechin equivalents (CE) and 338.29 mg tannic acid equivalents ((TAE)/100 mL, respectively). Among all alcoholic beverages, the beverage W3 (fermented with PMPR) exhibited the highest antioxidant activity (DPPH radical inhibition, 95.99 mg trolox equivalents and reducing capacity, 3.57 mmol Fe(II) /100 mL), total phenolics, flavonoids and tannins (239.71 mg GAE, 372.67 mg CE and 157.67 mg TAE/100 mL,

respectively). The beverage W2 (fermented with PMPR) had the highest anti-acetylcholinesterase activity (21.35% inhibition at 1:10,000 dilution).

Conclusion: The beverages B3, W2 and W3 contained valuable sources of natural antioxidants and acetylcholinesterase inhibitors, and may provide health benefits when consumed.

Keywords: medicinal plant, wine, grape, anti-Alzheimer's disease, antioxidant

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Magnolol affects cellular proliferation, polyamine biosynthesis and catabolism-linked protein expression and associated cellular signaling pathways in human prostate cancer cells *in vitro*

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ABSTRACT

Background: Prostate cancer is the most commonly diagnosed form of cancer in men in Canada and the United States. Both genetic and environmental factors contribute to the development and progression of many cancers, including prostate cancer.

Context and purpose of this study: This study investigated the effects of magnolol, a compound found in the roots and bark of the magnolia tree *Magnolia officinalis*, on cellular proliferation and proliferation-linked activities of PC3 human prostate cancer cells *in vitro*.

Results: PC3 cells exposed to magnolol at a concentration of 80 µM for 6 hours exhibited decreased protein expression of ornithine decarboxylase, a key regulator in polyamine biosynthesis, as well as affecting the expression of other proteins involved in polyamine biosynthesis and catabolism. Furthermore, protein expression of the R2 subunit of ribonucleotide reductase, a key regulatory protein associated with DNA synthesis, was significantly decreased. Finally, the MAPK (mitogen-activated protein kinase), PI3K (phosphatidylinositol 3-kinase), NFκB (nuclear factor of kappa-light-chain-enhancer of activated B cells) and AP-1 (activator protein 1) cellular signaling pathways were assayed to determine which, if any, of these pathways magnolol exposure would alter. Protein expressions of p-JNK-1 and c-jun were significantly increased while p-p38, JNK-1/2, PI3Kp85, p-PI3Kp85, p-Akt, NFκBp65, p-IκBα and IκBα protein expressions were significantly decreased.

Conclusions: These alterations further support the anti-proliferative effects of magnolol on PC3 human prostate cancer cells *in vitro* and suggest that magnolol may have potential as a novel anti-prostate cancer agent.

Key Words: prostate cancer cells, magnolol, polyamines, MAPK, PI3K, NFκB

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Protein hydrolysates and recovery of muscle damage following eccentric exercise

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ABSTRACT

Background: A whey protein hydrolysate (NatraBoost XR; WPH_{NB}) has been shown to speed repair muscle damage. We sought to determine whether this benefit is specific to this hydrolysate to evaluate a marker for quality control.

Methods: Three hydrolysates of the same whey protein isolate (WPI) were prepared (WPH_{NB}, WPH_1 and WPH_2). Isometric knee extensor strength was measured in 39 sedentary male participants before and after 100 maximal eccentric contractions of the knee extensors to induce muscle damage. Participants were then randomised to consume 250 ml of flavoured water (FW, n=9), or 250 ml of FW containing 25 g of either NatraBoost XR (n=3), WPH_1 (n=9), WPH_2 (n=9) or WPI (n=9). Strength was reassessed over the next seven days while the supplements were consumed daily. Fibroblasts were cultured for 48 hr in the presence of the different hydrolysates, WPI, saline or fetal bovine serum to ascertain effects on cell proliferation.

Results: Strength was reduced in all treatment groups after eccentric exercise ($P<0.001$). Strength recovered steadily over 7 days in the FW, WPI, WPH_1 and WPH_2 treatment groups ($P<0.001$), with no difference between treatments ($P=0.87$). WPH_{NB} promoted faster strength recovery compared with the other treatments ($P<0.001$). Fibroblast proliferation was greater with WPH_{NB} compared with saline, WPI or the other hydrolysates ($P<0.001$).

Conclusions: Promoting recovery from muscle damage seems unique to WPH_{NB}. *In vitro* fibroblast proliferation may be a useful marker for quality control. It is not clear whether effects on fibroblast proliferation contribute to the *in vivo* effect of WPH_{NB} on muscle damage.

Keywords: tissue repair, fibroblast proliferation, strength recovery, whey protein

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Secretion of angiopoietin-like 4 protein from intestinal cells

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ABSTRACT

Background: Angiopoietin-like 4 (ANGPTL4) has been suggested to play a role in lipid metabolism as a regulatory protein of lipoprotein lipase activity. Intestinal secretion of ANGPTL4, which is regulated by fatty acids, may inhibit the activity of circulating lipoprotein lipase; but, recent studies suggest that it could also inhibit pancreatic lipase in the gut and thereby reduce intestinal uptake of lipids. Secretion of the ANGPTL4 protein to either the lumen or tissue/blood side of the intestinal epithelial layer would indicate possible modes of action.

Methods: Caco-2 cells were grown on permeable membranes and cultured for 21 days to spontaneously differentiate into an intact monolayer of intestinal cells, mimicking the epithelial cell layer lining the intestinal wall. Cells were treated with 9 mM butyrate and the time dependent gene expression and protein secretion to the apical and basolateral side was analysed over a time-course of 24 hours. Possible feedback from ANGPTL4 protein was investigated by adding 0.25 ng/ml recombinant ANGPTL4 protein to culture media.

Results: Butyrate-induced *ANGPTL4* gene expression increased in Caco-2 cells after 2 hours, reaching a plateau of approximately 6 fold after 6-24 hours, while the ANGPTL4 protein secretion to both the apical and basolateral sides was increased 18-24 hours after stimulation. A negative feedback on apical and basolateral secretion was observed in the presence of recombinant ANGPTL4 on the apical and basolateral sides, respectively.

Conclusion: The present study indicates that, upon exposure to butyrate, the monolayer of epithelial cells secretes the ANGPTL4 protein to both the tissue/blood (basolateral) side and the luminal (apical) side of the monolayer which, in an *in vivo* situation, may be interpreted as potential inhibition of both the circulating and pancreatic lipase.

Keywords: Angiopoietin-like 4, Caco-2, Permeable membrane, Protein, Secretion, Intestine, Negative feedback.

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9-*cis* β-carotene inhibits atherosclerosis development in female LDLR-/- Mice

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ABSTRACT

Background: Several epidemiological studies have shown that diets rich in carotenoids are associated with a reduced risk of cardiovascular disease. However, administration of synthetic all-*trans* β-carotene was reported to have no effect on cardiovascular disease. We previously showed that the 9-*cis* β-carotene-rich powder of the alga *Dunaliella bardawil* inhibits atherogenesis and reduces plasma non-HDL cholesterol levels in mice.

Context and purpose of this study: We sought to study whether isolated 9-*cis* β-carotene inhibits atherogenesis in a murine model of atherosclerosis.

Results: Twelve-week-old female LDL receptor knockout mice (LDLR-/-) were pretreated for 2 weeks with regular chow diet fortified with the alga *Dunaliella* powder, 9-*cis* β-carotene isomer, all-*trans* β-carotene isomer, or 9-*cis* retinoic acid, followed by 10 weeks of a high-fat diet with the same fortifications. In contrast to *Dunaliella*, 9-*cis* β-carotene did not inhibit the high fat diet- induced elevation of plasma cholesterol. In addition, diet fortification with *Dunaliella* powder, β- carotene isomers, or 9-*cis* retinoic acid did not change the plasma retinol or retinoic acid levels. Nevertheless, 9-*cis* β-carotene significantly inhibited atherogenesis compared to the control mice (39% reduction).

Conclusions: The results suggest that 9-*cis* β-carotene should be considered as an anti- atherogenic agent in the human diet.

Key words: Atherosclerosis, *Dunaliella*, 9CBC, LDLR-/- mice

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European health claims for small and medium-sized companies – Utopian dream or future reality?

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ABSTRACT

Background: In December 2007, the European Regulation (EC) 1924/2006 on nutrition and health claims came into force. The European Union wanted to regulate the use of health claims on products. An online survey was carried out to evaluate the situation, particularly of small and medium-sized companies, dealing with the new regulation.

Methods: The online survey on health claims was conducted with 16 enterprises. To underline the findings a SWOT (Strength, Weaknesses, Opportunities, Threats) analysis was made of the nutrition and health claims regulation regarding small and medium-sized companies in the European food and drink market.

Results: The findings of this study indicated that the European Union did a step in the right direction. Most companies defined the decent competition, the simplified trade within the inner-European market, and the consumer protection as positive aspects. The biggest threat is seen in false investment conditioned by the limited research and development budgets, especially of small and medium-sized enterprises, and the cost intensive scientific evaluation to reach an authorized health claim.

Conclusions: Overall, there are several strengths and opportunities speaking for SMEs and health claims in the near future. The most promising ones are the publishing of the new European Union Register of Nutrition and Health Claims and the learning effects that will occur. The biggest threat is, and will remain to be, false investment and the possible loss of a lot of money. Nevertheless, health claims for small and medium-sized enterprises will inevitably be the future to keep the European food and drink market competitive.

Keywords: health claims, European Legislation, SME

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Water-soluble low-molecular-weight β-(1, 3–1, 6) D-Glucan inhibit cedar pollinosis

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ABSTRACT

Background: The incidence of allergic diseases such as allergic rhinitis, atopic dermatitis, asthma, and food allergies has increased in several countries. Mast cells have critical roles in various biologic processes related to allergic diseases. Mast cells express the high-affinity receptor for immunoglobulin (Ig) E on their surface. The interaction of multivalent antigens with surface-bound IgE causes the secretion of granule-stored mediators, as well as the *de novo* synthesis of cytokines. Those mediators and cytokines proceed the allergic diseases. We investigated the effects of water-soluble, low-molecular-weight β-(1, 3–1, 6) D-glucan isolated from *Aureobasidium pullulans* 1A1 strain black yeast (LMW-β-glucan) on mast cell-mediated anaphylactic reactions. We reported that LMW-β-glucan dose-dependently inhibited the degranulation of mast cells. Furthermore, we found that orally administered LMW-β-glucan inhibited the IgE-mediated passive cutaneous anaphylaxis (PCA) reaction in mice. Here, we examined if LMW-β-glucan had effects on Japanese cedar pollinosis.

Findings: In a clinical study, a randomized, single-blind, placebo-controlled, parallel group study in 65 subjects (aged 22−62) was performed. This study was undertaken 3 weeks before and until the end of the cedar pollen season. During the study, all subjects consumed one bottle of placebo or LMW-β-glucan daily and all subjects were required to record allergic symptoms in a diary. The LMW-β-glucan group had a significantly lower prevalence of sneezing, nose-blowing, tears, and hindrance to the activities of daily living than the placebo group.

Conclusions: These results suggested that LMW-β-glucan could be an effective treatment for allergic diseases.

Key Words: Mast cell, Anti-allergy, β-glucan, Cedar pollinosis

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Bioactive compounds in potatoes: Accumulation under drought stress conditions

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ABSTRACT

Background: Potato (*Solanum tuberosum*) is a valuable source of bioactive compounds. Besides starch, crude fibre, amino acids (AAS), vitamins and minerals, the tubers contain diverse phenolic compounds. These phenolics and AAS confer anti-oxidant protection against reactive oxygen species, tissue damage, and diseases like atherosclerosis, renal failure, diabetes mellitus, and cancer. Climate change and drought stress may become a major risk for crop production worldwide, resulting in reduced access for those who depend on the nutritional value of this staple crop.

Objective: The aim of this study is to determine the effect of drought stress on water, lipid soluble antioxidants, anthocyanins (Ac), soluble phenols, proteins, free AAS, peroxidase (POD) and lipid acyl hydrolase activity (LAH) in tuber tissue.

Methods: The study was carried out on three potato genotypes comprising one yellow-fleshed cultivar and two purple breeding clones. The plants were grown in pots (from April to September) in a glasshouse with sufficient water supply and under drought stress conditions. After harvest, the tubers of both variants were analysed for antioxidants measured as ascorbic acid (ACE) and Trolox equivalent (TXE) using a photo-chemiluminescent method. Amounts of anthocyanins (Ac), soluble phenols, proteins, as well as POD and LAH activities were analysed using a UV photometer. Finally, free AAS were measured by HPLC.

Results: The results revealed that drought stress significantly reduces tuber yield, but has no significant effect on antioxidants, Ac, soluble phenols and POD. Drought stress significantly increased the levels of soluble protein ($P < 0.0001$) and LAH ($P < 0.001$). Also, total amounts of free AAS were higher in the drought stressed tubers (+34.2%, on average) than in the tubers grown with a sufficient water supply. Above all, proline was elevated due to drought stress.

Key words: anthocyanins, antioxidants, free amino acids, phenols, proteins, tuber quality

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Structural basis for bitter taste receptor activation and its potential role in targeting diabetes

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ABSTRACT

Background: Taste receptors are G protein-coupled receptors that, besides being present in the taste buds, have also been shown to be present in the gastrointestinal (GI) system, respiratory system, and brain, though their function at these locations is not well understood.

Objective: To understand the nutrient mediated release of gut peptides like GLP-1 from enteroendocrine L-cells of the GI system, we focused on a bitter taste receptor TAS2R38 (based on animal models) to investigate the structural basis of its potential role in the release of gut peptides.

Methods: The atomic-level structure of bitter taste receptor TAS2R38 was predicted using GEnSeMBLE, a first-principle based GPCR structure prediction method. These structures were obtained for the dominant taster haplotype (PAV) as well as for the nontaster haplotype (AVI) of the receptor. The known ligands phenylthiocarbamide (PTC) and 6-n-propylthiouracil (PTU) were docked to these structures to provide a structural basis for the taster and nontaster haplotypes.

Results: Docking of known ligands PTU and PTC to taster and nontaster haplotypes of the bitter taste receptor showed a backbone hydrogen bond to residue 262 in taster but not in nontaster haplotype, suggesting a potential mode of action of these molecules in the activation of the bitter taste receptor.

Conclusion: These results, combined with the ability of PTC to release gut peptides from *in vitro* models of the enteroendocrine L-cells, suggest a potential structural basis for TAS2R38 activation that can lead to the release of those peptides. This release has a therapeutic benefit for type 2 diabetes and implies a role for bitter tasting (but safe) natural compounds targeting TAS2R38 as potential drug candidates for curing type 2 diabetes.

Key words: TAS2R38, GLP-1 release, PYY release, CCK release, enteroendocrine L cell, GPCR, protein structure prediction, GEnSeMBLE

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Vitamin C: optimal dosages, supplementation and use in disease prevention

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ABSTRACT

The importance of vitamin C as a way to prevent scurvy has been known for centuries. More recent research on vitamin C has expanded beyond scurvy prevention, providing promising evidence for additional health benefits and clinical applications. This review of scientific literature will evaluate many aspects of vitamin C including deficient versus optimal blood plasma levels, adequate daily amounts necessary to maintain ideal levels, and the safety of higher doses. It will also focus on the importance of vitamin C as a powerful bioactive compound, and its utilization in the prevention and management of different chronic diseases. This review is necessary to express the importance of alternative healthcare methods in both preventative and clinical care. Vitamin C was chosen as a representative of this concept due to its powerful antioxidant capacity, incredibly important physiological implications, and very minimal chance of side-effects. This review focuses on studies involving human participants that address how vitamin C is important for our health.

Keywords: Ascorbic acid, deficiency, disease, dose, health, supplementation, vitamin C

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Blood homocysteine and fasting insulin levels are reduced, and erythrocyte sedimentation rates increased with a glycophospholipid vitamin formulation: a retrospective study in older subjects

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ABSTRACT

Background: Elevations in Homocyteine (Hcys) levels in the blood have been correlated with increased risk for coronary heart disease and stroke, loss of cognition and memory, and other chronic medical conditions.

Objective: A retrospective study was initiated to determine if Hcys levels and other blood markers were altered in subjects taking an oral functional food supplement containing a mixture of phosphoglycolipids (NT Factor®) and vitamins.

Methods: Thirty-five patients (28 females, 7 males, Av. Age=60.7±9.6 years) who had used the functional food Advanced Physician's Formula™ with NTFactor® in tablet form each day were enrolled in a retrospective study on blood chemistry. This retrospective study followed a prospective study on the use of the same supplement to reduce fatigue in patients with chronic fatigue. Participants were patients with chronic fatigue syndrome (myalgic encephalomyelitis) or other fatiguing illnesses. Subjects had blood drawn over a 6-month period, and routine blood testing was performed. In this laboratory study, the results were analyzed for differences and statistical analyses were performed.

Results: All participants responded in the study and demonstrated an average reduction of 31.8% in Hcys levels (from 10.85±0.42 to 7.40±0.42 µmol/L; t-test, $p<0.001$; Wilcoxon, $p<0.001$). Women responded better than men: women (from 11.06±0.50 to 8.67±0.82 µmol/L, 34.4% reduction, t-test, $p< 0.001$; Wilcoxon, $p<0.001$) versus men (from 10.80±0.51 to 7.01±0.47 µmol/L, 21.6% reduction, t-test, $p< 0.0862$). Differences were also found in fasting insulin levels (from 12.80±3.11 to 5.30±1.77 µIU/mL, 58.6% reduction, t-test, $p<0.005$) and erythrocyte sedimentation rate (ESR). ESR increased from 10.5±2.21 to 20.19±3.20 mm/hr (92.2% increase, t-test, $p<0.0314$; Wilcoxon, $p<0.0154$). Other tests were not significantly different after 6 months of supplement, there were no side effects from the test supplement, and none of the participants had any cardiovascular events during the study.

Conclusions: The test formulation was effective in reducing Hcys and fasting insulin blood levels and increasing ESR rates in older subjects without adverse effects.

Keywords: Lipid Replacement Therapy, NT Factor®, fatigue, homocysteine, blood insulin, erythrocyte sedimentation rate, vitamin B complex

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Anti-atherosclerotic effects of konjac

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ABSTRACT

Definition: The Konjac plant comes from the genus Amorphophallus. Japanese food uses Konjac cake. Konjac contains almost no calories and has a great amount of dietary fiber. Here, we reviewed possible anti-atherosclerotic effects of konjac, using the search Pubmed ®. Konjac ingestion is beneficially associated with obesity, blood pressure, and lipid and glucose metabolism. However, evidence is lacking on the relationship between konjac ingestion and development of atherosclerotic diseases. To better understand the anti-atherosclerotic effects of konjac, future studies will be performed, preferably with larger numbers of subjects.

Keywords: atherosclerosis, body weight, glucose, konjac mannan, low-density lipoprotein-cholesterol

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Effects of taurine intake on serum lipids in young women

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ABSTRACT

Background: Taurine is an abundant amino acid in human cells, promoting ocular and biliary health, which is also used to treat congestive heart failure, hypertension, and hepatitis. Recently, taurine-enriched energy drinks have become popular with young adults, but the effects of taurine on serum lipids in young adults are unknown.

Objective: We studied the influence of oral administration of taurine on serum lipid levels in healthy young women.

Methods: Ten healthy young women with a mean body mass index of 20.0kg/m2, apolipoprotein E (apoE) phenotype 3/3 and normal menstrual cycles participated. Each subject was instructed to orally ingest 1g of taurine powder after each meal (3g/day) in addition to their usual diets during one menstrual cycle. Before and at the end of taurine intake, physical measurements and blood collection were performed in the morning after a 12-h fast, and 3-day weighted dietary records were obtained. Concentrations of serum lipids, apolipoproteins, and fatty acids in the serum phospholipid fraction were measured.

Results: The subjects showed good compliance with taurine intake and none reported adverse effects during the experimental period. After taurine intake, concentrations of total cholesterol, low density lipoprotein cholesterol (LDL-C), free cholesterol, and apolipoprotein B (apoB) increased ($p<0.05$), while phospholipids tended to increase ($p=0.051$). Fatty acids in the serum phospholipid fraction also significantly increased ($p<0.05$). However, triglyceride, remnant-like particle cholesterol, remnant-like particle triglyceride, apoE, the apolipoprotein A-1 (apoA- 1)/apoB ratio and the LDL-C/apoB ratio were unchanged. Furthermore, body weight was significantly increased ($p<0.01$) but did not correlate with changes either in serum lipids or nutrient intakes.

Conclusion: These results suggest that high taurine intake affects lipoprotein metabolism and increases serum lipids in slightly lean young women.

Key words: Taurine, slightly lean young women, serum lipids, remnant lipoprotein, fatty acids of the serum phospholipid fraction.

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Tolerance, bioavailability, and potential cognitive health implications of a distinct aqueous spearmint extract

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ABSTRACT

Background: Cognitive function can decline during the aging process and significantly reduce quality of life. Although a number of interventions have been investigated for cognitive dysfunction, including antioxidants, this prominent health concern warrants further exploration of additional methods to support cognitive health later in life. An aqueous extract from a proprietary spearmint line has been developed which contains a number of antioxidant compounds, including rosmarinic acid, at higher levels than typically found in commercially- bred spearmint. Therefore, this pilot trial assessed the tolerance, bioavailability, and potential cognitive health implications of a proprietary spearmint extract in men and women with self- reported memory impairment.

Methods: Subjects consumed 900 mg/day spearmint extract for 30 days. The sample population (N = 11) was 73% female and 27% male with a mean age of 58.7 ± 1.6 y. Tolerability parameters were assessed at baseline and end of treatment visits. Computerized cognitive function tests were completed, and blood was drawn at pre- and post-dose (0.5 to 4 h) timepoints during baseline and end of treatment visits. Subjective cognition was also assessed at the end of treatment.

Results: Neither serious adverse events nor clinically relevant findings were observed in any tolerability parameters. Plasma vanillic, caffeic, and ferulic acid sulfates, rosmarinic acid, and methyl rosmarinic acid glucuronide were detected in plasma following acute administration of the spearmint extract. Computerized cognitive function scores improved in reasoning (P =0.023) and attention/concentration (P = 0.002) after 30 days of supplementation. After acute administration, subjects had improved attention/concentration in two tests at 2 (P = 0.042 and P = 0.025) and 4 h (P = 0.001 and P = 0.002).

Conclusions: The results from this pilot trial suggest that the spearmint extract, which contains higher rosmarinic acid content relative to extracts from typical commercial lines, was well- tolerated at 900 mg/day. The extract was also bioavailable. Further investigation is warranted regarding its potential for supporting cognitive health.

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Randomized, double-blind, placebo-controlled, crossover study to evaluate the effects of beta-1,3/1,6 glucan on stress associated with daily lifestyle in healthy subjects

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ABSTRACT

Background: Fatigue is attributable to physical and psychological stress. Fatigue is also a common symptom which occurs in both sick and healthy individuals. Although its mechanism of cause is complex, fatigue from stress is known to affect the existing equilibrium of the immune system. However, nutrition, such as beta-1,3/1,6 glucan, has been reported to play an important role in regulating stress and fatigue states, via modulating a weakened immune system. In this study, a popular and healthy beverage in Okinawa, Japan, containing a soluble baker's yeast in black koji vinegar (*Moromisu*), was provided to healthy subjects with a non-strenuous daily lifestyle.

Results: By performing statistical analysis on the results of the Profile of Mood States (POMS) survey, we observed that overall study results (n=14) demonstrated significant differences in fatigue and confusion in the POMS factors.

Conclusions: In this study we confirmed that beta-1,3/1,6 glucan improved some of the factors related to stress and fatigue, as indicated by evaluation of POMS survey results.

Key Words: Beta-1,3/1,6-glucan, vinegar, POMS, stress

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A water-soluble high molecular weight substance isolated from Hyuganatsu orange (*Citrus tamurana*), suspected to be a polysaccharide, inhibits rat osteoclast cell formation

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ABSTRACT

Background: Osteoporosis is detrimental to aged women's health care. We previously reported that Hyuganatsu orange (*Citrus Tamurana*) contains active substances that inhibit osteoclast activities. Prior to conducting a human study, we sought to identify the biological active substance in the Hyuganatsu orange which suppresses osteoclast formation.

Methods: We isolated five fractions from a Hyuganatsu orange extract according to molecular weight. Each fraction was tested to determine its suppressive effect on the formation of osteoclasts in rats. We also used high-performance liquid chromatography (HPLC), infra-red (IR), and ^{1}H and ^{13}C NMR spectroscopy to evaluate its chemical structure. Data was recorded as mean ± standard error of the mean. The Mann-Whitney test was used, and a p-value of <.05 was considered statistically significant.

Results: The highest and lowest molecular weight fractions showed significant suppression activity on rat osteoclast formation ($p < .05$). The lowest molecular weight fraction was identified as hesperidin using thin layer chromatography. Additionally, IR absorption revealed that the highest molecular weight fraction was not a flavonoid. With regard to chemical structure, ^{1}H and ^{13}C NMR spectroscopy suggested that the highest molecular weight fraction had signals compatible with a polysaccharide such as galacturonic acid.

Conclusions: Hyuganatsu orange contains a biological active substance other than hesperidin that may be a polysaccharide and may suppress osteoclast formation.

Key words: *Citrus Tamurana*, TRAP positive cell, Polysaccharides, Rat osteoclast cell, in vitro study

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The effect of extracts of *Irvingia gabonensis* (IGOB131) and *Dichrostachys glomerata* (Dyglomera™) on body weight and lipid parameters of healthy overweight participants

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Running Title: IGOB131 and Dyglomera™ in weight management

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ABSTRACT

Background: Previous work reported the benefits of extracts of 2 Cameroonian spices – *Irvingia gabonensis* and *Dichrostachys glomerata*— on obese people with metabolic syndrome. Considering the physio-metabolic changes that accompany obesity, the present study investigates the effects of these extracts on healthy overweight participants over an 8-week test period.

Methods: The study was an 8 week randomized double-blind, placebo controlled design involving 48 overweight (BMI 26 – 30) participants (27 females and 19 males), divided into 3 groups – placebo, 300 mg *I. gabonensis* extract (IGOB131), or 300 mg *D. glomerata* extract (Dyglomera™). Capsules containing the placebo or the test formulations were administered once daily before the main meal of the day. No major dietary changes or changes in physical activity were demonstrated during the study. Weight and blood lipid parameters were measured at baseline, and at the 4 and 8 weeks interval.

Results: Compared to the placebo group, there were significant ($p<0.05$) reductions in weight of participants in both test groups over the 8 week period. However, these significant changes were not observed in the initial 4 weeks, even though the lipid parameters in the test groups changed significantly ($p<0.05$).

Conclusion: The extracts of *Irvingia gabonensis* and *Dichrostachys glomerata*, at a dose of 300 mg per day, were effective in reducing weight and positively modifying lipid parameters in healthy overweight participants.

Keywords: Overweight, *Dichrostachys*, *Irvingia*, waist-hip circumference, blood lipids.

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The efficacy and safety of a proprietary onion-pumpkin extract (OPtain120) on blood pressure: an open-label study

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ABSTRACT

Background: Nutraceuticals and functional foods are increasingly being used to help manage hypertension. Treatment with either pumpkin or onion can significantly lower systolic and diastolic blood pressure in animal studies. Traditionally, pumpkin has been used to support healthy blood pressure, glucose tolerance and lipid levels. Onion contains high levels of flavonoids, including quercetin, which decreases blood pressure and promotes restoration of healthy endothelial function. However, human trials on these food sources are limited, and the combined effects of pumpkin and onion have not been examined yet.

Objective: We performed an open-label clinical study to evaluate the effects of a proprietary onion-pumpkin extract (OPtain120) on systolic and diastolic blood pressure.

Methods: Healthy adults with systolic blood pressure (SBP) and diastolic blood pressure (DBP) in the elevated range of 140-159 and 80-90 mmHg, respectively, were enrolled in this study. Subjects consumed one capsule of onion-pumpkin extract twice daily for 12 weeks. Daily Home Blood Pressure Measurement (HBPM) was taken upon waking and before bed. Office Blood Pressure Measurement (OBPM) was taken in-clinic at Week 0, 6, and 12.

Results: 52 subjects were screened and 12 were enrolled in the study, with a total of 10 subjects completing the study. Systolic HBPM taken before bed demonstrated a statistically significant reduction from baseline (147.23 mmHg) to Week 12 (138.14 mmHg), representing a reduction of 9.09 mmHg (6.17%, p=0.021). Diastolic HBPM taken before bed demonstrated a decrease of 4.06 mmHg (4.46%, p=0.085), a significant reduction from baseline (91.07 mmHg) at Week 12(87.02 mmHg). Non-statistically significant reductions were seen in the early morning Systolic (3.14%) and Diastolic (2.57%) HBPM and in the Systolic (1.36%) OBPM.

Conclusion: OPtain120 was safely consumed over a 12-week period. OPtain120 appears to be effective in lowering Systolic Blood Pressure at bedtime in healthy individuals with slightly elevated blood pressure. This study suggests that onion-pumpkin extract may aid individuals who manage their cardiovascular risk factors with diet and lifestyle.

Key Words: pumpkin, onion, extract, blood pressure

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A new definition of functional food by FFC: what makes a new definition unique?

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ABSTRACT

Functional food science has gained momentum recently in response to the changing health status of developed countries. As healthcare costs and average life expectancy rise, the public has sought ways to become healthier and develop higher qualities of life. The concept of "functional food" developed as a convenient and inexpensive solution to chronic health problems and is becoming influential in numerous branches of science and policy. Since its conception in 1984, "functional food" changed its meaning per country and culture. The term migrated from Japan to the EU and the United States where it generated profit but bred confusion among experts and non-experts. In this chapter, we review how "functional food" has been defined and redefined over the past 30 years, as well as the benefits of our current definition. The goal of this new definition is to strengthen communication between nutrition scientists, the public, and other groups as well as legitimize functional food science around the world.

Keywords: Functional foods definition; bioactive compounds; biomarkers

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LC-MS determination of L-DOPA concentration in the leaf and flower tissues of six faba bean (*Vicia faba* L.) lines with common and rare flower colors

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ABSTRACT

Background: Parkinson's disease (PD) is the second most common neurodegenerative disorder characterized by the loss of muscle control, which causes trembling of the limbs and head as well as impaired balance. L-DOPA (L-3,4-dihydroxy phenylalanine) is the major ingredient of several prescription drugs used to treat PD. Faba bean (*Vicia faba* L.) is one of the few plant species that is known to produce L-DOPA and has the potential to be developed as a functional food crop for people suffering with PD.

Objective: Aimed to provide needed information for people who want to use faba bean as a natural remedy or functional food to relieve PD symptoms, this study analyzed the variation of L-DOPA concentration in the leaf and flower tissues of six faba bean lines with common and rare flower colors.

Methods: Leaf and flower samples were taken from field grown plants with different flower colors, namely, pink with purple lines and black dots, pure white, brown, and crimson. Samples were freeze-dried and L-DOPA was quantified by a LC-MS system consisting of an ACQUITY UPLC in line with a Synapt G2 HDMS quadrupole time-of-flight mass spectrometer. This experiment was carried out in two consecutive years (2012 and 2013) and the plants used in the second year were grown from the seeds harvested from the plants used in the first year.

Results and Discussion: Our two-year study revealed a high level of variation in L-DOPA concentration for leaf and flower tissues among the six faba bean lines studied. The average L- DOPA concentration based on dry weight (DW) in flowers ranged from 27.8 to 63.5 mg/g and 18.2 to 48.7 mg/g for leaf tissues. There was no significant correlation between L-DOPA concentrations in flowers and leaves. The L-DOPA concentration in flowers and in leaves of the same line varied but was not statistically significant between the two years. Ideally, the genotype with the highest average L-DOPA concentration in both flowers and leaves would be grown as a natural source of this medicinally important molecule. When developing faba bean as a functional food crop for PD patients, a careful selection of genotype seems necessary for exploiting the full potential of this natural remedy.

Conclusions: Faba bean has the potential to be developed as a functional food crop for PD patients. Consumption of young pods and leaves is the most practical means for direct intake or processing of L-DOPA from the faba bean plant. Favorable environmental conditions for growth will optimize L-DOPA yield. Further analysis of the genetic control of L-DOPA synthesis and metabolism will be valuable, with the possibility of developing environmentally

resilient cultivars that can produce desirable amounts of L-DOPA for pharmaceutical use.

Key words: Faba bean, L-DOPA, Parkinson's disease

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Safety and Efficacy of NEXT-II®, a Novel Water-Soluble, Undenatured Type II Collagen in Healthy Human Subjects Suffering from Occasional Knee Joint Pain

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ABSTRACT

Background and aim: Oral administration of a novel water-soluble undenatured type II collagen (NEXT-II®) has been demonstrated to ameliorate the signs and symptoms of rheumatoid arthritis (RA) in animal models. In the present investigation, we conducted a pilot study to examine the efficacy and safety of NEXT-II® in borderline subjects defined as healthy and non-diseased state, but with potential risks in knee joint health.

Method: We employed Western Ontario McMaster Index (WOMAC) score and Visual Analog Scale (VAS) scores to assess the extent of improvement in the knee joints in these volunteers following supplementation of 40 mg NEXT-II® (10 mg as undenatured type II collagen) over a period of 12 weeks.

Result: The results demonstrated that NEXT-II® treatment significantly reduced WOMAC and VAS scores compared to subjects at baseline. Specifically, in the evaluation using VAS, the borderline subjects at resting, walking, and going up and down the stairs revealed significant improvement when compared to the baseline.

Conclusion: The results of the studies demonstrated that NEXT-II® might be an ingredient which is safe and effective in the application of dietary supplement in ameliorating joint pain and symptoms of the borderline subjects without any adverse events.

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Tinospora cordifolia stem supplementation in diabetic dyslipidemia: an open labelled randomized controlled trial

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ABSTRACT

Background: Medicinal plants are powerful health promoting nutritional agents. Among the vast library of medicinal plants Tinospora cordifolia (Willd.) has been meagrely explored. It belongs to the family *Menispermaceae* and is a rich source of alkaloid and terpenes. It has hepatoprotective, antioxidant, immunostimulatory, hyperlipidemic, anticancer and antidiabetic properties. The stem contains berberine, palmatine, tembetarine, magnoflorine, tinosporin, tinocordifolin. The stem starch is highly nutritive and digestive. In modern medicine it is called the magical rejuvenating herb owing to its properties to cure many diseases. The stem contains higher alkaloid content than the leaves because of which it is approved for medicinal usage. With a host of phytochemical properties present in the stem, it may hold potential to manage dyslipidemia and dysglycemia, which otherwise has been proven only in pre-clinical studies.

Objective: To study the impact of tinospora cordifolia stem supplementation on the glycemic and lipemic profile of subjects with diabetic dyslipidemia.

Methods: Type 2 diabetics with dyslipidemia on oral hypoglycemic agents were enrolled. Baseline data on medical history, family history of lifestyle diseases, duration of diabetes diagnosis, drug profile, anthropometric data, dietary data and physical activity data was obtained along with a fasting blood sample for estimating high sensitivity C reactive protein (hs-CRP), hepatic, renal, lipid profile and glycated hemoglobin. The participants were randomized into either of the two groups; intervention group (n=29) received 250mg of encapsulated mature stem of tinospora cordifolia pre meal twice a day along with prescribed dyslipidemic agent and control group (n=30) only on dyslipidemic agents for a period of 60 days. After 60 days all the parameters were re-assessed to analyse the impact of the intervention.

Results: Majority of the subjects in both the arms were in the 50-60 years age bracket with a similar duration of diabetes, disease and drug profile. Tinospora cordifolia supplementation led to a significant decline in waist circumference (94.7 to 94.2cm, P 0.004), hip circumference (99.9 to 9.5cm, P 0.004), waist stature ratio (0.594 to 0.591, P 0.004) and systolic blood pressure (132.6 to 127.1mmHg, P 0.0017) vs. significant decline in hip circumference (100.02 to 99.7cm, P 0.01) and systolic blood pressure (134.5 to 130.1mmHg, P 0.0013) in controls. The intervention brought about a significant decline in hs-CRP (4.6 to 2.8mg/l, P 0.0007) and the prevalence of hs-CRP>3mg/l declined from 65.5% to 37.9% (P 0.037). Renal and hepatic parameters remained in the normal range. Decline in HbA1c, although non-significant, was more evident in the intervention arm (7.7 to 7.5%, P 0.09) than the controls (7.9 to 7.81%, P 0.52). Intervention led to significant reductions in total cholesterol, low density lipoprotein, triglycerides and very low density lipoprotein and among controls too, but of lesser intensity. The

number of dyslipidemic features declined by 28.6% (P 0.0036) in the intervention arm and by 19.4% in controls (P 0.020). The prevalence of metabolic syndrome decreased by 13.73% from 68.9% to 55.17% in the intervention arm and reduced by 6.7% from 56.7% to 50% among controls.

Conclusion: Tinospora cordifolia stem supplementation brought about more evident changes in the lipoprotein fractions, inflammatory markers and metabolic syndrome than the controls.

Keywords: Diabetic dyslipidemia, tinospora cordifolia, lipid profile, metabolic syndrome

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The effects of whey protein, resistant starch and nutrition education on body weight

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ABSTRACT

Background: Obesity is widely recognized as one of the most critical health threats to families and children across the country. Obesity is a very serious health problem for people in Louisiana and especially in African Americans Children with 40.5% in the State classified as either overweight or obese as compared to 41.2% nationally. African American women have the highest rates of being overweight or obese (79.8%) compared to non-Hispanic whites (57.9%). In 2007, African Americans were 1.4 times as likely to be obese as whites. Therefore this study was designed to test the impact of dietary whey protein (WP) and resistant starch (RS) shakes/smoothies on reduction of body fat via increased satiety and increased energy expenditure in African Americans.

Methods: Thirty-three African American males and females aged between 21 and 43 were randomly assigned to two groups (15 controls, and 18 treatments). Twenty-eight (85%) of the participants (13 controls, 15 treatments) completed the study. For a period of 24-weeks, the treatment group consumed WP and RS shakes/smoothies for breakfast and received nutrition education. For the same period, the control group consumed the same shakes/smoothies but with starch powder and received nutrition education. The data was analyzed using SAS version 9.3.

Results: At the end of the 24 week study, the treatment group lost a mean body weight of approximately 6 kg with standard deviation of 8.38 kg ($p < 0.029$). In control group, weight did not differ significantly ($p < 0.209$) between week 0 and 24. In addition, the treatment group exhibited a significant decrease of about 6 cm in waist circumference ($p < 0.023$). There was no significant effect on mean blood pressure in treatment and control group.

Conclusion: The findings from this study suggest that a combination of WP and RS in the form of shakes/smoothies consumed for breakfast along with a nutrition education component may be an effective method in decreasing body weight, waist circumferences and cumulative food intake in African American males and females.

Key words: Whey Protein, Resistant Starch, Obesity, Breakfast shakes, Nutrition education

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/210/415

The effect of VMP35 supplement ingredients encapsulated in a novel Phospholipid Prodosome SK713 SLP nutrient delivery technology observed as a result of changes in properties of live human blood

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ABSTRACT

Background: In North America digestive malfunction in terms of disintegration, dissolution, and absorption of food and nutrients, is a widespread malady. Malabsorption is also an exacerbating factor in most chronic degenerative diseases that might benefit from dietary supplementation. The purpose of this experiment was to evaluate absorption following the sublingual administration of VMP35 SK713 encapsulated nutraceutical formulation.

Method: Changes in peripheral blood smears from 38 subjects were observed using peripheral live blood cell imaging (LBCI) with phase contrast microscopy. Observation of changes in properties of live blood was made and compared to placebo and baseline at five and 30 minutes after administration.

Results: Compared to baseline and control, the VMP35 formulation SK713 SLP technology effected positive changes in the blood. They were demonstrated by morphological, hematological and rheological changes observed five minutes from the intake and were sustained for at least 30 minutes post intake.

Conclusions: These observable changes showed that the SK713 SLP system can make a key contribution to increasing the potential benefits of dietary supplementation for those patients with compromised digestive processes. We encourage additional research on the effects of this novel neutraceutical formulation and delivery system.

Keywords: digestive malfunction live blood cell imaging, peripheral blood smear, cell aggregation, rheology, phospholipids, nutrient encapsulation, multinutrient complex.

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/212/417

Use of lysozyme from chicken egg white as a nitrite replacer in an Italian-type chicken sausage

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ABSTRACT

Background: Sodium or potassium nitrite is widely used as a curing agent in sausages and other cured meat products. Nitrite has strong antimicrobial and antioxidant effects and generates cured meat color. Nitrite, however, can react with secondary or tertiary amines in meat to form carcinogenic, teratogenic and mutagenic N-nitroso compounds. Several findings have been suggested that high consumption of processed meat may increase the risk of cancer, and emphasized that dietary nitrosamines are positively associated with cancer. Lysozyme is one of the major egg proteins that have antimicrobial and antioxidant characteristics. Therefore, lysozyme can be used in meat processing to prevent microbial growth and oxidative degradation in meat products during storage. This study was focused on evaluating the antimicrobial and antioxidant effects of lysozyme extracted from egg white as a replacer of nitrite in a cooked Italian-type chicken sausage.

Methods: Four curing treatments including 100% nitrite (control), 100% lysozyme (treatment 1), 25% nitrite + 75% lysozyme (treatment 2) and 50% nitrite + 50% lysozyme (treatment 3) were used to prepare Italian-type chicken sausage samples. Recipe was developed with 64% meat, 17% binder (bread crumble), 12% ice, 4% vegetable oil, 2% salt, spices 1% (chili, black pepper, cardamom). Prepared samples were cooked in an 80 °C smoke house to a core temperature of 65 °C and cooled in cold water to 20-25 °C subsequently packed in polyethylene and stored in a freezer (-18 °C). The antimicrobial effect lysozyme was tested using *Escherichia coli* and *Salmonella.* The growth of these pathogens at 0, 3 and 5 days of storage of spore inoculation was determined. Antioxidant activity of lysozyme was determined using the TBARS value during the 25 d storage period. The redness (a*), lightness (L*), and yellowness (b*) of sausages were analyzed using a Minolta color meter (CR 410, Konica Minolta Inc., Japan). The proximate composition (AOAC, 2002) of frozen (-18 °C) sausage samples and sensory properties of cooked samples were determined.

Results: 50% nitrite + 50% lysozyme (treatment 3) was as effective as control (100% nitrite) in suppressing the growth of *Escherichia coli, Salmonella* and limiting lipid oxidation in the Italian- type chicken sausage. Treatment 3 was not significantly different from the control for the lightness (L*), redness (a*) and yellowness (b*) values ($P > 0.05$) but showed the best sensory characteristics among the treatments ($p=0.002$). Moisture content of control sample was significantly higher ($p=0.000$) than other treatments while crude protein, crude fat, crude fiber and ash content were not differ significantly. In term of the cost, both treatment 3 and control have shown approximately equal values.

Conclusion: This study demonstrated that lysozyme can be used as an effective nitrite replacer in the Italian-type chicken sausage. Replacing 50% of nitrate salt with 50% lysozyme did not show any negative effects in controlling microbial growth, preventing lipid oxidation, and color changes but improved the sensory characteristics.

Keywords: Italian-type chicken sausage, nitrite, lysozyme, antimicrobial, antioxidant

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Impact of nutritional stress on early embryonic survival

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Running title: Nutritional Stress and Early Embryonic Survival

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ABSTRACT

Low reproductive efficiency is the utmost critical predicament faced by the modern livestock industry across the globe. Early embryonic loss is one of the major causes of poor reproductive efficiency resulting in delayed pregnancy, fewer calves born, reduced milk production, slower genetic progression, and substantial financial loss to the beef and/or dairy industry. The establishment of pregnancy results from the interaction between the embryo and the dam and is the culmination of a series of events initiated with development of the follicle and gametes. Among numerous internal and external factors, nutrition has the potential to alter the microenvironment of the oocyte and the embryo, making it more hostile to optimal fertilization and pre-implantation embryonic growth. Understanding the impact of nutritional stress on oocyte function, embryo development and reciprocal signaling networks between the embryo and uterus will lead to alleviation of the problems associated with early embryonic mortality.

Keywords: Early embryonic loss, establishment of pregnancy, maternal recognition of pregnancy, interferon-tau, progesterone, nutritional stress, oocyte function, embryo development

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Protection of renal function by four selected plant extracts during *Plasmodium berghei* infection

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ABSTRACT

The weakening of renal function from reactive oxygen species, which is generated during malaria infection, is one of the prominent causes of death in prevalent regions throughout the world. The potential toxicity of free radical generated by malaria parasites are counteracted by a large number of cytoprotective phytochemicals. Therefore, this study examined the influence of extracts of five selected antimalarial plants (*Azadirachta indica, Parquetina nigrescens, Citrus paradisi*, and *Khaya senigalensis*) on the reduction of inflammation in renal tissue, blood urea nitrogen, and creatinine levels during malaria infection using *Plasmodium berghei* infected Swiss albino mice. For *in vivo* assay, mice were inoculated with 1×10^7 parasitized erythrocytes and plant extracts were subsequently administered orally at 100 mg/kg body weight once a day for 17 consecutive days. The chemo-suppressive and prophylaxis effects of the plant extracts against *P. berghei* were investigated and compared with those of standard antimalarial drug, chloroquine. Tail bleeding was performed to check the percentage parasitaemia by making a thin film smear on a slide, stained in Giemsa. The numbers of parasited cells against the unparasitised cells were counted using a microscope. The effect of malaria infection on renal tissue was assessed by histological analysis and measurement of blood urea nitrogen and creatinine levels in plasma. At 100 mg/kg per body weight, aqueous extract of *K. senegalensis, A. indica, C. paradisi* and *P. nigrescens* exhibited significant ($p<0.05$) percentage inhibition and chemo-suppressive effects in comparison with the chloroquine treated mice. The results of the untreated group showed that there was a significant ($p<0.05$) increase in the level of plasma urea, while the level of the groups treated with plants extract stabilized the level of urea and creatinine in the blood. Additionally, there was a pathological lesion on the kidney tissue of the untreated group, whereas the group treated with aqueous extract of *A. indica, Khaya senegalensis* and *C. paradisi* showed no lesion. Therefore, it can be assumed that the extracts can protect and preserve renal function during malaria infection. These findings justified the use of the extracts in traditional medicine practice, for the treatment of malaria infection.

Key words: *Plasmodium berghei*, antimalarial plants, renal function, antiplasmodium

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A randomized double-blind study of a green and black tea agent, AssuriTEA®, in healthy male subjects

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Study Design: A double blind, randomized placebo controlled clinical study

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ABSTRACT

Background: Green and black teas have known anti-oxidant and anti-inflammatory properties. The current study was a prospective randomized, double-blind, placebo controlled study of 3 doses of a water-extracted green and black tea agent (AssuriTEA® [AT]).

Methods: Subjects who met inclusion criteria were randomized to one of four groups: 1000, 500, or 250 mg AT or placebo for 28 days. At baseline (BL) and day 28, serum antioxidant capacity, quality of life and safety were assessed.

Results: Of the 55 subjects screened, 43 were considered evaluable. Age was 56.77 ± 2.83 years (mean ± SEM). Evaluable subjects demonstrated improved antioxidant status, as measured by ferric iron reducing antioxidant power at all doses over the placebo ($p < 0.05$). There was significant improvement in cellular antioxidant protection in the 1000 mg AT group versus the placebo ($p=0.032$). Glucose levels were higher in the placebo group versus the 250 mg AT group ($p=0.023$) and there was a significant improvement in systolic blood pressure in the 250 mg AT group at day 28 versus BL ($p=0.048$). In the 1000 mg AT group, there was a significant decrease in systolic blood pressure at day 28 versus BL ($p=0.017$). There was a significant improvement in the vitality category in the 1000 mg AT group ($p=0.029$). Overall, AT was safe and well tolerated with no differences in adverse events or serum chemistries between groups.

Conclusions: Results demonstrate that the administration of AT resulted in improvement of serum antioxidant status, vitality level, blood glucose, and systolic blood pressure in test subjects.

Key Words: Green tea, black tea, *Camellia sinensis*, antioxidant status, blood glucose, systolic blood pressure, and quality of life

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Immune and homeostatic surveillance are positively modulated in cancer- like and cancer conditions by a number of natural products

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ABSTRACT

Endometriosis, a non-lethal cancer-like inflammatory condition, and cancer share many common features. These shared features include the inability of the human body to confront the cause of disease initiation, due to incompetent immune and homeostatic surveillance. Additionally, both diseases can be detected using the same diagnostic tools. Moreover, alternative, non-chemical treatment can be successfully achieved by a number of common substances found in nature that can fortify the human body to combat disease. Therefore, this commentary focuses on and discusses how remedial action pine bark extracts (Pycnogenol®), almond skins, Agaricus Blazei murrill, oleuropein and oleocanthal may have positive benefits for a destabilized organism which has failed to combat illness by its own efforts. The selection of the natural products discussed within this article has been accomplished via a thorough literature search. Although this article focuses on maintaining the two key processes of immune and homeostatic surveillance, more systems should be further investigated for reaching definite and credible conclusions.

Key Words: Surveillance, homeostasis, endometriosis, cancer, natural products

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Recent researches on prebiotics for gut health in Thailand

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ABSTRACT

Background: In the food industries, several oligosaccharides have received increasing attention as key components for functional foods and nutraceutical products. Prebiotics are non-digestible oligosaccharides which have been shown to have properties that can modulate gastrointestinal problems and improve gut health and well-being. Recent researches much pay attention to find alternative sources, improve specific properties and proof on health benefits of these prebiotics.

Methods: This is the summary of research works have been done by our research group on prebiotics and gut health in Thailand. These works aimed to study sources of prebiotics from fruits and vegetables in Thailand, production by enzymatic synthesis of prebiotics, purification by microbial fermentation and membrane technology and applications of the prebiotics in nutraceuticals and functional foods.

Results: Among the 30 parts of 14 plants, six appear to have the highest potential for commercialization based on extract yield and the amount and type of indigestible oligosaccharides. These include dragon fruit, palm flesh, palm embryo, jackfruit flesh, jackfruit seed, and okra pod. At least three of them, dragon fruit, jackfruit flesh and seed, were confirmed on their prebiotic property by selectively *in vitro* colonic microflora fermentation in an artificial colon system. Among 52 LAB isolates for production of GOS, BFP32 showed highest intracellular β-galactosidase activity and GOS yield. It was identified as *Lactobacillus pentosus* var. *plantarum* by 16S rDNA sequencing. Composition of GOS consisted of oligosaccharides with having DP of 3, 4 and 5. A mixture of GOS was purified successful by sequential bacterial and yeast fermentation whereas nanofiltration could be used for partial purification. Prebiotic index (PI) of the GOS produced was1.19 in batch culture. A crude extract from tubers of Jerusalem artichoke (*Helianthus tuberosus* L.) had transfructosylating activity for biosynthesis of FOS from sucrose. Optimal conditions for production of FOS were 0.26 U FTase, incubated with 0.46 M sucrose as substrate at pH 5.4 and 35ºC for 144 h. A maximum yield of scFOS (DP<5) was obtained (54.46%). The scFOS showed prebiotic property with PI of 1.29 in batch culture. Four formulas of canned tuna in spring water and tuna in mayonnaise and pouched tuna in salad cream and tuna in thousand island cream with added inulin were developed for commercial production. An addition of 5 % inulin for tuna in spring water and 7 % inulin for tuna in mayonnaise, tuna in thousand island and tuna in salad cream are recommended. The highest prebiotic index (PI) scores of tuna in spring water and tuna in salad cream added 5% inulin were 1.82 and 0.93, respectively in three-stage continuous culture. In clinical study of tuna products, it was found that 5% inulin addition helps on improve of bowel regularity. By-product from rubber wood sawdust could be used as alternative source of XOS. Among eight edible commercial mushrooms, *Schizophyllum commune*had highest total β-glucan content (59.87% dry basis).

Conclusions: Research on prebiotics in Thailand had two mainly approaches including by extraction from natural occurring in fruits and vegetables and by enzymatic approach using hydrolysis and transferase activities from agricultural by-products and low cost raw materials. Prebiotic researches are covered *in vitro*, *in vivo* in rat and being investigated in clinical study related to gut health functional and immunity.

Keywords: Prebiotic, Functional carbohydrate, Gut health, Fecal fermentation, Clinical study

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Evaluation on prebiotic properties of β-glucan and oligo-β-glucan from mushrooms by human fecal microbiota in fecal batch culture

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ABSTRACT

Background: β-glucan is dietary fiber, a structural polysaccharide, β-linked linear chains of D- glucose polymers with variable frequency of branches. β-glucan is isolated from different sources such as cell walls of baker's yeast (*Saccharomyces cerevisiae*), cereals (oat and barley) and various species of mushrooms. Among 8 mushrooms in the study, *Schizophylum commune* Fr and *Auricularia auricula* Judae had the highest in β-glucan contents and the cheapest cost of mushroom per content of β-glucan, respectively. Even the function of β-glucan on immune modulation has been known however no report on interaction between β-glucan and human gut microbiota. Gut microbiota is thought to have health effects by interaction with non-digestible component particular fermentable dietary fiber. It is important to correlate the specific groups of the microbial communities associated with β-glucan fermentation and the consequential SCFA profiles. β-glucan from mushroom may has potential prebiotic function similar to those from commercial yeast (*Saccharomyces cerevisiae*) β-glucan.

Objective: To evaluate on prebiotic properties of soluble β-glucans and oligo-β-glucans from *Schizophylum commune* Fr and *Auricularia auricula* Judae by fecal fermentation in batch culture.

Methods: *In vitro* fecal fermentation in anaerobic batch cultures under simulated conditions similar to human colon with human faecal samples from three donors were performed. Comparison on 3 β-glucans and 2 oligo-β-glucans have been studied. Sample was taken at 0 h, 24 h and 48 h to analyze the numbers of bacterial changes by fluorescent *in situ* hybridization (FISH) technique. Short chain fatty acids (SCFA) were analyzed by HPLC. The prebiotic index (PI) was calculated according to the change of 5 specific bacterial genus within 48 h fermentation.

Results: Soluble β-glucan from *Auricularia auricula* Judae increased numbers of bifidobacteria and lactobacillus significantly ($P<0.05$). The PI of soluble β-glucan and oligo-β-glucan from *Schizophylum commune* Fr were 0.01 and -0.01, respectively. β-glucan and oligo-β-glucan from *Auricularia auricula* Judae were 0.11 and -0.07, respectively. Whereas PI of β-glucan from commercial yeast (*Saccharomyces cerevisiae*) was 0.03. Acetate was the most prevalent SCFA found in all treatments followed by propionate, butyrate and lactate, respectively.

Conclusion: The study confirmed that β-glucan from *Schizophylum commune* Fr and *Auricularia auricula* Judae are candidate prebiotics.

Keywords: β-glucan, oligo-β-glucan, prebiotic, mushroom, fecal batch culture

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The effects of bioactive compounds on biomarkers of obesity

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ABSTRACT

The world is presently facing a prolonged struggle without a predictable cure. Obesity causes hundreds of thousands of fatalities each year, along with holding a position as a primary contributor to several other virulent chronic diseases. This review of scientific literature will examine the current state of obesity along with the mechanisms and biomarkers that lay the foundation for the development of the disease. Furthermore, this article will assess several functional foods and the bioactive compounds they contain that play an influential role in the prevention and treatment of obesity as a chronic disease. By presenting many relevant functional food research studies, this review aims to offer auxiliary support to traditional obesity treatments. The topic of functional foods and their relation to obesity is an extremely important topic to explore due to the severe expansion of obesity in the past few decades. Overall, the purpose of this review is to supply a comprehensive description of obesity and examine results of functional foods in clinical trials that may offer innovative benefits.

Keywords: obesity, bioactive compounds, disease, health, functional foods, clinical trials

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Water-insoluble fractions of botanical foods lower blood ethanol levels in rats by physically maintaining the ethanol solution after ethanol administration

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ABSTRACT

Background: Several studies have analyzed the functions of foods and dietary constituents in the dynamics of alcohol metabolism. However, few studies have reported the function of dietary fibers in the dynamics of alcohol metabolism.

Objective: We assessed the effects of botanical foods that contain dietary fibers on alcohol metabolism.

Methods: The ability of the water-insoluble fraction (WIF) of 18 kinds of botanical foods to maintain 15% (v/v) ethanol solution was examined using easily handled filtration. A simple linear regression analysis was performed to examine the correlation between the filtered volumes and blood ethanol concentration (BEC) in F344 rats 4 h after the ingestion of 4.0 g/kg of ethanol following dosage of 2.5% (w/v) WIF of the experimental botanical foods. Furthermore, the supernatant (6.3 Brix; water-soluble fraction) and precipitate (WIF of tomato), with a strong ethanol-maintaining ability, were obtained and BEC and the residual gastric ethanol in rats were determined 2 h after the administration of 4.0 g/kg of ethanol and the individuals fractions.

Results: The filtered volumes of dropped ethanol solutions containing all the botanical foods tested except green peas were decreased compared with the ethanol solution without WIF (control). There was a significant correlation between the filtered volumes and blood ethanol concentration (BEC). There was no significant difference in the residual gastric ethanol between controls and the supernatant group; however, it was increased significantly in the WIF group than in controls or the supernatant group. Consistent with this, BEC reached a similar level in controls and the supernatant group but significantly decreased in the WIF group compared with controls or the supernatant group.

Conclusions: These findings suggest that WIFs of botanical foods, which are mostly water-insoluble dietary fibers, possess the ability to absorb ethanol-containing solutions, and this ability correlates strongly with the inhibition of the blood ethanol response.

Key words: Botanical food, tomato, water-insoluble fraction, dietary fiber, blood ethanol concentration

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A methanolic extract of *Trigonella foenum-graecum* (fenugreek) seeds regulates markers of macrophage polarization

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ABSTRACT

Background: Macrophages are key cellular mediators in diabetes-related inflammation. Molecular cues such as cytokines found in the tissue microenvironment regulates the polarization of macrophages into an M1 (pro-inflammatory) or M2 (immunoregulatory) phenotype. Recent evidence suggests that M1 macrophages in diabetic patients may contribute to the complications associated with the disease such as atherosclerosis. *Trigonella foenum- graecum* (*Tfg:* fenugreek) seeds have been used in traditional medicine in Asia, Africa and the Middle-East for their alleged anti-diabetic properties.

Objective: To identify the molecular mechanism(s) through which *Tfg* seeds exert their effects, we investigated the role of a crude methanolic extract of *Tfg* seeds (FME) on macrophage polarization *in vitro*.

Method: THP-1 macrophages (Mφ) were treated with gBSA in the presence/absence of FME and the release and expression of M1 and M2 markers/cytokines were analysed. The role of FME on NF-κB activity was also explored using transfected HEK-293T cells.

Results: This study found that the *FME* significantly ($P<0.05$) decreased gBSA-induced secretion of M1 cytokines (TNF-α, IL-1β, IL-6 and IL-8) in THP-1 Mφ cells. In the presence of gBSA, FME also significantly increased the gene expression of the M2 marker Dectin-1, but had no effect on IL-10, IL-1Ra. FME also significantly decreased TNF-α induced NF-kB reporter activity.

Conclusion: These results suggest that FME can regulate the expression of M1 and M2 markers in THP-1 Mφ cells. This may be potentially through the modulation of NF-kB activity. Further work should be carried out to identify precise mechanism(s) involved in the effects of FME and *Tfg* seeds in diabetes and other conditions.

Keywords: chronic inflammation, macrophage polarization, diabetes, glycated BSA, THP-1 cells, *Trigonella foenum graecum,* fenugreek seeds, NF-κB,

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Enhancement of quercetin water solubility with steviol glucosides and the studies of biological properties

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ABSTRACT

Background: Quercetin, a flavonol contained in various vegetables and fruits, has numerous biological activities which include anticancer, antiviral, anti-diabetic, and anti-oxidative properties. However, quercetin also has low oral bioavailability, due to its insolubility in water. Thus, the bioavailability of quercetin administered to human beings in a capsule form was reported to be less than 1%, with only a small percentage of ingested quercetin getting absorbed in the blood. This leads to certain difficulties in creating highly effective medicines.

Methods: Quercetin-rubusoside and quercetin-rebaudioside were prepared. The antioxidant activities of quercetin and Q-rubusoside were evaluated by DPPH radical scavenging method. Inhibition activities of quercetin and Quercetin-rubusoside were determined by measuring the remaining activity of $3CL^{pro}$ with 200 µM inhibitor. The inhibition activity of quercetin, rubusoside and quercetin-rubusoside were determined by measuring the activity of human maltase, which remains at 100 µM rubusoside or quercetin-rubusoside. The mushroom tyrosinase inhibition was assayed with the reaction mixture containing 3.3 mM L-DOPA in 50 mM potassium phosphate buffer (pH 6.8), and 10 U mushroom tyrosinase/ml with or without quercetin or quercetin-rubusoside.

Results: With 10% rubusoside treatment, quercetin showed solubility of 7.7 mg/ml in water, and its solubility increased as the concentration of rubusoside increased; the quercetin solubility in water increased to 0.83 mg/ml as rubusoside concentration increased to 1 mg/ml. Quercetin solubilized in rubusoside solution showed DPPH radical-scavenging activity and mushroom tyrosinase inhibition activity, similar to that of quercetin solubilized in dimethyl-sulfoxide. Quercetin-rubusoside also demonstrated 1.2 and 1.9 folds higher inhibition activity against $3CL^{pro}$ of SARS and human intestinal maltase, respectively, than those of quercetin in DMSO.

Conclusions: Quercetin can be solubilized in water with rebaudioside or rubusoside treatment. As Ru concentration increases, the solubility of quercetin in water increases. The solubilization of quercetin in Ru solution did not reduce its biological functions such as the DPPH radical- scavenging and mushroom tyrosinase activity. Additionally, quercetin-rubusoside increased the inhibition activity against the $3CL^{pro}$ of SARS and human

intestinal maltase, when compared with the activity of quercetin in DMSO. Therefore, rubusoside and rebaudioside are promising compounds which enhance the solubility of poorly water soluble compounds.

Keywords: rubusoside, rebaudioside, flavonol, quercetin, human maltase, $3CL^{pro}$

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Glucosylglycerol on performance of prebiotic potential

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ABSTRACT

Background: Glucosylglycerol (GG), an organic compound constitutes a structurally diverse group of small organic molecules, which has a glycosidic chemical structure, a powerful osmolyte which is catalyzed by sucrose phosphorylase in the presence of sucrose and glycerol as a donor and acceptor substrate.

Context and purpose of this study: This research aims to study the potential of prebiotic properties from GG compared with three commercial oligosaccharides (FOS, inulin and lactulose) which also have prebiotic properties.

Results: The cultures with GG and FOS showed statistically significant difference ($P<0.05$) capacity to stimulated both probiotic strains *(Lactobacillus acidophilus* and *Lactobacillus plantarum*) and presented high ability to inhibit four intestinal pathogens (*Bacillus cereus*, *Escherichia coli*, *Samonella paratyphi* and *Staphyloccous aureus*), as displayed from wider inhibition zone compared with the culture without oligosaccharide. The tolerance ability of different gastrointestinal conditions (alpha-amylase, bile extract and HCl) in the culture medium with GG presented the highest percentage of survival (6.50%) after being incubated with HCl for 3 hours (significant difference as $P<0.05$). The culture of *L. acidophilus* with GG in the medium displayed maximum lactic acid concentration (1.46 mg/mL) after 48 incubation hours.

Conclusions: GG has high potential of prebiotic properties for probiotic growth stimulation, pathogenic inhibition and gastrointestinal tolerance. Additionally, GG can introduce probiotic for high production of lactic acid concentration in the culture media. From these results, GG is promising for application and development to become an effective functional food in the coming future.

Keywords: glucosylglycerol, prebiotic, probiotic, pathogen inhibition, gastrointestinal tolerance, lactic acid

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Antihyperglycemic, insulin-sensitivity and antihyperlipidemic potential of *Ganoderma lucidum*, a dietary mushroom, on alloxan- and glucocorticoid- induced diabetic Long-Evans rats

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ABSTRACT

Background: Reishi (*Ganoderma lucidum*) is a well-known and popular edible mushroom eaten all over the world. It has been used as an alternative medicine for many years in China, Korea, Japan, Malaysia, and in eastern Russia. This mushroom is reported to exhibit a number of medicinal properties including antitumor, antioxidant, immunomodulating, anti-inflammatory, hepatoprotective, and hypoglycemic activities, due to the presence of bioactive polysaccharide. Glucocorticoids, which are usually prescribed for the treatment of arthritis to protect inflammation and reduce pain, can induce hyperglycemia or aggravate the hyperglycemic condition. For example, causing very high glucose levels in diabetic patients. However, no report has been published for its effect on glucocorticoid-induced diabetes.

Objective: To investigate the effect of *Ganoderma lucidum* on alloxan- and glucocorticoid- induced diabetes in Long-Evans rats.

Methods: Alloxan monohydrate (150 mg/kg) was intraperitoneally administered to Long-Evans rats as a single dose. The same volume of normal saline was injected to control rats. Three days after alloxan injection, rats with plasma glucose levels higher than 12 mmoL /L were identified as diabetic and included in the study. Reishi mushroom was collected from the Mushroom Development Institute, Ministry of Agriculture, Savar, Dhaka, Bangladesh, where it was identified by a Taxonomist. Petroleum ether extract (PEE), known as petroleum spirit in the USA, and Methanol extract (ME) were prepared by maceration and distillation techniques. The extracts were orally administered once a day at doses of 200, 400, 600 and 800 mg/kg, respectively for 7 days. Metformin (150 mg/kg) was orally administered as a standard antidiabetic drug. Glucose levels were measured at 0 and 7th days of treatment. The rats were allowed to rest for 1 week without treatment. The animals were again injected with dexamethasone (2 mg/kg) through intra-muscular route for 3 days and glucose levels were monitored regularly. Rats were then further treated with PEE and ME and metformin for another 7 days and glucose levels were determined at 0 and 7th days of treatment.

Results: The PEE and ME of Reishi mushroom dose-dependently reduced the plasma glucose levels in alloxan-and steroid-induced fasting diabetic rats. The maximum reduction of fasting plasma glucose levels observed by PEE (800 mg/kg) and ME (800 mg/kg) were 55.57% and 36.01% in alloxan-induced and 51.41% and 32.02% in steroid-induced diabetic rats, respectively. On the other hand, metformin (150 mg/kg) resulted in the diminution of fasting blood glucose levels by 60.02 and 51.12% in the alloxan- induced and steroid-induced diabetic rats respectively. Both the PEE (800 mg/kg) and ME (800 mg/kg) significantly augmented plasma insulin levels (***P < 0.001 and **P < 0.01) and reduced HbA1c (**P < 0.01 and *P < 0.05) in alloxan-and steroid-induced diabetic rats. Additionally, treatment of diabetic rats with PEE (800 mg/kg) and ME (800 mg/kg) controlled the 2-h post prandial elevated glucose levels in blood plasma. The same dose of the extracts also significantly reduced the levels of total cholesterol (TC) (***P < 0.001 and ***P < 0.01), triglyceride (TG) (***P < 0.001 and **P < 0.01) and low-density lipoprotein-cholesterol (LDL-c) (***P < 0.001 and ***P < 0.001), as well as increased the level of high density lipoprotein cholesterol (HDL-c) (**P < 0.01 and **P < 0.01, respectively).

Conclusion: Our study demonstrated that edible mushrooms-Reishi has antihyperglycemic, insulin-sensitivity, and hyperlipidemic effects against both alloxan and corticosteroid-induced diabetes rats. The bioactive chemicals responsible for those activities are most probably the polysaccharides available in the mushroom. Therefore, usage of Reishi mushrooms as vegetables or as extract will be beneficial for the management of diabetes.

Keywords: Antihyperglycemic, antidiabetic, insulin-sensitizer, anti-hyperlipidemic, Gano mushroom, Reishi mushroom, *Ganoderma lucidum*, Lingzhi, alloxan-induced diabetes, Steroid induced diabetes, Glycated haemolgobin (HbA1c), Oral glucose tolerance test (OGTT), Hyperlipidemia

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Chemopreventive effects of magnesium chloride supplementation on hormone independent prostate cancer cells

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ABSTRACT

Background: Lifestyle significantly impacts the risk factors associated with prostate cancer, out of which diet appears to be the most influential. An emerging chemopreventive approach, which involves the adequate intake of dietary constituents, has shown great potential in preventing the occurrence or progression of cancer. Magnesium is known to be an essential cofactor for more than 300 enzymatic processes and is responsible for the regulation of various cellular reactions in the body. A plethora of studies have shown evidence that changes in the intracellular levels of magnesium could contribute to cell proliferation and apoptosis in some normal and malignant cells. The aim of the study was to investigate the effects of magnesium chloride ($MgCl_2$) in DU- 145 prostate cancer cells.

Methodology: Cultured DU-145 cells were subjected to graded concentrations or doses (50-500 µM) of $MgCl_2$ for 48 hours. The cell viability was assessed using MTT and Resazurin reduction assays. NBT assay was also used to assess the treatment-induced intracellular ROS levels. Acridine Orange/Ethidium Bromide (AcrO/EtBr) and Rh123/EtBr fluorescent stains were used to assess the cell death type and mitochondrial membrane potential ($\Delta\psi m$) respectively.

Results: The results revealed a dose-dependent decrease ($P < 0.05$) in cell viability in treated DU-145 cells after 48 hours. The NBT assay also revealed a dose dependent biphasic response ($P < 0.05$) in intracellular levels of ROS. There was a drop ($P < 0.05$) in ROS levels in all groups except at 100 µM, where ROS level was higher than the control. Apoptosis was the primary mode of cell death as observed in the fluorescence analysis.

Conclusion: Our finding suggests that $MgCl_2$ may be potentially chemopreventive for prostate cancer. This justifies further studies into its mechanism of action in DU-145 and other prostate cancer cell types.

Keywords: Prostate cancer, Magnesium chloride, Chemoprevention, Apoptosis, Reactive Oxygen Species.

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The effects of long-term ubiquinol intake on improving the quality of life of community residents

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ABSTRACT

Background: Ubiquinol is widely used as an anti-aging supplement. In this study, we evaluated the effects of long-term ubiquinol intake on improving or maintaining the quality of life (QOL) of community residents.

Methods: 124 adult (aged 22-86) residents (36 male, 88 female) participated in this trial. Each consumed 100-120 mg of ubiquinol per day for 6 months (n=22) or 12 months (n=102). We measured serum ubiquinol levels and QOL scores by SF-36 at baseline and after ubiquinol intake.

Results: In female participants, the SF-36 scores of role physical (RP), vitality (VT), social functioning (SF), mental health (MH), and mental component summary (MCS) increased significantly. On the other hand, significant score changes were not shown in male participants. After stratifying baseline serum ubiquinol levels by tertiles, we found a significant improvement of mental QOL scores in the low and middle ubiquinol level groups of female participants, but not in the highest tertile.

Conclusions: This trial indicates that ubiquinol supplementation has effects on female participants' psychological QOL, especially for those whose baseline serum ubiquinol levels are in the low to middle range.

Trial Registration: UMIN Clinical Trial Registry UMIN000012612

Key Words: ubiquinol, coenzyme Q10, energy production, quality of life, clinical trial

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Preparation of function-enhanced vegetable oils

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ABSTRACT

Background: Highly purified commercial vegetable oils, such as rape seed/canola oil, corn oil, safflower oil and soybean oil have virtually no antioxidant activity against lipid peroxyl radical scavenging activity ($ROO^{\cdot}$) (Figure 1), and peroxy nitrite ($ONOO^{-}$).

Methodology: Dried tomato-juice-waste-residues or dried wine-ferment-waste-residues were incubated with a highly purified oil obtained from the market, which is low-functional-grade oil (eg. canola oil), at room temperature for more than 2-3 weeks. Their antioxidant activities were then examined as described below

Results: Antioxidant lipid soluble components such as lycopene/carotenoids, flavonoids, and chlorophylls, originally present in tomato-juice-waste-residue, wine-ferment-waste-residues and dried spinach leaf, etc,, were transferred to such pure yet low-functional-grade vegetable oils. Peroxide value, acid value, and TBARS (thiobarbituric acid reactive substances) measurement, as well as spectroscopic characterization, demonstrated that such treatment much improved the properties of the low-functional-grade oils; namely low-functional-grade oils became high- functional-grade oils. The absorption spectrum of dried waste of tomato-juice-waste-residue treated canola oil indeed became much improved against various oil-deteriorating effects.

Conclusions: This method provides an easy procedure to convert low-functional-grade oils to high- functional-grade oils, using various vegetable-waste-residues.

Keywords: antioxidant components, enrichment of edible oils, lipid peroxidation, dried vegetable-waste-residues.

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Nutritional characteristics and consumer acceptability of sausages with different combinations of goat and beef meats

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ABSTRACT

Background: Obesity and cardiovascular heart diseases are becoming more prevalent in the United States. This is partly due to the increasing consumption of red meats, such as pork and beef. However, goat meat has the potential to replace these traditionally consumed meats. Rice bran is a rich source of antioxidants, including vitamin E, which can be utilized as a binder in meat and meat-related products.

Methods: Goat meat/beef sausages were formulated to contain either 50/50, 75/25 or 100/0 percent goat meat/beef, with either no added rice bran (NRB) or 3 percent stabilized rice bran (RB). Proximate analysis, fatty acids, α-tocopherol and cholesterol concentrations of the six cooked formulations were determined. The six sausage formulations were compared in a consumer acceptability taste test.

Results: The fat concentration of the NRB and RB formulations decreased linearly with increasing percentages of goat meat ($p < 0.001$). The sum of the saturated fatty acids decreased linearly with increasing percentages of goat meat ($p < 0.01$). Polyunsaturated fatty acids (PUFA), omega-3(n-3) and omega-6 (n-6) fatty acid and conjugated linoleic acid (CLA) concentrations demonstrated linear increase ($p < 0.05$), with increasing percentages of goat meat in both the NRB and RB sausage formulations. The α-tocopherol concentration of the NRB formulations did not change across the goat meat percentages, but with the RB formulations there was a linear increase with increasing percentages of goat meat ($p < 0.001$). The cholesterol concentration decreased linearly with increasing percentages of goat meat in both the NRB and RB formulations ($p <0.01$, < 0.05 respectively). The tasters preferred the NRB with higher goat meat percentage to the RB formulations.

Conclusions: The NRB and RB sausage formulations with higher percentages of goat meat had higher concentrations of α-tocopherol, CLA (18:2 cis 9 Trans 11), total n-3, total PUFA, total n- 3/total n-6 ratio, and a lower cholesterol concentration. The RB sausage formulations with higher percentages of goat meat had lower amount of saturation, in addition to an acceptable ratio of stearic acid (C18:0) + Oleic acid (C18:1) to palmitic acid (C16:0). The NRB formulations with greater percentage of goat meat were more acceptable by the tasters than the RB formulations.

Key words: Goat meat; rice bran; fatty acids; α-tocopherol; cholesterol

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Alterations in drug metabolizing activities in acute hepatosteatosis induced by intake of a high-carbohydrate/fat-free diet after food deprivation

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ABSTRACT

Background: Lipid accumulation in hepatocytes constitutes a major component in the pathogenesis of chronic liver injury. However, the impact of lipid deposition in liver on drug metabolizing capacity remains unclear.

Purpose of the study: The present study was undertaken to evaluate the changes in hepatic cytochrome P-450 (CYP) enzymes in acute hepatosteatosis.

Methods: The rat subjects fasted for 48 h, and then were provided with a high- carbohydrate/fat-free diet (FH) or a normal diet (FN) for 48 h.

Results: Hepatic lipid accumulation was significant in the FH group compared to the FN group. In the FN group, there was a small increase in microsomal *p*-nitrophenol hydroxylase, *p*- nitroanisole *O*-demethylase, and erythromycin *N*-demethylase activities. In contrast, aminopyrine *N*-demethylase activity significantly decreased. However, the microsomal enzyme activities were all inhibited by FH intake. Immunoblotting analysis revealed that CYP2E1, CYP1A, CYP3A, and CYP2B1/2 proteins decreased in the FH group. Expression of corresponding CYP mRNAs was also down-regulated. A dose of CCl_4, a CYP2E1 substrate, was administered to rats fed with different diets. The liver injury was significantly lower in the FH group compared to the FN group, as determined by the elevation of serum enzyme activities and histopathological examination.

Conclusions: The results revealed that acute hepatosteatosis may result in a significant alteration in hepatic CYP-mediated metabolizing capacity, which can precipitate erratic responses of liver to various endogenous and exogenous substances.

Key words: hepatosteatosis, cytochrome P450, non-alcoholic fatty liver disease, drug metabolizing capacity

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A comparative study: long and short term effect of a nutrition sensitive approach to delay the progression of HIV to AIDS among people living with HIV (PLWH) in Nigeria

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ABSTRACT

Background: Malnutrition has a negative impact on optimal immune function, thus increasing susceptibility to morbidity and mortality among HIV positive patients. Evidence indicates that the prevalence of macro and micronutrient deficiencies (particularly magnesium, selenium, zinc, and vitamin C) has a negative impact on optimal immune function, through the progressive depletion of CD4 T-lymphocyte cells, which thereby increases susceptibility to morbidity and mortality among PLWH.

Objective: To assess the short and long term effects of a nutrition sensitive intervention to delay the progression of human immune-deficiency virus (HIV) to AIDS among people living with HIV in Abuja, Nigeria.

Methods: A randomized control trial was carried out on 400 PLWH (adult, male and female of different religious background) in Nigeria between January and December 2012. Out of these 400 participants, 100 were randomly selected for the pilot study, which took place over six months (January to June, 2012). The participants in the pilot study overlapped to form part of the scale-up participants (*n* 400) monitored from June to December 2012. The comparative effect of daily 354.92 kcal/d optimized meals consumed for six and twelve months was ascertained through the nutritional status and biochemical indices of the study participants (*n*=100 pilot interventions), who were and were not taking the intervention meal. The meal consisted of: Glycine max 50g (Soya bean); Pennisetum americanum 20g (Millet); Moringa oleifera 15g (Moringa); Daucus carota spp. sativa 15g (Carrot).

Results: At the end of sixth month intervention, mean CD4 cell count (cell/mm^3) for Pre-ART and ART Test groups increased by 6.31% and 12.12% respectively. Mean mid upper arm circumference (MUAC) for Pre-ART and ART Test groups increased by 2.72% and 2.52% within the same period (*n* 400). Comparatively, participants who overlapped from pilot to scale- up intervention (long term use, *n* 100) were assessed for 12 months. Mean CD4 cell count (cell/mm^3) for Pre-ART and ART test groups increased by 2.21% and 12.14%. Mean MUAC for Pre-ART and ART test groups increased by 2.08% and 3.95% respectively. Moreover, student's t-test analysis suggests a strong association between the intervention meal, MUAC, and CD4 count on long term use of optimized meal in the group of participants being treated with antiretroviral therapy (ART) (P<0.05).

Conclusion: Although the achieved results take the form of specific technology, it suggests that a prolong consumption of the intervention meal will be suitable to sustain the gained improvements in the anthropometric and biochemical indices of PLWHIV in Nigeria.

Keywords: HIV; AIDS; Nutrition-sensitive approach; CD4 cell count; Macro and Micronutrients; ART; Tailored Functional Recipe-TFR.

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Anti-inflammatory effects of enzyme-treated asparagus extract and its constituents in hepatocytes

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ABSTRACT

Background: Asparagus (*Asparagus officinalis* L.) is one of the most ancient vegetables in the world, and is rich in asparagine. Enzyme-treated asparagus extract (ETAS™; Amino Up Chemical Co., Ltd., Sapporo, Japan) is the final product of enzyme-treatment of asparagus stems and subsequent extraction. Two constituents were purified from ETAS and identified: 5-hydroxymethyl-2-furfural (HMF), an abundant constituent, and (*S*)-asfural, a novel constituent, which is a derivative of HMF. ETAS has been reported to increase the expression of heat shock proteins (HSPs), which are essential for the repair or removal of defective proteins. The expression of *Hsp* family genes is regulated by the transcription factor heat shock factor 1 (HSF1). It is unknown whether ETAS and its constituents elicit anti- inflammatory effects, such as the suppression of nitric oxide (NO), an inflammatory mediator synthesized by inducible nitric oxide synthase (iNOS) in interleukin (IL)-1β-treated hepatocytes.

Objective: To examine the anti-inflammatory effects of ETAS, we treated rat hepatocytes with ETAS, or its constituents (*S*)-asfural or HMF, and IL-1β, before then analyzing the expression of the *iNOS* gene and other genes involved in inflammation.

Methods: Primary cultured rat hepatocytes were prepared by collagenase perfusion. ETAS, (*S*)-asfural, or HMF was added to the medium with IL-1β and incubated at 37 °C. When necessary, an inhibitor of HSF1 was added. NO in the medium was measured by the Griess method, and the half-maximal inhibitory concentration (IC_{50}) values were determined. To analyze the mRNA expression, a reverse transcription-quantitative polymerase chain reaction was performed. Antibody arrays were used to determine the levels of cytokines and chemokines in the medium.

Results: ETAS suppressed NO production in IL-1β-treated hepatocytes without causing cytotoxicity. ETAS decreased the levels of both iNOS mRNA and the antisense transcript, whereas it increased the levels of Hsf1 mRNA and Hsp70 mRNA. ETAS also suppressed the production of pro-inflammatory cytokines and chemokines in hepatocytes. When (S)-asfural and HMF were added to the medium, they suppressed NO production and iNOS gene expression. The IC50 value of (S)-asfural was approximately 3-fold lower than that of HMF. In contrast, (S)-asfural increased the levels of Hsf1 mRNA. Interestingly, the KRIBB11, an inhibitor of HSF1, reduced the expression of the iNOS gene. When both (S)-asfural and KRIBB11 were added, the level of iNOS mRNA was lower than when (S)-asfural alone was added.

Conclusion: ETAS and its constituents (*S*)-asfural and HMF suppressed NO production and the expression of pro-inflammatory cytokines and chemokines, thus showing anti- inflammatory effects. Our data suggest the possibility that the increased HSF1 level is involved in suppression of NO by ETAS and its constituents, although HSF1 is essential for the expression of the *iNOS* gene.

Keywords: nitric oxide, inducible nitric oxide synthase, inflammation, heat shock factor, asparagus

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Anti-cancer effect of EGCG and its mechanisms

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ABSTRACT

Background: Epidemiological analysis demonstrated that there are negative correlation between green tea consumption and the risk of non-Hodgkin lymphoma and prostate cancer. Recent studies show (–)-epigallocatechin-3-*O*-gallate (EGCG), or major green tea polyphenol, suppresses the proliferation of cancer cells and induces cell death without adversely affecting normal cells. As a result, several molecular mechanisms have been suggested to be responsible for this effect. For example, 67-kDa laminin receptor (67LR) was recently identified as the sensing molecule for EGCG. 67LR overexpresses in cancer cells and plays a crucial role in the selective toxicity of EGCG. Moreover, possible downstream mechanisms were suggested in 67LR-dependent the anti-cancer effect of EGCG. This review focused on the molecular mechanism of EGCG and developing a novel strategy to amplify its effect.

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Nutrition by design: a review of biotechnology in functional food of plant origin

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ABSTRACT

Medical institutions in industrial and developing countries are increasingly turning to functional foods as intervention in chronic disease. Advances in genetic engineering have provided methods of purposefully designing functional foods and bioactive compound-producing organisms. This literature review examines the recent history of biotechnological applications in functional food, the state of bioagricultural engineering for high-value compound production, and the challenges that developers face in promulgating functional foods from biotechnological sources. Based on the literature reviewed, it is predicted that adding biotechnologically-produced compounds will be more successful in producing novel functional foods.

Keywords: Biotechnology; functional food; genetic engineering, golden rice, algae

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Randomized study of nutritional status and treatment toxicities of oral arginine, glutamine, and Omega-3 fatty acids during concurrent chemoradiotherapy for head and neck cancer patients

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ABSTRACT

Background: Patients with head and neck cancer (HNC) undergoing concurrent chemoradiotherapy (CCRT) are at high risk for dysphagia, malnutrition, and immunosuppression. Accordingly, arginine, glutamine, and Omega-3 fatty acidsare immune- enhanced nutrition can promote cellular immunity. We aimed to examine the impact of immunonutrition diet on nutritional status, in addition to CCRT toxicities, within this group of patients.

Methods: Forty patients with HNC who were treated with curative CCRT were randomized into group A (n = 20), patients who received a regular diet and dietary counseling by a protocol dietician, and group B (n = 20), patients who received a regular diet plus immune- enhanced nutrition supplements and dietary counseling by the same protocol dietician. Outcome measures were weight loss, protein and energy intake, serum pre-albumin and albumin, and toxicities of CCRT were evaluated at baseline, weekly and at the end of treatment.

Results: Both groups were well balanced at baseline. One patient from group A (1/20) withdrew consent. Seven patients from group B (7/20) withdrew from the study; 1 patient could not tolerate the side effect of chemotherapy and 6 patients could not tolerate the taste of oral immune-enhanced nutrition. A significant loss in total body weight was observed in group A patients ($p<0.001$), whereas in group B there no significant weight loss ($p=0.109$). Median percentage change from baseline of energy intake was 19.6%, and 22.9% at the end of treatment for group A and B respectively. The circulating levels of nutritional markers, pre-albumin and albumin, decreased after CCRT in both groups. There was a significantly decreased level of albumin in group A compared to that of group B, at the end of treatment. During CCRT; 4 patients (20%) in group A and 1 patient (5%) in group B developed grade 3 mucositis, respectively. One patient (5%) in group A had grade 3 radiation dermatitis. Grade 3–4 hematologic toxicities, mainly in absolute neutrophil count (ANC), were significantly higher in group A than group B: 20% versus 0% ($p=0.035$). Over the 7-week period of CCRT, both the intention to treat analysis and per protocol analysis revealed similar results in scaled for all endpoints.

Conclusions: Nutritional counseling and immuno-nutrition can reduce the deterioration of nutrition status and also significantly reduced hematologic and non-hematologic toxicity of CCRT in head and neck cancer.

Keywords: immune-enhanced nutrition, concurrent chemoradiotherapy, head and neck cancer

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/230/468

Correlation of pasting behaviors with total phenolic compounds and starch digestibility of indigenous pigmented rice grown in upper Northern Thailand

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ABSTRACT

Background: Thailand has one of the most important rice genetic resources with white, light brown, brown, red, and purple rice bran colors. The latter forms are believed to have the potential for health benefits due to their phenolic content. Recently researchers have indicated that starch digestive enzymes, including salivary and pancreatic α-amylases and α- glucosidases, can be inhibited by phenolic compounds. Although pasting properties of rice flour are key determinants of quality significantly impacting the final product texture, there is no in-depth study on their correlation with phenolic compound and starch digestibility.

Methods: Rice flour from twelve varieties, three from each of five bran colors (white, brown, red, and purple), were evaluated for pasting properties (RVA-3D), total phenolic compounds, amylose content, resistant starch and estimated glycemic index. Simple correlation coefficients were calculated for the relationships between pasting properties (final viscosity, breakdown, setback and pasting temperature) and total phenolic compounds, resistant starch and estimated glycemic index**.**

Results: Within each rice variety, red and purple pigmented flours had higher total phenolic compounds (TPC) and more resistant starch than that of white flours. The TPC and resistant starch content of the flours ranged between 7.83- 47.3 mg/L and 2.44–10.50% respectively, and producing 60-80 of estimated glycemic index. Viscosity behavior showed that pigmented with low amylose rice had lower viscosity temperature than that of pigmented with high amylose rice flour, but higher in peak viscosity. Correlation coefficients of pasting temperature, final viscosity, break down and setback with TCP was observed to be inversely related to glycemic index. However, it was positively correlated to the resistant starch and amylose content.

Conclusions: Pigmented rice flour is a better source of TPC and resistant starch, which in turn provides low glycemic index. This could help reduce the onset of type 2 diabetes and other related chronic diseases. In addition, this study provides impact of pasting behavior – TPC- resistant starch of rice flour relationships, which have important implication for utilization in food industry.

Keywords: total phenolic compounds, amylose content, resistant starch, glycemic index

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Effectiveness of aronia berries for reduction of mild fibrosis and gene expression analysis in livers from mice fed a high-fat diet with aronia berries

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ABSTRACT

Background: Aronia berries have many potential effects on health, including an antioxidant effect, effect for antimutagenesis, hepatoprotection and cardioprotection, an antidiabetic effect and inhibition of cancer cell proliferation. Previous human studies have shown that aronia juice may be useful for treatment of obesity disorders.

Objective: To reveal relationship between beneficial effect and the gene expression change by aronia berries, we analyzed mice livers using RNA sequencing and RT-qPCR.

Method: At 28 days after starting a normal diet, a high fat diet and a high-fat diet containing 10% freeze-dried aronia berries, serum was obtained from veins of mice after isoflurane anesthesia, and liver tissues were isolated and weighed. Triglyceride, total cholesterol and LDL cholesterol levels were measured and total RNAs were extracted. cDNA libraries were prepared according to Illumina protocols and sequenced using an Illumina HiSeq2500 to perform 100 paired-end sequencing. RNA-sequence reads mapping was performed using a DNA nexus. Gene expression analysis was performed. The liver tissue specimens were fixed and embedded in paraffin. After 5-µm-thick paraffin sections had been cut, they were stained with hematoxylin-eosin using the standard procedure and also with Sirius Red.

Results: In this study, we found that mild fibrosis induced by a high-fat diet was reduced in livers of mice fed a high-fat diet containing aronia berries. RNA sequencing and RT-qPCR analyses revealed that gene expression levels of *Igfbp1* and *Gadd45g* were increased in livers from mice fed a high-fat diet containing aronia berries. Furthermore, results of an enzyme-linked immunoassay showed that a secreted protein levels of FABP1 and FABP4 were reduced in serum from mice fed a high-fat diet containing aronia berries. The results suggest that aronia berries have beneficial effects on mild fibrosis in liver.

Conclusion: Aronia berries have a beneficial effect on liver fibrosis. The recovery from liver fibrosis is associated with expression levels of *Gadd45g* and *Igfbp1* in the liver. The beneficial effects of aronia berries on liver fibrosis reduce the risk of liver cancer diseases and insulin resistance, resulting in reduction of serum FABP1 and FABP4 levels.

Keywords: aronia; fibrosis; liver; Igfbp1; Gadd45g

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Utilization of tuna roe and using inulin as oil replacer for producing value added omega-3 mayonnaise product

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ABSTRACT

Background: The fishery industry has been important for Thailand's economy for more than 30 years. For example, Thailand is the world's largest canned tuna producer and exporter. However, only ordinary meat or white meat is used for raw material in canned tuna products. While roe, viscera, head and dark meat are sold at cheap prices, with these by-products being used to feed plant or local human food, its nutritive values with fat, protein and minerals are still high. It is well known that tuna is a good source of polyunsaturated fatty acid (PUFA), including Eicosapentaenoic acid (EPA) and Docosahexanoic acid (DHA). People around the world pay more attention to eating salads consisting of fruits and vegetables, in addition to dressing. Generally, mayonnaise, a kind of salad dressing, consists of chicken egg yolk (12-15%) and soybean oil (30-65%). Both of these ingredients contain very high saturated fatty acid contents. Therefore, because normal mayonnaise is high in fat content and low in polyunsaturated fatty acid, this product is not ideal for people on a diet or those who are trying to control their weight.

Objective: To increase omega-3 through tuna roe substitution and to replace fat content using inulin gel.

Methods: Tuna roe was prepared by soaking in galangal solution extracted with 95% ethanol for removal fishy/rancidity odor. Inulin powder 45 g was suspended in 55 ml of water before being brought to heat at temperature 80°C for 30 min to form a gel and stored at 4°C. Treatment of making omega-3 mayonnaise product was started using 100% tuna roe substitution for egg yolk. Thereafter, inulin gel was added to replace vegetable oil at 0, 25, 50, 75 and 100%. Basic mayonnaise containing egg yolk and 0% inulin gel (100% soy bean oil) was used as the control sample. Color and emulsion stability tests were monitored for physical quality. pH value, peroxide value (PV) and thiobarbituric acid reactive substances (TBARS) were used for chemical quality analyses. Total viable count (TVC), yeast and mold, lactic acid bacteria (LAB) and coliforms were measured for microbiological quality. Sensory evaluation using 9-point hedonic scale technique was also monitored.

Results: When there was increased inulin gel in the mayonnaise, L* value significantly increased while a* and b* values significantly decreased ($p<0.05$). Without addition of inulin gel, tuna roe mayonnaise (IG0) had lower emulsion stability compared with control sample containing egg yolk. It was found that using the inulin gel significantly increased moisture contents and water activity of the mayonnaise. However, there was no significantly difference found in pH value in any sample. In addition, the tuna roe mayonnaise with and without added inulin gel possessed higher lipid oxidation products determined as PV and TBARS value compared with basic mayonnaise using egg yolk (control sample). All microbiological quality indices were very low and passed through a standard regulation of mayonnaise product. Although consumer acceptability of the mayonnaise producing from tuna roe was lower than that of control, 50% of inulin gel substitution (IG50) seemed to obtain higher sensory score when

compared with other inulin gel substitution groups. Therefore, sensory improvement of the tuna roe mayonnaise product substituted with inulin gel needs to be studied further.

Conclusions: The mayonnaise produced from tuna roe and replaced fat with inulin gel between 25 to 100% were successful when determined by emulsion stability, pH value and microbiological quality. However, sensory score of the mayonnaise using 100% tuna roe with and without inulin gel substitution was lower than that of control. The tuna roe mayonnaise substituted with 50% inulin gel (IG50) should be selected for sensory improvement in the further work.

Keywords: Tuna roe, Mayonnaise, Inulin, Omega-3

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Examining the potential benefits of (-)-epicatechin, (+)-catechin, and rutin on maternal and offspring cardiovascular outcomes in LDLr-/- mice exposed to an atherogenic environment during early development

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ABSTRACT

Background: Maternal nutritional status can impact numerous early developmental processes. In certain cases, these effects can influence the risk their offspring can have for select chronic diseases later in life. Consequently, in this article we report on the effects of maternal consumption of high levels of certain flavonoids on the development of coronary artery disease (CAD) in an atherosclerosis-prone mutant mouse model.

Methods: LDLr -/- mutant mice were fed a control fat (CF), high fat (HF), or the HF diet supplemented with epicatechin and catechin (HFEC) or rutin (HFRU), prior to pregnancy and during lactation, in order to explore whether the flavonoids influenced markers of vascular health in the lactating dams (lactation day (LD) 21). Post-weaning (postnatal day (PND) 22), offspring were challenged with an atherogenic environment (HF diet in the absence of flavonoids) and vascular health markers were assessed in the adult offspring (PND 60).

Results: Dams fed the HF diet had elevated markers of atherosclerosis on LD 21 when compared to the dams fed with the control diet. Flavonoid consumption prior to pregnancy and during lactation had inconsistent effects on maternal markers of atherosclerosis (plasma cholesterol, aortic lipid accumulation, and oxidative stress biomarkers) at LD 21 compared to dams fed the HF diet without flavonoids. At PND 60, there were no differences in vascular health markers among the groups of LDLr -/- offspring whose mothers consumed the CF or the HF diet with or without flavonoids during lactation.

Conclusions: Maternal consumption of the flavonoid-supplemented HF diets had modest effects on maternal markers of atherosclerosis. The exposure of offspring to the flavonoid-supplemented HF diets during early lactation had little effect on the cardiovascular parameters assessed in the adult offspring.

Key Words: (-)-epicatechin, (+)-catechin, rutin, flavonoids, flavanols, flavonols, coronary artery disease, lactation, development

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/232/482

Evaluation of harmful heavy metal (Hg, Pb and Cd) reduction using *Halomonas elongata* and *Tetragenococcus halophilus* for protein hydrolysate product

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ABSTRACT

Background: Many health claims surrounding antioxidative, antihypertensive and anti- inflammatory properties have been addressed in natural protein hydrolysates, including fermented fish. Besides being sold as animal feed, tuna viscera is used for for the production of fermented products like fish sauce and Tai pla, fermented viscera. However, toxic heavy metals including Hg, Pb and Cd have been found in various food items, particularly within the internal organs of tuna. Therefore, the consumption of fermented tuna viscera containing heavy metal involves health risks. Consequently, the detoxification and reduction of these toxic elements are relevant and important issues, particularly with the use of their bacterial cells and metabolic products. *Halomonas elongata* is a moderately halophilic bacterium which has the ability to remove heavy metal, and is normally found in hypersaline environments. *Tetragenococcus halophilus* is a moderately halophilic lactic acid bacterium and probiotic which is found in fermented food products, such as fish sauce, shrimp paste, and fermented fish. Some scientific studies have reported using *T. halophilus* improves amino acid profiles and desirable volatile compounds, in addition to reducing biogenic amine content in fish sauce product. Therefore, it was hypothesized that using *H. elongata* and *T. halophilus* could reduce heavy metal content and improve the organoleptic quality of fermented fish viscera product (Tai pla).

Objective: This present work attempted to determine the growth characteristic of *H. elongata* and *T. halophilus* reared at various NaCl concentrations: 10, 15, 20 and 25%. Consequently, heavy metal reduction using these microorganisms reared at optimum NaCl concentration was evaluated.

Methods: *H. elongata* and *T. halophilus* were reared in saline nutrient broth (SNB) and de Man, Rogosa and Sharpe (MRS-broth) added with NaCl at concentration 10, 15, 20 and 25%, respectively. Cultures at each NaCl content were added with mercury (Hg), lead (Pb) and cadmium (Cd) at concentration, 0.5, 1, and 3 mg/L, respectively. Subsequently, the supernatant of each condition was incubated at 48h and taken for heavy metal analysis at 96 h.

Results: The results showed that higher NaCl content resulted in slower late log and stationary phases, particularly in *T. halophilus*. This may due to *T. halophilus* not producing special metabolite such as exopolysaccharide, which was found in *H. elongata*. Regardless of heavy metal concentration, the results revealed that Cd at 3 mg/kg caused more cell death of *H. elongate*, but not that of *T. halophilus*. Furthermore, removal of Hg, Pb and Cd was 12.70, 84.78 and 75.83% respectively, by rearing with *H. elongata* for 48 h and by rearing with *T. halophilus* for 96 h was 12.68, 91.27 and 95.12%, respectively.

Conclusion: *H. elongata and T. halophilus* prefered SNB containing NaCl concentration between 10-20%. At higher NaCl concentration, 20-25%, the log phase was extended. Both *H. elongata and T. halophilus* were able to remove

all test heavy metals. However, *T. halophilus* appeared to have higher Pb and Cd removal capability compared with *H. elongata.* Therefore, using *H. elongata* and *T. halophilus* for fermented tuna viscera is possible.

Keywords: *Halomonas elongata, Tetragenococcus halophilus*, Heavy metal, NaCl

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Polyphenol compounds of *Mahkota Dewa* (*Phaleria macrocarpa* [Scheff.] Boerl) up-regulated caspase-3 and apoptosis index in balb/c strain mice

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ABSTRACT

Background: Polyphenol compounds of *Mahkota Dewa* (*Phaleria macrocarpa* [Scheff.] Boerl (PMD) can potentially be used as anticancer treatment by scavanging radical molecules. The effect *in vivo* is still limited to Indonesia.

Purpose: This research was aimed to validate the activity of PMD in increasing caspase-3 expression and apoptosis in Balb/c mice, induced by Benzo(a)pyrene (BaP).

Methods: A post test control group was implemented and used by 40 Balb/c mice at the age of 1-2 weeks, with the body weight of 20-30 g. The tumor induction was administered to the mice using BaP. The animals were randomized into two groups called the control group and the PMD treatment group, the latter of which was given a dosage of 50mg. Lung tumor growth was assessed through surgery at week 8, 17, and 26. The results of caspase-3 expression and apoptotic index from IHC-TUNEL staining were analyzed using Kruskal-Wallis, Mann- Whitney, One-way ANOVA, and Post hoc test LSD with significant levels of $p<\alpha$ (0,05). This research was approved by Ethical Clearance.

Results: Oral administration of 50mg PMD significantly increased caspase-3 expression and apoptotic index in the treatment group animals at weeks 8, 17, and 26. Carcinogenesis incidence in the control group were respectively found at 2,32±0,26 and 3,93±0,46 at weeks 8 and 26, while those of the treatment group were 1,88±0,38 and 0,88±0,22 (p=0,001). The apoptotic index in the control group was 0,00±0,00 at 8 weeks and 0,92±0,22 at 26 weeks, whereas the indexes of the treatment group were 1,12±0,71 and 2,02±1,05 (p=0,001). In the control group, the caspase-3 expression at weeks 8 and 26 were 0,28±0,17 and 0,56±0,16, while those in the treatment group were 0,60±0,14 at week 8 and 2,52±0,33 at week 26 (p=0,001).

Conclusion: The treatment of PMD effectively induced cell apoptosis in the Balb/c mice via up-regulation of the caspase-3 expression, thereby increasing the apoptotic index. This shows that PMD has anticancer abilities to inhibit lung carcinogenesis in Balb/c mice.

Keywords: polyphenol, mahkota dewa (*Phaleria macrocarpa* [Scheff.] Boerl), cell proliferation, apoptotic index, Balb/c strain mice, Benzo(a)pyrene (BaP).

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Improvement of nutritional value and bioactivity of ricegrass as affected of priming induced by fish protein hydrolysate

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ABSTRACT

Background: Wheatgrass (*Triticum aestivum* L.) is consumed worldwide and has been used for health benefits and as functional food or nutraceuticals. While ricegrass (*Oryza sativa* L.) is still not well documented, which is also in the grass family (Poaceae) as wheatgrass. Also, similar to wheatgrass, ricegrass is produced with aged around 8-10 d. Moreover, priming is a process for enhancing seed vigour properties and improving bioactive compounds. Utilization of fish protein hydrolysate (FPH) for liquid fertilizer is more interesting in order to increase the nutritional value and bioactive compounds as well as antioxidant activity of many plants.

Objective: To investigate the nutritional value and bioactivity of ricegrass affected by the priming process of fish protein hydrolysate.

Methods: The Chainat 1 rice seeds were soaked with FPH at 0, 5, 10, 15 and 20 ppm at a ratio of rice seed to FPH as 1:5 and grown for 7 d, thereafter, the ricegrass seed vigour properties, nutritional value and bioactive compounds such as chlorophyll, carotenoids, total phenolic and phytic acid were determined. The ricegrass was extracted with water at a ratio 1:2 (ricegrass:water), then homogenized and centrifuged at 10000xg for 20 min. Then the supernatant was brought to freeze dry. The freeze-dried powder was dissolved in distilled water and brought to measure total phenolic content by Folin-Ciocalteu method. Antioxidant activities were determined by 3 assays as ferric reducing antioxidant power (FRAP), 2,2-diphenyl-1-picryl hydrazyl radical (DPPH) and 2,2'-azino-bis-3-ethylbenzthiazoline-6-sulphonic acid radical (ABTS) methods.

Results: The results showed that FPH at 10 ppm significantly improved (p<0.05) seed vigour properties including germination percentage, germination rate, height and fresh weight and nutritional values such as ash, protein, fat and carbohydrate. In addition, bioactive compounds including chlorophyll a and b, total chlorophyll and carotenoid content in ricegrass primed with 10 ppm FPH were higher than control. Phytic acid content in ricegrass primed with FPH at 5 and 10 ppm but not 15 and 20 ppm was lower than control. The ricegrass primed with FPH at 10 ppm yielded highest total phenolic content. Though ABTS activity was not highest in rice primed with FPH at 10 ppm, DPPH and FRAP assays were highest.

Conclusion: The seed vigour property, nutritional value, bioactive compounds and antioxidant activity of ricegrass primed with FPH was significantly improved. The appropriate content of FPH for priming ricegrass was 10 ppm because it demonstrated improvement in seed vigour, nutritional value and bioactive compounds including chlorophyll, carotenoid, total phenolic content and antioxidant activity determined as FRAP, DPPH and ABTS and reduced the anti- nutrient compounds as phytic acid.

Keywords: Ricegrass, Fish protein hydrolysate, Nutritional value, Bioactive compound, Antioxidant

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A new method for aldo-sugar analysis in beverages and dietary foods

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ABSTRACT

Background: Carbohydrates are a common part of our everyday diet. However, sugar analysis is difficult and inconvenient when it comes to food materials such as beverages, fruits, and vegetables. Consequently, in our article we discuss a new method for labeling the sugar ingredients in beverages and plant foods. This method provides a highly sensitive and efficient tool for sugar compositional analysis by labeling the aldoses in beverages and foods with 2,3- naphthalenediamine via an iodine-promoted oxidative condensation reaction to form highly fluorescent aldo-naphthylimidazole (NAIM) derivatives. We have also separated the natural glycosides from dietary foods: for example, solanines from tomato and potato. The various types of solanines with different sugar moieties were analyzed by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) and electrospray ionization tandem mass spectrometry (ESI-MS/MS). The solanine glycans were released by acidic hydrolysis, and the sugar components were subjected to NAIM labeling. These aldo-NAIM derivatives not only demonstrated enhanced mass signaling, but also provided fluorescent moiety at the reducing end of sugar, thereby assisting detection in HPLC analysis.

Objective: To develop a rapid and sensitive sugar detection method for research and commercial use, as well as to determine the sugar composition in a selection of dietary beverages and functional foods.

Results: Five beverages in Taiwan were examined for the composition of six common sugars. Two Solanaceae samples extracted from the potato and tomato plants were measured by MALDI MS and ESI-MS/MS. The structures of solanines were elucidated and the glycan moieties were converted to the fluorescent NAIM derivatives to confirm their composition.

Conclusions: The results suggest that aldo-NAIM, accompanied with LC and MS, is an efficient and rapid method for evaluation of sugar composition and concentration in beverages and foods.

Key words: beverages, foods, potato, tomato, aldose, sugar analysis, fluorescence, NAIM kit

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/251/478

Oral administration of an ethanolic extract of *Hypericum gentianoides* attenuates spontaneous colitis in mdr1a$^{-/-}$ mice

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ABSTRACT

Background: Nutraceuticals (i.e., complementary and alternative medicines) are gaining ground as therapeutic modalities for inflammatory and autoimmune disorders, primarily due to their low toxicity and high patient compliance. Several species of *Hypericum* have been shown to possess immunomodulatory capabilities in many disease models. However, the therapeutic potential of the chemically unique *Hypericum gentianoides* (HG) is largely untested. We investigated the efficacy of an orally administered ethanolic extract of HG (HGEE) to prophylactically inhibit/ameliorate the spontaneous colitis that develops in mdr1a deficient (mdr1a$^{-/-}$) mice.

Methods: Beginning at six weeks of age, vehicle (5% ethanol), HGEE (4.8 mg/day) or metronidazole (0.75 mg/mL) were orally administered daily to mdr1a$^{-/-}$ or FVB^{WT} mice until they reached 20 weeks of age or had lost ≥ 15 % of their body weight. Macroscopic disease assessment included measurement of weight loss, colon shortening, and combined colonic/cecal macroscopic lesion scores. Colonic/cecal inflammation was also scored histologically. Inflammatory responses were assessed using myeloperoxidase (MPO) assay and analysis of serum cytokines/chemokines.

Results: Daily administration of HGEE significantly ($p < 0.05$) delayed the onset of clinical signs of disease, reduced the associated morbidity, and attenuated macroscopic and microscopic disease/inflammatory scores in mdr1a$^{-/-}$ mice. After 14 weeks of treatment, there were no adverse macroscopic or microscopic effects observed following the daily administration of HGEE to wild type FVB mice. Histological evaluation of colonic tissue revealed a decrease in neutrophil infiltration in HGEE treated mdr1a$^{-/-}$ mice, which was substantiated by a significant decrease ($p \leq 0.05$) in colonic MPO activity. Compared to vehicle treated mdr1a$^{-/-}$ mice, levels of G-CSF, KC, and TNFα were significantly lower in the serum of mdr1a$^{-/-}$ mice treated with HGEE.

Conclusions: Oral administration of HGEE was shown to be safe, effectively ameliorating mucosal inflammation and disease severity in mdr1a$^{-/-}$ mice. The attenuation of mucosal inflammation correlated with a reduction in the production of pro-inflammatory cytokines and the recruitment of inflammatory granulocytes to the intestinal mucosa, which suggests that extracts of *H. gentianoides* have the potential to be used as a CAM product for mucosal inflammation.

Keywords: *Hypericum gentianoides*, colitis, IBD, mdr1a deficient mice, botanical

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Antioxidant activity of *Rosa multiflora* Thunb. flower extract and suppressive activity on proinflammatory mediator production in lipopolysaccharide- stimulated RAW 264.7 macrophages

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ABSTRACT

Background: Oxidative stress and inflammation are associated with various age-related chronic diseases. The fruits and roots of *Rosa multiflora* Thunb. have been used in medicine for the treatment of edema and inflammatory diseases in Eastern Asia. Dried *Rosa multiflora* Thunb. flowers (RMF) are consumed as a tea in Korea, but reports on the biological activity of RMF are lacking. We evaluated the *in vitro* antioxidant and anti-inflammatory effects of an ethanol extract from RMF as well as various solvent fractions from the extract.

Methods: The ethanol extract (Et) of RMP was fractionated sequentially by hexane (Hx), dichloromethane (DM), ethyl acetate (EA), n-Butanol (Bt), and water (DW). Total phenolic and flavonoid contents, scavenging activities of the 2,2-diphenyl-1 picrylhydrazyl radical, 2,2'- azinobis-3-ethylbenzothiazoline-6-sulfonic acid radical, and ferric-reducing antioxidant power were measured. Anti-inflammatory effects in terms of levels of nitric oxide (NO), prostaglandin (PG) E2, and production of pro-inflammatory cytokines such as interleukin (IL)-6, tumor necrosis factor (TNF)-α in lipopolysaccharide (LPS)-treated RAW 264.7 macrophages were measured. The expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase (COX)- 2 were measured by the Western blot analysis.

Results: EA demonstrated the highest total phenolic and flavonoid contents and strongest antioxidant activity, followed by Bt and Et. Treatment with Et, Hx, DM, EA, Bt, and DW significantly suppressed ($p<0.05$) NO production in a dose-dependent manner in LPS-treated RAW 264.7 macrophages via reduction of expression of iNOS protein. Treatment with Et, DM, and EA significantly suppressed ($p<0.05$) PGE2 production induced by LPS treatment; however, only Bt treatment significantly reduced ($p<0.05$) the expression of COX-2 protein. Treatment with EA and Bt suppressed IL-6 production significantly ($p<0.05$) in LPS-treated RAW 264.7 macrophages. Treatment with Et, DM, EA, and Bt suppressed TNF-α production significantly ($p<0.05$).

Conclusion: These data suggest that the ethanol extract of *Rosa multiflora* Thunb. Flowers and its dichloromethane, ethyl acetate and n-Butanol fractions have potent antioxidant and/or anti- inflammatory activities.

Keywords: *Rosa multiflora* Thunb, flowers, antioxidant activity, anti-inflammatory activity, RAW 264 7, macrophages, cytokines, iNOS, COX-2

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/248/486

Increasing of bioactive compounds in *Mentha cordifolia* Opiz., kitchen mint via $ZnSO_4$ biofortification during plantation

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ABSTRACT

Background: Plant growth generally requires both macronutrients and micronutrients. One of the most important micronutrients for plants is zinc. Zinc is an essential nutrient for every life form, including plants. In particular, zinc aids enzymatic processes and many biochemical reactions. When plants receive an inadequate amount of zinc, it leads to the loss of imperative biochemical reactions, which is also related to inhibition of plant growth. Therefore, the yield of the plant is relatively low. Interestingly, some scientific evidence have demonstrated a positive relation between zinc intake and the amount of essential oil and yield of plants. *Mentha cordifolia* Opiz., kitchen mint, is one of the top seven vegetables consumed in Thailand. The increase of some essential minerals in plants or biofortification during plantation has resulted in the increase of essential oils and chlorophyll. The bioactive compounds of essential oil provide antibacterial benefits. Additionally, chlorophyll can be utilized for against sinusitis, purifying the blood, and cleansing of toxins from intestines.

Objective: Our study aimed to evaluate the effects of fortifying zinc into plantation soil on growth characteristics, essential oil droplets, and overall quality of *Mentha cordifolia* Opiz.

Methods: *Mentha cordifolia* Opiz were planted in soil fortified with $ZnSO_4$ at 0 (control), 100, and 200 ppm and grown for 3 months. During the growth period, physical characteristics were observed. After harvesting, proximate analyses were conducted as well as determination of minerals, and chlorophyll content, were conducted. Microbiological and sensory tests were also performed.

Results: The increase of growth characteristics correlated with the increase of zinc concentration. The sizes of mint leaves were larger, the stalks were plumper, and the length of the roots were longer—although not significantly different—and the production of essential oil significantly increased. The approximate composition contents including protein, fat, ash, and fiber of plants grown in fortified $ZnSO_4$ soil, increased when compared to the control. The leaves grown from the soil containing the 100 ppm $ZnSO_4$ treatment possessed the highest chlorophyll content, related to lowest in a* value. Overall, the kitchen mint fortified with 100 ppm $ZnSO_4$ seemed to be the most tolerable sample when analyzed for color and sensory attributes. Furthermore, it was discovered that 200 ppm $ZnSO_4$ treatment demonstrated the highest production of essential oil and lowest number of microorganisms.

Conclusion: In conclusion, soil fortified with $ZnSO_4$ at 100 ppm during seeding increased greenness, chlorophyll content, and consumer acceptability of the mint leaves. Darker and larger oil droplets were found in the mint leaves obtained from plants grown in soil fortified with 200 ppm $ZnSO_4$.

Keywords: Fortification, Growth characteristics, Zinc deficiency, kitchen mint, oil drop

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/252/492

Polyphenol content and glycemic load of pasta enriched with *Faba bean* flour

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ABSTRACT

Background: Legumes contain elevated levels of health functional components. The objective of the present paper was to evaluate the nutritional properties and the post-prandial glycaemic responses of pasta obtained using 35% *Vicia Faba* (VF) bean flour, which is an important source of fiber and phytochemical compounds.

Results: Protein and fiber content were higher in VF pasta compared with durum wheat semolina (DWS) pasta. The total phenol content in VF pasta was about two fold higher compared to that of DWS pasta. A higher total flavonoid content, higher antioxidant activity against peroxyl radicals evaluated by oxygen radical absorbance capacity (ORAC) assay was also observed in VF pasta. The comparison of post-prandial increase of glucose after VF intake or DWS demonstrated significant differences and VF pasta exhibited a lower glycemic index value, a lower glycemic load and higher glycemic profile compared with DWS pasta.

Conclusion: The results suggest that enrichment with 35% *Vicia faba* bean has potential health benefits and that VF flour can be used as an ingredient to prepare added-value products.

Key words: Glycemic Index; Glycemic load; Glycemic Profile; polyphenols, flavonoids; diabetes

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Vegetable derived antioxidant and vitamin D: effects on oxidative stress and bone mineral metabolism of aged patients with renal disease

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ABSTRACT

Background: Aging and chronic kidney disease (CKD) are associated with bone mineral metabolism disorders, in addition to disarrangement of trabeculae structure and bone architecture. Increased alkaline phosphatase (ALP) and parathyroid hormone (PTH) have been related with abnormal bone turn over. Lycopene, a plant derived micronutrient, has strong quenching and free radical scavenging attitude.

Objectives: This study aimed to evaluate the effects of lycopene and calcifediol (25 OH D3) based Integrated Medicine on ALP, PTH and oxidative stress.

Methods: In octogenarians, nonagenarians and centenarians with chronic kidney disease (GFR :45 ±10,4 ml/min/1,73 m^2), vitamin D deficiency and abnormal ALP, PTH blood values, the effects of daily lycopene supplementation on blood oxysterols and on 4-hydroxy-2,3-trans- nonenal (4-HNE) as markers of oxidative stress were evaluated. The effects of calcifediol administration together with daily lycopene supplementation on PTH and ALP blood concentrations were also investigated.

Results: Daily lycopene supplementation induced a reduction of oxysterols (α-triol: 0.40 ± 0.07 µg / L *vs* 0.32 ± 0, 04 µg / L and β-epoxi cholesterol: 5.3 ± 1.3 µg / L *vs* 3.7 ± 0.6 µg / L) but not of 4-HNE (0.27 ± 0.18 nmol / L *vs* 0.25 ± 0.20 nmol / L). Vitamin D added to lycopene for two weeks decreased the blood values of ALP (106 ± 40 U / L *vs* 69 ± 19 U / L) and PTH (108 ±42 pg/ml *vs* 66± 21 pg/ml).

Conclusion: Tomato derived lycopene, with daily supplements, decreased cholesterol oxidation products. Calcifediol and vegetable derived antioxidant daily supplementations were associated to normalization of ALP and PTH.

Keywords*:* oxysterols; 4-hydroxynonenal; lycopene; alkaline phosphatase; parathyroid hormone; chronic kidney disease (CKD)

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Drinking functional coherent mineral water accompanies a strengthening of the very low frequency impact on heart rate variability, and mono and multifractal heart rhythm dynamics in healthy humans

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Study Design: A double blind, randomized pre-post cross-over clinical study.

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ABSTRACT

Background: Research on functional water has revealed its physiological functions and health-beneficial effects. Accordingly, this study explored the effects of drinking an average dietary volume of functional coherent mineral water (FCMW) on blood pressure, short-term cardiovascular variables, fractal heart rhythm dynamics, and salivary immunoglobulin A.

Methods: Fifteen healthy subjects were randomized in a pre-post crossover design, selected the morning after an overnight fast. Short-term electrocardiography (ECG) was measured before and after drinking either control mineral water (CMW) or FCMW on two separate occasions. Saliva was collected for four minutes before the start of each ECG measurement. Blood pressure was monitored in five-minute intervals for one hour.

Results: Drinking 100 ml of FCMW temporarily increased arterial blood pressure at 20 to 25 minutes in the 60 minutes post-drinking. Drinking CMW led to a significant reduction in the heart rate, while all-time domain and Power Spectral Density parameters (PSD) were unaffected. Consumption of FCMW resulted in a highly significant difference and decrease in heart rate, and an increase in NN interbeat intervals, and in two of the PSD parameters. A large increase in total power had a significant increasing effect on 2–3-minute oscillations of the very low frequency (VLF) power, indicating a specific change in the heart's intrinsic cardiac rhythm that is fundamental to health and well-being. An extension in mono and multifractal scaling of heart rate dynamics defines a healthy function and non-local adaptability, indicating a higher capacity to respond to unpredictable stimuli and stresses, a function which improves autonomic stability. The effect on the heart rate and VLF power suggest an efficient cellular metabolism and a stabilizing effect on mucosal immunoglobulin A.

Conclusions: Functional coherent mineral water with an apparent non-local electromagnetic identity triggered in healthy subjects a sustainable sympathetic response in cardiac VLF power, which is considered an intrinsic health-promoting rhythm produced by the heart itself that accompanies adaptive mono and multifractal heart rhythm dynamics.

Keywords: functional water, VLF-power, heart rate variability, fractal scaling, health improvement

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Dietary fat and insulin resistance: a connection through leptin and PPARγ activation

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ABSTRACT

Insulin resistance refers to reduced insulin action in peripheral tissues and impaired suppression of endogenous glucose production, a state which is critical for maintaining normal glucose homeostasis. Insulin resistance is partly explained by genetic factors and is strongly influenced by the individual's habitual lifestyle. Investigating factors that may influence the development of insulin resistance and their mechanisms of action is highly significant; one of these factors include dietary fat. Both quantitative and qualitative terms of dietary fat have been known to play an important role in the development of insulin resistance, although the mechanism underlying this effect is not fully understood. In this regard, the classical view has been that dietary fat quality mainly affects cell membrane fatty acid composition and consequently the membrane function. Recently, the relationship between dietary fat and insulin resistance has entered an advanced level due to the discovery that different fatty acids can regulate gene expression, transcriptional activity and adipocytokines secretion. In essence, this provides new mechanisms by which fatty acids exert their cellular effects. The present review critically assesses the effect of dietary fat quality on the development of insulin resistance in relation to the adipocytokine, leptin and the activation of the transcription factor, peroxisome proliferator-activated receptor gamma (PPARγ). It is evident that fat quality influences the development of insulin resistance and has a more important role than quantity. Leptin and PPARγ prove to be potential candidates linking dietary fat with insulin resistance. However, the exact role or mechanism of action of various types of dietary fat in the development of insulin resistance is still uncertain. Further well-controlled studies in humans are necessary to establish better evidence-based dietary fat recommendations for diabetes prevention and its clinical management.

Keywords: dietary fat, insulin resistance, diabetes, PPARγ activation, leptin.

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The effects of bioactive compounds on Alzheimer's disease and Mild cognitive impairment

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ABSTRACT

As the prevalence and rate of Alzheimer's disease are increasing around world, identifying effective treatments to manage cognitive impairment and neurodegeneration has become a global health priority. Decades of scientific research have led to a more comprehensive understanding of Alzheimer's Disease and Mild Cognitive Impairment (MCI), a transitional stage of accelerated cognitive decline. This understanding has enabled researchers to envision and develop novel Alzheimer's Disease therapies, including the use of bioactive compounds found in plants and animals. Within the past 15 years, a significant amount of clinical research has been published documenting the effects specific bioactive compounds have on patients with Alzheimer's Disease and MCI. This article reviews the results of this research, along with relevant epidemiological studies, measures of cognition, and disease pathologies to discuss whether sufficient evidence exists to support the use of specific bioactive compounds by individuals diagnosed with Alzheimer's Disease and MCI. The results of clinical trials within the last 15 years do not conclusively prove that the studied quantities of vitamin B, Omega-3 fatty acids, or bioactive compounds within Fortasyn Connect are beneficial for use in the management of Alzheimer's Disease or MCI. Additionally, the documented effects of these bioactive compounds do not warrant development of a functional food product to help manage AD or MCI.

Keywords: Bioactive compounds, Alzheimer's Disease, Mild cognitive impairment, Dementia, Vitamin B, Omega-3 fatty acids, DHA, EPA, Fortasyn Connect, Souvenaid.

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Charnoly body as a novel biomarker of nutritional stress in Alzheimer's Disease

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ABSTRACT

Background: The Charnoly body (CB) was discovered as a universal biomarker of cell injury in the developing undernourished rat cerebellar Purkinje neurons and in the intrauterine Domoic acid and Kainic acid-exposed mice hippocampus and hypothalamic neurons. The incidence of CB increased with the severity of nutritional and environmental neurotoxic insult.

Purpose: We proposed that stress (nutritional and environmental) induced cortisol release augments, whereas metallothioneins (MTs), insulin-like growth factor (IGF-1), and brain-derived neurotropic factor (BDNF) inhibit CB formation to prevent progressive neurodegeneration, early morbidity, and mortality in Alzheimer's disease (AD).

Results: CB is a pre-apoptotic biomarker of compromised mitochondrial bioenergetics, formed in the most vulnerable cell in response to nutritional stress, intrauterine infection, environmental toxins, and/or drug abuse due to free radical overproduction and mitochondrial genome down- regulation. It appears as a pleomorphic, electron-dense multi-lamellar, quasi-crystalline stack of degenerated mitochondrial membranes in highly susceptible neurons and may be induced by microbial infection. CB formation was accompanied with stunted neuritogenesis in the aging mitochondrial genome knock out (RhO_{mgko}) human dopaminergic (SK-N-SH, SHS-Y-5Y) neurons due to down-regulation of ubiquinone NADH oxidoreductase (complex-1). Transfection of RhO_{mgko} neurons with ubiquinone NADH oxidoreductase (complex-1) gene and CoQ_{10}, inhibited CB formation and augmented neuritogenesis, as confirmed in α-synuclein- metallothioneins triple knock out and weaver mutant mice. CB formation was attenuated in MTs- over-expressing weaver mutant mice.

Findings: Accumulation of CB at the junction of axon hillock impairs axoplasmic transport of enzymes, neurotransmitters, hormones, neurotropic factors (NGF, BDNF), and mitochondria at the synaptic terminals cause cognitive impairment, early morbidity, and mortality. Nonspecific induction of CB causes alopecia, myelosuppression, and GIT symptoms in multi-drug-resistant malignancies. Antioxidants and MTs inhibit CB formation as free radical scavengers by zinc- mediated transcriptional regulation of genes involved in growth, proliferation, differentiation, and development. Consequently, drugs may be developed to prevent CB formation and/or enhance charnolophagy as a basic molecular mechanism of intracellular detoxification to avert cognitive impairments in AD.

Conclusion: Brain regional monoamine oxidase-specific CBs can be detected by ^{11}C or ^{18}F- labeled MAO-A or MAO-B inhibitors *in vivo*, in addition to ^{18}FdG-PET neuroimaging to quantitatively assess and improve the mitochondrial

bioenergetics in AD.

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Glycemic index of some traditional fortified staple meals on the postprandial blood glucose responses of Nigerian undergraduate students: an open-label study

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ABSTRACT

Background: Staple meals, or meals that are eaten routinely, inexpensive, and are readily available, constitute a dominant portion of the standard diet in a given population. Most of the indigenous staple foods available are based on starchy foods, as is the case in Nigeria. The development of diabetes mellitus, obesity, cancer and cardiovascular disease (CVD) has been reported to be linked to the intake of high starchy foods. Consequently, there is a strong need to determine the glycemic index of commonly consumed fortified staple foods, as well as to determine the extent of their effects on the postprandial blood glucose responses of Nigeria undergraduate students.

Methods: Fifteen volunteers, non- diabetic undergraduate students aged 20–25yrs, on which a standard oral glucose tolerate test was performed were selected randomly after excluding those with family history of diabetes, in addition to smokers and alcoholics. The subjects reported by 8 am at the study centre each day after overnight fasting (10 – 12hrs) with certain precautions for a period of 6 days for the different prepared test meals, including: the glucose tolerance test (control), beans, rice, yam, unripe plantain and garri stews. Fasting blood samples (2ml each) were collected from the prominent arm veins of each student prior to the eating of one of the test meals of each day. Each test meal contained 50g carbohydrate portion per meal. After each meal had been eaten, 2ml venous blood samples were collected at 30 minutes interval for 120 minutes each day from each student and put into the specimen bottles for blood glucose estimations. The random sugar was determined 2hours later. A glucometer was used for measuring the blood sugar using test strips. The mean values of postprandial glucose blood sugar for each test meals from the randomly selected volunteered students were obtained. The glycosylated haemoglobin in the blood of the subjects was determined by the formulae method.

Results: The mean glycosylated haemoglobin of the students was 4.7%±0.002, with fasting blood sugar of 89.02±4.41mg/dl. The ratio of protein and fat contents of the serving portion containing 50g carbohydrate were highest in unripe plantain stew 7.84g and 5.31, respectively, but were lowest in yam stew 4.19g for protein and 2.02 for fat in beans vegetable stew. The glycemic index of the commonly consumed fortified staple test meals was highest in rice stew (107.7± 8.4), followed by yam stew (102.4±1.8), garri and stew (101.4±11.8), beans stew (86.9±6.7), and unripe plantain stew (81.8±8.4) in that order. The carbohydrate content of the commonly consumed fortified staple test meals was highest in garri with stew (68.2±0.2g) and lowest in unripe plantain stew while the fibre content was highest in plantain stew (5.8±0.4g) and lowest in rice stew (2.8±0.12g). The mean blood oral glucose tolerance test of the students was below 120mg/dl, but had the mean peak after an hour interval (112.8±7.3mg/dl). The increment on the postprandial blood glucose after ingestion of the test

meals was highest for garri and stew meal (93.1±2.4mg/dl), but lowest for unripe plantain stew meal (74.3±11.6mg/dl) after 120 minutes the test meals were ingested.

Conclusion: Unripe plantain stew meal had the lowest glycemic index value, with lowest postprandial blood glucose response for the period of time the staple test meals were ingested. This could be attributed to the relatively higher level of fibre content of the unripe plantain than the other staple test meals.

Key Words: glycemic index, postprandial blood glucose concentrations, glucose tolerance test, glycoslated haemoglobin

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Antioxidant, ACE-Inhibitory and antibacterial activities of *Kluyveromyces marxianus* protein hydrolysates and their peptide fractions

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ABSTRACT

Background: There has been evidence that proteins are potentially excellent source of antioxidants, antihypertensive and antimicrobial peptides, and that enzymatic hydrolysis is an effective method to release these peptides from protein molecules. The functional properties of protein hydrolysates depends on the protein substrate, the specificity of the enzymes, the conditions used during proteolysis, degree of hydrolysis, and the nature of peptides released including molecular weight, amino acid composition, and hydrophobicity.

Context and purpose of this study: The possibility of using strain of *Kluyveromyces marxianus* as a source of yeast extract with antioxidant, antibacterial, and ACE-inhibitory activity was the subject of this research.

Results: Autolysis and enzymatic hydrolysis were completed respectively, after 96 h and 5 h. Overall, trypsin (18.52% DH) and chymotrypsin (21.59% DH) treatments were successful in releasing antioxidant and ACE inhibitory peptides. Autolysate sample (39.51% DH) demonstrated poor antioxidant and ACE inhibitory activity compared to trypsin and chymotrypsin hydrolysates. The chymotrypsin 3-5 kDa (301.6±22.81 µM TE/mg protein) and trypsin < 3 kDa (280.16±39.16 µM TE/mg protein) permeate peptide fractions showed the highest DPPH radical scavenging activity. The trypsin <3 kDa permeate peptide fraction showed the highest ABTS radical scavenging (1691.1±48.68 µM TE/mg protein) and ACE inhibitory (IC_{50}=0.03±0.001 mg/mL) activities. The fraction (MW=5-10 kD) obtained after autolysis treatment showed antibacterial activity against *St. aureus* and *Lis. monocytogenes* in well diffusion screening. The minimum inhibitory concentration (MIC) value was 13.3 mg/mLagainst *St. aureus* and *Lis. monocytogenes* calculated by turbidimetric assay and it showed bactericidal activity against *St. aureus* at 21.3 mg/mL protein concentration.

Conclusions: Altogether, the results of this study reveal that *K. marxianus* proteins contain specific peptides in their sequences which can be released by enzymatic hydrolysis and autolysis.

Key words: *Kluyveromyces marxianus*, Antioxidant activity, ACE-inhibitory, Antimicrobial activity, Protein hydrolysate, Bioactive peptide.

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A pilot study to determine the effects of lean beef consumption on markers of metabolic syndrome

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ABSTRACT

Statement of Objective: To determine the effects of a diet that provides 30% energy from protein with ½ as lean, red meat on risk factors of metabolic syndrome in humans.

Design, Setting, and Participants: A 3-month, randomized, control, intervention trial with 33 participants (Beef-Intervention n=18; DASH-Control n=15) with markers of metabolic syndrome. Registered Dietitians Nutritionists recruited and educated participants on Beef- Intervention Lean Beef Pattern, (30% of energy from protein with ½ as lean red meat, 40% carbohydrate, 30% fat) or DASH-Control dietary pattern, (15% of energy from protein, 55% carbohydrate, and 30 % fat). Of the 33 participants who completed the study; 21 were female and 12 male.

Outcome Measures and Analysis: Bodyweight (BW), fasting serum lipoproteins [total cholesterol (TC), LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), and triglycerides (TG)], hemoglobin A1C (HbA1C), dietary satisfaction, and general health status were assessed at baseline and post intervention**.** A three-day diet journal was collected to assess for calorie and macronutrient intake at baseline and post-intervention. Repeated measures analysis was used to determine group differences from baseline to post-intervention and for interactions. Variables were checked for normality, and non-normal variables were transformed prior to analysis. Statistical significance was set at $p \leq 0.05$.

Results: There were no significant changes in total cholesterol, LDL-C, and HDL-C. There was a significant time by group interaction effect for TG (baseline to post; Beef-Intervention 207±87mg/dL to 148±53; DASH-Control, 200±88 to 193±96.) Both groups had decreased BW and HgA1c from baseline to post. Those assigned to Beef-Intervention demonstrated compliance with dietary instructions that included ½ of 30% total calories from protein as lean red meat (baseline to post-intervention; 34.8%±17.7% to 30%±26.8%). Both groups reported a higher level of current dietary satisfaction, a higher level of general health, and walking minutes and total increases in physical activity.

Conclusion and Implications: Lipid parameters, BW, and HbA1C of participants with metabolic syndrome randomized to the Beef-Intervention promoting 30% energy from protein with ½ as lean, red meat had outcomes that were similar or improved to those randomized to DASH-Control diet. The implication is, although larger studies in greater numbers still need to be done, that the inclusion of LRM in calorie-reduced diets may be used short term as an alternative to the DASH diet for those with MetS for weight and TG reduction.

Keywords: Metabolic Syndrome, Beef, Serum Lipid levels

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Extract of the sea cucumber, *Holothuria scabra*, induces apoptosis in human glioblastoma cell lines

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ABSTRACT

Background: Glioblastoma is the most aggressive primary brain tumor resistant to conventional treatment, and has a frequent recurrence. *Holothuria scabra* is the most widely consumed sea cucumber in Thailand and Asian countries. Sea cucumber extracts have valuable bioactive ingredients that are utilized in Chinese traditional medicine for several therapeutic measures including anti-cancer. In this study, we aimed to test the anticancer activity of *H. scabra* body wall extract in ethyl acetate fraction against two human glioblastoma cell lines A172 and U87MG.

Material and methods: The anticancer effect of the ethyl acetate fraction of body wall extracts from *H. scabra* (HSBWEA) was tested against two human glioblastoma cell lines A172 and U87MG to determine cell viability, apoptotic cell analysis, mitochondrial membrane potentials, nuclear condensation and expression of apoptotic molecules. The bioactive compound in the extract was characterized by LC-MS/MS.

Results: The extract exhibited strong cytotoxic effect to A172 and U87MG cells with IC50 4.23 and 4.46 µg/ml, respectively. The extract also induced both early and late stages of apoptosis, loss of mitochondrial membrane potentials and nuclear condensation and fragmentation. After treatment with the extract for 24 h, the cells expressed increasing amounts of a pro-apoptotic Bax and caspase-3 while an anti-apoptotic Bcl-2 was decreased in a concentration-dependent manner. The major bioactive components in this extract are triterpene glycosides similar to those described previously in *H. scabra* as well as in other related sea cucumber species.

Conclusion: The crude extract from the body wall of *H. scabra* exhibited anticancer activity against human glioblastoma cells through the mitochondrial-mediated apoptotic pathway, and the compounds in the extract might be a novel candidate for anti-glioblastoma.

Keywords: Sea cucumber, *Holothuria scabra*, Glioblastoma, Triterpene glycoside, Apoptosis

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Effect of kefir on *Fusobacterium nucleatum* in potentially preventing intestinal cancer

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ABSTRACT

Background: *Fusobacterium* spp. are known to be part of mouth and intestinal microbiota. *Fusobacterium nucleatum* is an obligate anaerobe, Gram negative, non-spore forming pleomorphic bacillus that can cause diseases not only in the mouth and teeth but also in the brain, pleura, lungs and liver. It was noted that *F. nucleatum* induces fetal death (fetal demise) in pregnant women. Recent studies indicate that *F. nucleatum* could lead to colon cancer by binding to the epithelial tissue. Kefir is produced from kefir grains that are a source of probiotics. Fermented dairy products and especially kefir and yogurt are significant for functional nutrition. In kefir grains, lactic acid bacteria, acetic acid bacteria and yeasts are embedded in a polysaccharide matrix, called kefiran. When kefir grains are added to milk and incubated for approximately 22 h at 25°C, microorganisms in the grains continue to proliferate in milk with the production of functional metabolic compounds. While yogurt has mainly two bacteria, authentic kefir has its characteristic *Lactobacillus kefiranofaciens*, *Lactobacillus kefir* and *Lactobacillus kefirgranum*, in addition to many other types of lactic acid bacteria (LAB). Previous studies have indicated that fermented dairy products can cause probiotic effects such as improvement in digestive system health, reduction in serum cholesterol, improvement in lactose tolerance, improvement in immune function, control of irritable bowel symptoms, and anticarcinogenic properties.

Objective: The aim of this research was to report the effects of fermented dairy products *in vitro* on the growth of *F. nucleatum*. Milk, kefir made from natural kefir grains, commercial kefir produced from kefir starter culture, yogurt produced from natural yogurt starter culture and commercial yogurt produced from yogurt starter culture were used against *F. nucleatum*.

Methods: *F. nucleatum* (ATCC 25586) was grown in Fluid Thioglycollate Medium at 37°C for 3 days under anaerobic incubation. Kefir was made from authentic kefir grains with 2% by volume inoculation at 25°C for 22h fermentation. Yogurt was made using a natural starter culture. The inhibition effects of fermented dairy products were determined *in vitro* against *F. nucleatum*. Zone inhibition tests were conducted using sterile disks that were immersed into kefir and yogurt samples and subsequently placed on Brucella Blood Agar with Hemin and Vitamin K1 inoculated with *F. nucleatum*; plates were incubated at 37°C for 3 days under anaerobic conditions. Inhibition zones were determined after the incubation was completed. Additionally, lactic acid bacteria (counted on MRS and m17), yeast (PDA) and related pathogen were observed after anaerobic incubation by adding a certain amount of kefir and yogurt cultures into *F. nucleatum* inoculated medium.

Results: Authentic kefir samples exhibited distinct inhibitory zone against *F. nucleatum* after incubation agar plates. The largest zone of inhibition (with 9.5 mm) was caused by natural kefir samples made from kefir grains. Yogurt samples provided 8.25 mm zone inhibition against *F. nucleatum*. The milk used to make kefir and yogurt did not cause any zone of inhibition. It was also discovered that number of *F. nucleatum* in Thioglicollate Medium

decreased depending on inoculated concentrations of kefir and yogurt cultures.

Conclusion: Kefir is known to have positive effects on health and especially intestinal health. Therefore, these findings are important for showing an inhibition effect of fermented dairy products against a pathogen and possible carcinogen. These results suggest that regular consumption of natural fermented dairy products especially kefir should be included in a functional diet. The impact of these cultured dairy products could be promising and warrants further investigation with *in vivo* studies.

Keywords: *Fusobacterium nucleatum*, pathogen, carcinogen, fermented foods, kefir, kefir grains

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Pharmacokinetic of ^{3}H-deacetylasperulosidic acid in mice

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ABSTRACT

Background: An investigation was conducted to determine the fate of the iridoid derivative deacetylasperulosidic acid (DAA) after oral application to mice.

Methods: DAA was extracted from *Morinda citrifolia* leaf and purified by preparative HPLC. The identity was verified by MS and NMR spectroscopy. A sample of DAA was radioactively labelled with tritium and applied to mice by gavage. The pharmacokinetic of the radioactivity was investigated in blood, organs, urine and feces. Metabolites were isolated in blood and urine by HPLC and identified by LC-MS. In vitro incubation of DAA with mouse duodenum and liver homogenate and human fecal bacteria was performed and possible metabolites were separated by HPLC.

Results: DAA was rapidly absorbed and excreted mainly via the kidneys with a half-life of 30 minutes. Radioactivity was present in all organs with highest concentrations in kidney and liver. Almost 100% of the radioactivity isolated from urine and organs could be identified as unchanged DAA. Additionally, no metabolism could be observed after in vitro incubation of DAA with mouse small intestine or liver homogenate. However, a total breakdown of the molecule was observed after incubation of DAA with human intestinal bacteria.

Conclusion: The absorption and excretion of glycosides such as DAA in mammals without hydrolysis is a potential defense mechanism of animals against the toxicity of these compounds.

Keywords: Deacetylasperulosidic acid, DAA, tritium label, pharmacokinetic, iridoid, metabolism

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Effects of selected antioxidant food extracts on postprandial glucose responses in healthy individuals

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ABSTRACT

Background: Obesity and diabetes are highly prevalent in Western countries. Both of these conditions can be associated with impaired glucose control and hyperglycemia. Studies have identified that antioxidants have the ability to regulate blood glucose levels. However, the effects of specific high-antioxidant food extracts on blood glucose levels have not been well characterized. Thus, this study aimed to measure the effects of selected antioxidant food extracts on postprandial glucose responses in healthy individuals.

Methods: Ten healthy individuals were recruited into a randomized, single-blinded study. Participants consumed five different high-antioxidant food extracts (one per session, each >48 hours apart) that were matched for total antioxidant content 10 mins prior to ingestion of 50 g of available carbohydrate from either a glucose load or white bread (with ham) after an overnight fast. Blood glucose levels were measured using capillary sampling every 15 mins for two hours and the incremental area under the glucose curve (IAUC) was also measured. The IAUC values for the test foods were compared to the glucose-only and bread-only controls.

Results: Amla berry-, grape seed- rooibos tea- and green tea- extracts as well as propolis tincture were all strong glycemic modulators, significantly decreasing the IAUC by 25-40% compared to the glucose-only or white bread controls (all $p < 0.05$).

Conclusion: Antioxidants are able to modulate postprandial glucose responses in healthy subjects. These results suggest that further research is warranted to determine whether these antioxidant-rich foods are beneficial to people with prediabetes or type 2 diabetes mellitus.

Keywords: Antioxidants, glycemic response, blood glucose levels, postprandial response

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Glycaemic index values and physicochemical properties of five brown rice varieties cooked by different domestic cooking methods

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ABSTRACT

Background: The prevalence of diabetes has increased dramatically in recent decades in the regions where people excessively consume white rice. Due to higher nutritional values and bioactive components, low to medium glycaemic index (GI) brown rice could be a potential alternative to white rice in these regions.

Methods: Five varieties, Chiang (CH), Sungyod (SY), Lepnok (LP) from Thailand, Long grain specialty 1 (LS1) and Long grain specialty 2 (LS_2) from Malaysia were tested for GI. Ten test foods were prepared from 5 varieties by 2 cooking techniques (pressure cooker, PC and rice cooker, RC). Overnight fasted 10 healthy subjects were fed with 25 g glucose as a reference food (RF) on 3 occasions and amount equivalent to 25 g available carbohydrate portion of test food (TF) on 1 occasion in separate days. Fasting and post-prandial capillary blood glucose was measured via finger-prick methods at 0, 15, 30, 45, 60, 90 and 120 min, and the incremental area under curve (iAUC) was determined. The GI of each TF was calculated as percentage of incremental area under curve (iAUC) of TF over RF.

Results: The mean GI values of SY (72 – 81, high), CH and LP (59 – 65, medium) and LS_1 and LS_2 (64 – 73, medium to high) for cooking were discovered by PC and RC methods. The GI did not vary significantly ($p>0.05$) among varieties as well as between cooking methods. GI showed a significant negative correlation with the amylose content ($r = –0.70$, $p<0.05$) and significant positive correlation with cold peak viscosity ($r = 0.80$, $p<0.01$).

Conclusions: All five rice varieties irrespectively of the cooking method used are classified as medium to high GI foods. Medium GI varieties could have potential of being used in diabetic diet. Cooking methods did not significantly alter the glycaemic characteristics of the studied varieties. Amylose content and pasting properties can be used for predicting GI of brown rice. It is urgent to explore low GI brown rice varieties in these regions.

Keywords: Glycaemic index, diabetes, brown rice, cooking methods

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Accumulation of solvent-soluble and solvent-insoluble antioxidant phenolics in edible bean sprouts: implication of germination

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ABSTRACT

Background: Edible bean sprouts are popular fresh vegetables widely recognized for their nutritional quality. However, while their antioxidant capacity and phenolic composition in both solvent-soluble and solvent-insoluble extracts has not been systematically evaluated.

Methods: The antioxidant capacity and phenolic composition in both solvent-soluble and solvent-insoluble fractions of 12 cultivars of edible bean sprouts were evaluated, and relationships of antioxidant capacity and total phenolic content were also analyzed.

Results: Sprouts demonstrated a wide range of antioxidant capacity and total phenolic content, with lower but substantial antioxidant capacity and total phenolic content in the solvent-insoluble fractions. Highest levels were found in the green mung bean sprout. Phenolic compounds, such as catechin, ellagic acid, ferulic acid, gallic acid and *p*-coumaric acid were widely detected in these sprouts. Additionally, a positive correlation was discovered between antioxidant capacity and total phenolic content in these edible bean sprouts.

Conclusions: Germination generally resulted in the accumulation of antioxidant phenolics in the most edible bean sprouts. Edible bean sprouts with high antioxidant phenolics can be valuable natural sources of dietary antioxidants for the prevention of oxidative stress-related chronic diseases.

Keywords: Bean sprout, Germination, Antioxidant capacity, Radical scavenging capacity, Phenolic composition, Solvent-insoluble phenolics

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Sauerkraut: A probiotic superfood

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ABSTRACT

Background: Sauerkraut could potentially be a probiotic superfood. Sauerkraut does not require the use of a starter culture to cultivate these beneficial bacteria. All that is needed is a measure of salt and the cabbage. Naturally made, unprocessed sauerkraut contains probiotic microorganisms called Lactic Acid Bacteria (LAB). LAB is one of the most significant organisms and has established benefits. For example, Lactic Acid Bacteria has established benefits with the treatment of diarrhea, constipation, irritable bowel syndrome, infections (urogenital, urinary and candida). LAB have also been shown to enhance immune system function to help prevent various illnesses and promote lactose digestion. Nevertheless, there is very little conclusive evidence on how much LAB is in sauerkraut and if there is enough present to confer benefits.

Purpose: Determine if various serving sizes of homemade sauerkraut (2 Tbsp., ½ cup, & 1 cup) meets the recommended CFU range in comparison to a control (supplement probiotic).

Methods: Sauerkraut was prepared with no starter culture. Modified Lactobacillus Media was used to culture LAB. The capsule serving (0.8g) was diluted with 99.2g PBS (1/100) and 10g of sauerkraut was diluted with 90g PBS (1/10). For serial dilutions, 1mL of each of the samples was diluted into 9 mL MRS broth for the dilutions (10^{-1}-10^{-10}). Then 1mL from each test tube is transferred into corresponding petri dishes. Melted Lactobacillus MRS agar is then mixed into each of the petri dishes. All petri dishes are then placed into a candle light jar and placed in an incubator at 37 degrees Celsius (98.6^{o}F) for 5 days. After five days, the petri dishes with 25-250 visible cultures were counted. The number counted was multiplied by the dilution which gave the total number CFUs/g. The LAB concentration of the sauerkraut was calculated by multiplying the CFU/g times the serving size.

Results: The results were calculated as the mean of CFUs recorded from the 3 trials for both the control (supplement) and the sauerkraut. The control group was calculated as a mean of 4.3x107 CFUs with a Relative Standard Deviation (RSD) of 3.5% CFUs. The sauerkraut averages were calculated for each of the serving sizes. The 2 Tbsp. serving has a mean of 1.5x106 (RSD= 32%), the ½ cup has a mean of 5.9x106 (RSD= 31%), and the 1 cup serving has a mean of 1.2x107 (RSD= 30%).

Conclusion: The study concludes that sauerkraut (even the two Tbsp. serving) meets the recommended CFU range. Based on these findings, sauerkraut can be considered a “probiotic superfood”.

Keywords: Sauerkraut, probiotic superfood, supplement probiotic, Lactobacillus

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Lactobacillus gasseri SBT2055 stimulates immunoglobulin production and innate immunity after influenza vaccination in healthy adult volunteers

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ABSTRACT

Background: *Lactobacillus gasseri* strain SBT2055 (LG2055) is a human intestine-originating probiotic bacterium and potent probiotic known to exert various health promotion effects, including prevention of abdominal adiposity in rats and humans. A recent finding in mice has suggested that oral administration of LG2055 induces a protective effect against influenza A virus infection. In this context, evidence for the efficacy of LG2055 using a human clinical trial was imminently required.

Methods: To confirm this in humans, a randomized, double-blind, placebo-controlled, parallel-group study in healthy adult volunteers was conducted to examine the effect of drinkable yogurt (DY) containing LG2055 on influenza, with vaccine-specific antibody responses as the primary objective and innate immune responses as the secondary objective. Subjects were asked to consume 100 g/day of DY with LG2055 (LG2055 group; n = 94) or without LG2055 (placebo group; n = 94) for 16 weeks. After 4 weeks, all subjects received a trivalent influenza vaccine.

Results: We found that the intake of LG2055 DY increased hemagglutination inhibition titers against influenza viruses A/H1N1 and B and the rate of seroprotection against influenza B after vaccination as compared with the intake of placebo DY by healthy volunteers. In support of this result, we confirmed that total IgG and IgA levels in plasma and sIgA production in saliva were also higher in the LG2055 group than in the placebo group. Furthermore, the intake of LG2055 DY enhanced natural killer cell activity and myxovirus resistance A gene expression, which is one of the antiviral genes stimulated by type I or type III Interferons in peripheral blood mononuclear cells.

Conclusions: These results strongly indicate that LG2055 activates both the innate and adaptive human immune responses, suggesting the potential to prevent influenza virus infections by providing specific probiotics as complementary foods.

Keywords: human clinical trial, innate immunity, influenza virus, *Lactobacillus gasseri*, vaccine

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Effects of grape wine and apple cider vinegar on oxidative and antioxidative status in high cholesterol-fed rats

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ABSTRACT

Background: Oxidative stress is the result of an imbalance between the rates of free radical production and elimination via endogenous antioxidant mechanisms such as antioxidant enzymes, which include glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), and catalase (CAT). There are mainly two vinegar production methods. The first is the surface method which is also known as the traditional method. The second method is known as the industrial method or submerged method which involves the use of a submerged culture with supplemented aeration.

Objective: The aim of this study is to determine the effects of grape and apple cider vinegar consumption against oxidative stress in rats fed a high cholesterol diet.

Methods: Fifty-four male, adult Wistar albino rats were included in this study. Rats were fed for 7 weeks by oral gavage as given in the experimental procedure. Rats were sacrificed at the end of the experiment and blood samples were collected. Catalase (CAT) activity, malondialdehyde level (MDA), glutathione peroxidase (GSH-Px) activity, superoxide dismutase (SOD) activity were analyzed. Grape and apple vinegar fermentation products prepared using both the surface culture method and submerged methods were prepared. The total antioxidant activity of vinegar samples were measured by Oxygen Radical Absorbance Capacity (ORAC) and 2,2'-azinobis (3-ethlybenzthiazoline)-6-sulfonic acid (ABTS) methods.

Results: Levels of CAT, GSH-Px, SOD in high cholesterol diet group (CHCNT) were significantly decreased while MDA levels were significantly increased in control rats fed with the high-cholesterol diet (CHCNT) when compared to the Control group (CNT) ($P<0.05$). Levels of MDA, which is the end-product of lipid peroxidation, were significantly decreased in the apple cider vinegar administered groups when compared to the CHCNT ($P<0.05$). GSH-Px levels were significantly increased in rat groups, which were fed with the vinegars produced by traditional surface methods ($P=0.03$, $P=0.001$ respectively) as compared to the CHCNT. SOD levels of rat groups which were fed with all the vinegars were significantly increased as compared to CHCNT group ($p<0.05$).

Conclusions: This study indicated that a high cholesterol diet increased lipid peroxidation and consumed the antioxidant enzymes. Although the impact of vinegars on antioxidant enzyme activity differs, the use of vinegar and especially vinegars produced by surface culture methods seem to have favorable effect *in vivo*.

Keywords: Oxidative stress, grape vinegar, apple cider vinegar, glutathione peroxidase (GSH- Px), superoxide

dismutase (SOD), malondialdehyde (MDA), catalase (CAT)

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Vitamin B12 supplementation and cognitive scores in geriatric patients with Mild Cognitive Impairment

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ABSTRACT

Background: The Neurodegenerative diseases are increasingly affecting the elderly with a severe impact on their brain health. There is a wide gap in supplementation based studies for increasing the cognition levels of the geriatric population, especially in developing countries like India which are at extreme risk of developing neurological disorders. And recently Vitamin B12 has drawn considerable attention due to its ability to improve the cognitive status. Current literature has linked the possibility of alleviating neurological disorders in the elderly with effective vitamin B12 management. Abundant animal and human models have proved that supplementation of vitamin B12 is beneficial for the restoration of cognitive functions.

Objective: To supplement vitamin B12 deficient mild cognitively impaired geriatric patients with injectable doses of vitamin B12 followed by impact evaluation.

Methods: Screening of the mild cognitively impaired patients was carried out using the Mini- Mental State Examination and Yamaguchi Fox Pigeon Imitation test. Baseline information was elicited from the patients residing in urban Vadodara (a district in the state of Gujarat), India. This included socio-demographic, medical and drug history, anthropometric and physical activity pattern, in addition to biochemical parameters comprising of serum vitamin B12 and glycated haemoglobin profile. A sub-sample of 60 patients with mild cognitive impairment (MCI) demonstrating severe vitamin B12 deficiency were conveniently enrolled for injectable doses of Vitamin B_{12} in the dosage of 1,000 µg every day for one week, followed by 1,000 µg every week for 4 weeks & finishing with 1,000 µg for the remaining 4 months. An intervention six- month after the experiment with all the parameters were elicited.

Results: Vitamin B12 supplementation resulted in a significant ($p<0.001$) improvement in the MMSE scores of the patients with a rise of 9.63% in the total patients. Gender-wise division also highlighted a significant increase ($p<0.001$) in the scores by 6.79% and 12.46% in overall males and females and a 10.20% and 8.24% rise for young-old (60-69 yrs) and old-old (70-85 yrs) categories, respectively. As a result, 27 patients progressed towards the normal category from the MCI state being assessed by MMSE scores. In the same manner, YGFPIT too demonstrated a 38% increase in normal with 35% males, 42% females, 41% young–old and 31% old-old moving to normal status. Thus, a total number of 28 patients progressed to the normal condition as per YGFPIT.

Conclusion: Ultimately, vitamin B12 supplementation was discovered to be significantly effective, as the placing of serum vitamin B12 within MCI patients caused a turn from the deficiency state to sufficient levels and in turn increased their performance in MMSE and YFPIT scores.

Keywords: Mild Cognitive Impairment, vitamin B12, geriatrics, cognition

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The cytotoxic and anti-proliferative activity of high molecular weight pectin and modified citrus pectin

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ABSTRACT

Background: Pectin is a heterogeneous polysaccharide mainly present in citrus fruits and has different biological activities.

Objective: High molecular weight Citrus Pectin and modified citrus pectin (MCP) were tested for their cytotoxic, anti-proliferative, and anti-oxidant activity.

Methods: The cytotoxicity of pectin was studied against HaCaT cell line (human keratinocyte cell line) using Trypan blue method and LDH-cytotoxicity assay. Anti-proliferative activity was assayed using a WST-1 proliferation kit. Antioxidant activity was determined using the DPPH scavenging assay.

Results: MCP and Pectin both reduced the viability of HaCaT cells in a dose dependent manner; however, MCP was found to be more cytotoxic than high molecular weight citrus pectin since it had a lower IC_{50} (300ug/ul). At non-cytotoxic concentrations, the viability of cells decreased with increase of concentration of MCP as determined by the WST-1. MCP exhibited a higher antioxidant effect than pectin (SC_{50} at a concentration range between 2 and 4mg/ml).

Conclusion: This study suggests that MCP exhibits a stronger cytotoxic and anti-proliferative effect on HaCaT cell line than pectin. The most probable explanation of this observation is the different effects due to the variable molecular weight and exposed side-chains of MCP and high molecular weight citrus pectin.

Keywords: Cytotoxic, Anti-proliferative, Pectin, MCP, HaCaT cell line

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Decaffeinated coffee consumption induces expression of tight junction proteins in high fat diet fed rats

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ABSTRACT

Background: Recent evidence indicates that gut microbiota plays a key role in the development of NAFLD through the gut-liver axis. An altered gut permeability induced by alterations of tight junction (TJ) proteins allows the passage of bacteria and substances leading to liver inflammation, hepatocyte damage and fibrosis. This study aims to evaluate the influence of decaffeinated coffee on gut permeability in a rat model of fat liver damage induced by a high fat diet (HFD).

Methods: Twelve male Wistar rats were assigned to 3 groups. The first group received HFD for 5 months and drank water. The second group received HFD for 5 months and drank water added with 1.2mL decaffeinated coffee/day starting from the 4th month. The third group received standard diet (SD) and drank water. Protein and mRNA expression levels of Toll-Like Receptor- 4 (TLR-4), Occludin and Zonula occludens-1 (ZO-1) were assessed in rat intestines.

Results: A significant reduction of Occludin and ZO-1 was observed in HFD fed rats (0.97±0.05 vs 0.15±0.08 $p<0.01$, and 0.97±0.05 vs 0.57±0.14 $p<0.001$ respectively. This reduction was reverted in HFD+COFFEE rats (0.15±0.08 vs 0.83±0.27 $p<0.01$ and 0.57±0.14 vs 0.85±0.12 $p<0.01$ respectively). The TLR-4 expression up-regulated by HFD was partially reduced by coffee administration.

Conclusions: HFD impairs the intestinal TJ barrier integrity. Coffee increases the expression of TJ proteins, reverting the altered gut permeability and reducing TLR-4 expression.

Key Words: HFD, coffee, Occludin, Zonulin-1, rat model, TLR-4.

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Comparison of the amino acid and peptide composition and postprandial response of beef, hydrolyzed chicken, and whey protein nutritional preparations

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ABSTRACT

Background: Increasing dietary protein intake synergistically improves the effect of exercise to stimulate muscle protein synthesis. The purpose of this study was to evaluate the plasma amino acid response of two novel protein nutritional preparations, beef protein isolate (BeefISO™) and hydrolyzed chicken protein isolate (MyoCHX™).

Methods: The postprandial plasma amino acid response over 3 hours was monitored in young adults (n=6) following consumption of 23 grams of WPC, BeefISO™, or MyoCHX™. Amino acid compositional analysis and molecular weight distributions of each protein were performed by HPLC. Statistical analyses were performed using one-way or two-way ANOVA where appropriate and corrected for multiple comparisons to account for the cross-over design.

Results: Compositional evaluations revealed similar levels of essential and branched-chain amino acids for WPC and MyoCHX™. While the results of this study predictably demonstrated plasma amino acids levels increased following consumption of the different proteins, the kinetics of the postprandial response was unique to each protein source. WPC and MyoCHX™ were rapidly absorbed with maximum plasma amino acid concentrations observed at 30 and 15 min, respectively. The slightly faster absorption of MyoCHX™ was associated with the increased peptide content of MyoCHX™ (greater than 76% of protein is <2kDa). BeefISO™ exhibited sustained release characteristics as evidenced by increased post prandial amino acid concentrations after 3 hours.

Conclusions: The protein preparations studied each had different amino acid profiles and absorption kinetics. WPC and MyoCHX™ contained a higher essential amino acid content and were rapidly absorbed with plasma amino acid concentrations peaking within 30 minutes following consumption. BeefISO™ contained a higher proportion of conditionally essential amino acids that steadily increased in plasma over 3 hours, indicating a sustained release profile for BeefISO™. Each of these three protein preparations have been shown to facilitate similar improvements in body composition following a resistance-exercise training program. The paradoxical finding that proteins with varying composition, molecular weight, and digestibility can lead to similar effects on body composition suggests the need to evaluate proteins based on total nutritional potential rather than as a delivery vehicle for single amino acids.

Key Words: Protein digestibility; amino acids; body composition; beef protein; chicken protein

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Enhancement of water soluble wheat bran polyphenolic compounds using different steviol glucosides prepared by thermostable β-galactosidase

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ABSTRACT

Background: Production of wheat bran (WB) for human consumption is estimated to be about 90 million tons per year. WB contains an abundant source of dietary fiber, minerals, vitamins, and bioactive compounds. WB is a by-product of milling and contains an abundant source of carbohydrate (60%), protein (12%), fat (0.5%), minerals (2%), and bioactive compounds such as phenolic acids, arabinoxylans, flavonoids, caroteinoids alkylresorcinol and phytosterols. These are known for health promoting properties such as controlling glycemic index, reducing plasma cholesterol level, antioxidant, anti-inflammatory, and anticarcinogenic activities. Several terpene glycosides such as mogroside V, paenoiflorin, geniposide, rubusoside (Ru), stevioside (Ste), rebaudioside A (RebA), steviol monoside, and stevioside glucoside have been discovered to enhance the solubility of a number of pharmaceutically and medically important compounds that normally show poor solubility in water.

Context and purpose of this study: In this study, in order to increase soluble extraction of polyphenol compounds of WB using Ru, the expression of β-galactosidase from *Thermus thermophilus* (*T. thermophilus*) was optimized using different *E. coli* hosts and a different concentration of lactose inducer rather than of isopropyl-1-thio-β-D-galactopyranoside (IPTG) for industrial production. Additionally, the effect of different steviol glucosides (Ru, Ste, RebA, and SG) on the enhancement of polyphenol compounds extraction from wheat bran was studied.

Results: β-galactosidase from *T. thermophilus* was used for the specific conversion of stevioside (Ste) to rubusoside (Ru) with 92% productivity. The enzyme was optimized to be expressed in *E. coli.* With 7 mM lactose, the β-galactosidase activity expressed was 34.3, 14.2, or 34.4 ± 0.5 U/mL in *E. coli* BL21(DE3)pLysS, Rosetta(DE3)pLysS, or BL21(DE3) at 37°C, and 9.8 ± 0.2, 7.0 ± 0.5, or 7.4 ± 0.2 U/mL at 28°C respectively. The expression of β-galactosidase was dependent on the lactose concentration and the highest activity was obtained with the conditions of 5 mM lactose in *E. coli* Rosetta(DE3)pLysS, 53.3 ± 1.5 U/mL. 78% of the mesophilic proteins was

eliminated by heating at 70°C for 15 min with 89% β-galactosidase activity recovery. The total polyphenol content of WB extracted by water, Ru, Ste, rebaudioside A (RebA), and steviol glucosides (SG) were 533.8 ± 9.6 µg/mL, 633.3 ± 1.25 µg/mL, 604.4 ± 10.1 µg/mL, 654.8 ± 26.5 µg/mL, and 601.2 ± 33.4 µg/mL, respectively. The DPPH radical scavenging activity prepared by water, Ru, Ste, RebA, and SG extraction were 8.76 ± 0.3 mg/mL, 4.87 ± 0.3 mg/mL, 5.34 ± 0.22 mg/mL, 7.27 ± 0.1 mg/mL, and 7.82 ± 0.02 mg/mL respectively.

Conclusions: To increase soluble extraction of polyphenol compounds of WB using Ru, the expression of β-galactosidase from *T. thermophilus* was optimized using different *E. coli* hosts and a different concentration of lactose inducer rather than isopropyl-1-thio-β-D-galactopyranoside (IPTG) for industrial production of the enzyme. The highest antioxidant activity was shown in WB extracted by Ru. The number of glucosyl units attached to steviol can possibly affect the efficiency of antioxidant activity of WB extracted by steviol glucosides.

Keywords: Rubusoside, β-galactosidase, lactose induction, immobilized enzyme, wheat bran, steviol glucosides

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Effect of some tropical eggplant fruits (Solanum Spp) supplemented diet on diabetic neuropathy in male Wistar rats *in- vivo*

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ABSTRACT

Background: Eggplant is a popular crop grown in the subtropics and tropics for its fruits. Although it is a perennial plant, its fruits are grown commercially as an annual crop. The fruit is primarily used as a vegetable for various dishes. The eggplant has various kinds of species, which are highly variable in color, shape, and size.

Content and Purpose of this study: This study focused on comparing the effect of dietary tropical eggplants *Solanum kumba* (PG) *Solanum gilo* (PW) and *Solanum aethiopicum* (PGW) species. Type-II-Diabetes was induced experimentally by high fat fed/low dose streptozotocin (STZ) 35 mg/kg body weight on male wistar rats. The diabetic subjects were fed diets supplemented with 20–40% eggplant fruits of different species for 14 days. The effect of the diets on the blood glucose level, pancreatic α-amylase, intestinal α-glucosidase and angiotensin-I-converting enzyme (ACE) activities, plasma antioxidant status were determined, in addition to the quantification of the fruits polyphenols using High Performance Liquid Chromatography/ diode array detection fingerprinting (HPLC/DAD).

Results: The results revealed that there was no significant ($P < 0.05$) difference in the average feed intake in all the groups. Supplementation with eggplant diet gradually reduced blood glucose level and hypertension in the diabetic rats (treatment groups) when compared to diabetic rats (negative control) without treatment and metformin-treated (positive control group). The treated group with eggplant diet demonstrated elevated levels of antioxidant status such as glutathione peroxidase GPX, glutathione transferase GST, reduced glutathione GSH, Catalase and Ascorbic acid. The supplemented diet reduced the free radicals produced as typified (TBARS).

Conclusion: This study showed that the eggplant may attenuate hyperglycemia, hypertension and oxidative stress in the type-2-diabetes condition with *Solanum kumba* having the highest activity, which is not far fetched due to its synergistic activities of polyphenols as revealed in the HPLC/DAD analysis.

Keywords: Solanum spp, Polyphenols, Diabetes, Enzymes, HPLC/DAD analysis

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Safety and toxicological evaluation of a novel *Citrus sudachi* extract powder

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ABSTRACT

Background: *Citrus sudachi*, an evergreen tree primarily found in the prefecture of Tokushima, Japan, is a widely used popular citrus fruit used in cooking and consumed as a juice. *Citrus sudachi* peels are rich in flavonoids including sudachitin (5,7,4'-trihydroxy-6,8,3'- trimethoxyflavone), and exhibit potent antioxidant, antimicrobial and anti-diabetic properties; additionally, several limonoids and their glucosides are found in its seeds. We examined the broad spectrum safety of a novel light yellow to golden yellow *Citrus sudachi* Extract Powder (CSEP), organic, nutritive from the dried fruit rind (25:1 herbs to extract ratio) containing no less than 1% sudachitin in various toxicology models in GLP-approved laboratories.

Methods: The acute oral toxicity study was conducted in female Sprague-Dawley rats with an up and down procedure. The single dose acute dermal LD_{50} of CSEP was assessed in both male and female rats. The primary skin irritation toxicity of CSEP was assessed in female New Zealand Albino rabbits in order to determine the potential for CSEP to produce irritation after a single topical application, while primary eye irritation index of CSEP was conducted in female New Zealand Albino rabbits. Ames' bacterial reverse mutation assay was conducted to determine the ability of CSEP to induce reverse mutation at selected histidine loci in five tester strains of *Salmonella typhimurium* viz. TA1535, TA97a, TA98, TA100, and TA102 in the presence and absence of a metabolic activation system (S9) at the doses of 5000, 1500, 500, 150 and 50 mg/plate. The mutagenic potential of CSEP was also evaluated in an *in vitro* mammalian cell gene mutation test using the thymidine kinase gene of L5178 Tk+/- 3.7.2C mouse lymphoma cell line.

Results: The acute oral LD_{50} of CSEP was found to be greater than 5000 mg/kg body weight. The single dose acute dermal LD_{50} of CSEP was found to be greater than 2000 mg/kg body weight in both male and female rats. In the primary skin irritation test, CSEP was found to be slightly irritating to the skin. The primary dermal irritation index (PDII) calculated for CSEP was found to be 0.8. In the primary eye irritation test, the maximum mean total score (MMTS) of CSEP was found to be 2.7. Thus, CSEP was classified as minimally irritating to the eye. In both Ames' bacterial reverse mutation assay and *in vitro* mammalian cell gene mutation test, no mutagenicity was observed.

Conclusion: Overall, these toxicological evaluations demonstrate the broad spectrum safety of CSEP.

Keywords: *Citrus sudachi* Extract Powder (CSEP); acute oral toxicity; acute dermal toxicity; primary dermal

irritation; primary eye irritation; Ames' bacterial reverse mutation assay; *in vitro* mammalian cell gene mutation assay

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/301/545

Biomarkers in Mild Stages of Alzheimer's disease: Utility in clinical practice and their relation with nutritional and lifestyle factors

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ABSTRACT

Background: The use of biomarkers in basic and clinical research as well as in clinical practice has become so common that their presence as primary endpoints in clinical trials is now accepted. A biomarker refers to a broad subcategory of medical signs. The aims of this article are to consider the of use biomarkers in Mild stages of Alzheimer's disease (AD) in research and clinical settings, in addition to defining their utility in clinical practice relating this with nutritional and lifestyle factors as possible treatment.

Methods: We searched MEDLINE, PubMed, and AgeLine databases using different keywords.

Conclusions: A summary of the utility of biomarkers in AD and nutritional and lifestyle factors used as treatment in mild stages are described.

Key words: Biomarkers, Alzheimer's disease, Dementia, Utility, Clinical practice, Nutritional and Lifestyle Factors, Early treatment

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/299/539

Protective effects of active hexose correlated compound in a rat model of liver injury after hepatectomy

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Running title: AHCC prevents liver injury

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ABSTRACT

Background: Recent evidence has indicated that a functional food, active hexose correlated compound (AHCC), has liver-protective effects via suppression of inflammatory mediators, such as inducible nitric oxide synthase (iNOS) and tumor necrosis factor (TNF)-α.

Objective: This study aimed to investigate whether AHCC has beneficial effects in a rat model of endotoxin-induced liver injury after partial hepatectomy, in addition to clarifying the mechanisms of action of AHCC.

Methods: Rats were treated with 70% of partial hepatectomy and lipopolysaccharide (PH/LPS) to induce acute liver injury. A normal diet with or without 2% AHCC was administered orally 10 days before 70% hepatectomy. Inflammatory mediators were analyzed.

Results: AHCC improved the survival rate by 70% in PH/LPS rats. AHCC prevented an increase in serum transaminase levels, and histopathological changes and apoptosis in the liver. AHCC reduced iNOS mRNA and protein expression in the liver, resulting in inhibition of nitric oxide production. AHCC also reduced TNF-α, cytokine-induced neutrophil chemoattractant-1, and interleukin-6 mRNA expression, but enhanced expression of interleukin-10. An electrophoretic mobility shift assay with hepatic nuclear extracts demonstrated that AHCC reduced the activation of nuclear factor (NF)-κB induced by PH/LPS treatment.

Conclusion: AHCC inhibits induction of inflammatory mediators, including iNOS and TNF-α, in part through inhibition of NF-κB activation in a rat model of liver injury. Our findings suggest that AHCC prevents postoperative liver failure after liver resection.

Keywords: active hexose correlated compound, inducible nitric oxide synthase, liver injury, nuclear factor-κB, tumor necrosis factor-α

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Dehydrated melon containing antioxidants and calcium from grape juice

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ABSTRACT

Background: Grape juice has a high antioxidant potential, capable of fighting oxidative processes in the body. The juice is mainly marketed in its concentrated form, which has a high content of glucose and fructose. The juice concentrate may then be used as an osmotic agent to dehydrated fruit with a relatively short shelf-life at room temperature, such as melon. The osmotic dehydration process can also be combined with conventional drying in order to further reduce the water activity (a_w) of the product. Finally, the antioxidant-rich melon meets the consumers' demand for foods which contain ingredients that may impart health benefits.

Results: Melon dehydrated by osmotic process at 200, 400 and 600 mbar, using grape juice concentrate (GJC), showed no significant differences in physical characteristics (a_w, °Brix, and moisture content). Higher efficiency was observed when dehydration was performed at 200 mbar. After osmotic dehydration with GJC, both plasmolysis of the melon cells and an increase in intercellular spaces were observed by optical microscopy, with no negative impact on the mechanical properties (True stress, Hencky's strain and deformability modulus). Calcium present in GJC was impregnated into the melon matrix, thus contributing with the mineral composition and mechanical properties of the final product. No significant differences were observed for the antioxidant capacity of melon dehydrated both with GJC and GJC followed by air-drying at 50 and 70°C. This demonstrates that it is possible to combine the two processes to obtain a product with intermediate moisture without decreasing its antioxidant capacity. The samples scored above the acceptable limit (>5) varying between like slightly to like moderately, resulting in a purchase intent with average scores between 3 (maybe/maybe not buy) and 4 (probably would buy).

Conclusions: A product with intermediate water activity, acidic, firm, high antioxidant capacity, rich in calcium and in naturally occurring sugars, and potential sensory acceptance can be obtained using grape juice concentrate in the osmotic dehydration process, followed by air- drying process.

Keywords: osmotic dehydration, air-drying, fruit juice, optical microscopy, antioxidants, calcium.

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/281/551

Evaluation of functional potentiality of selected commonly consumed foods of Bangladesh

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ABSTRACT

Background: Rising tide of chronic nutrition related non-communicable diseases yoked with extant under nutrition problems makes it imperative to carry out scientific research towards the discovery of functional foods. Although the emergence of these diseases are believed to be related to a constellation of dietary, socio-economic and lifestyle related risk factors, central to the pathogenesis of these diseases (or disease states) are free radicals, oxidative stress, and inflammatory processes typically accompanied by pain. Therefore, functional whole foods with physiologically active antioxidants, anti-inflammatory, and analgesic compounds seem to be the most promising option to deal with the pathogenesis of existing and emerging chronic diseases burden of Bangladesh.

Methods: Edible portions of 70 commonly consumed Bangladeshi foods – including one cereal, five legumes, fourteen vegetables, four tea varieties, five oil seeds, twenty spices, and twenty-one fruits – were evaluated for total phenol content (TPC) by Folin-Ciocalteau assay. To evaluate functional potentiality, in vitro antioxidant capacity (AC) of selected food items were evaluated by DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging assays, in vitro anti-inflammatory potential by observing the production of pro-inflammatory cytokine TNF-α using J774A.1 cells stimulated with lipopolysaccharide (LPS), in vivo anti-inflammatory potential by measuring carrageenan induced rat paw edema reduction, and in vivo analgesic potential by acetic acid induced writhing test in mice.

Results: Spices, oilseeds, and teas showed high concentration of TPC among the analyzed foods, while spices and teas exhibited notable AC. Green tea showed highest concentrations of TPC (2349 mg Gallic Acid Equivalent / g) and AC (2432 µmole Trolox Equivalent/g). Fourteen food items showed potential in vitro anti-inflammatory activity with confirmatory dose response effect shown by 8 items. In vivo, black sesame and yellow mustard expressed anti-inflammatory and analgesic effects in a dose dependent manner.

Conclusion: This study found commonly consumed food items representing different food groups of Bangladesh to contain diverse range of polyphenols and antioxidant capacities. Out of the tested food items, black sesame and yellow mustard both demonstrated anti-inflammatory and analgesic potential in the animal model. The findings of this study can be used to promote polyphenols rich foods through dietary guidelines and facilitate epidemiological research investigating diet-disease relationships.

Key words: Polyphenols**,** Total phenol content, Antioxidant capacity, Anti-inflammatory activity, Analgesic activity, Functional foods

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/278/553

Polyphenol characterization, anti-oxidant, anti-proliferation and anti-tyrosinase activity of cranberry pomace

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ABSTRACT

Background: Cranberry pomace (CP), an underutilized by-product from juice processing, contains a wide range of biologically active compounds that can be recovered and used in a variety of applications in functional foods and nutraceuticals.

Methods: In this study, analytical chemical techniques such as solvent extractions and characterization of extracts in respect with their phenolic content were performed using ultra- high performance liquid chromatography mass spectrometry (UPLC-MS) and spectrophotometry. Crude CP extract and its phenolic acids, flavonols, anthocyanins and proanthocyanidins–rich fractions were then evaluated for their anti-oxidant capacity, tyrosinase inhibitory activity, and anti-proliferation activity against hepatocellular carcinoma HepG2 cells.

Results: On a dry weight basis, the different CP fractions contained seven major anthocyanins (0.1-125 mg/g), six major phenolic acids (0.8-31 mg/g), seven flavonols (1-126 mg/g) and five flavan-3-ols (0.1-12 mg/g). Fractions rich in flavonols exhibited the most potent antioxidant capacities with ferric ion reducing antioxidant power values of 1.8-1.9 mmole/g and 2, 2- diphenyl-1-picrylhydrazyl radical scavenging IC_{50} values of 15.1-15.2 mg/L respectively. On the other hand, fractions rich in phenolic acids and flavan-3-ol monomers demonstrated the most potent anti-tyrosinase activity (IC_{50}=6.1-6.2 mg/L) and anti-proliferative activity (IC_{50}=7.8-15.8 mg/L). Generally, all the fractions exhibited a dose-response relationship in the selected biological activity assays.

Conclusion: This study suggests an effective utilization of CP to obtain biologically active fractions with potential to be used in functional foods and nutraceuticals designed for the prevention of chronic diseases associated with oxidative stress.

Keywords: *cranberry pomace, polyphenol, anti-tyrosinase, anti-proliferation, nutraceuticals, functional foods*

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Dietary Nitrite: from menace to marvel

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ABSTRACT

The health benefits of nitrite are now indisputable when administered in a clinical setting for specific diseases. Currently, most published reports identify the production of nitric oxide (NO) as the mechanism of action for nitrite. Basic science, in addition to clinical studies, demonstrate that nitrite and/or nitrate cannot restore NO homeostasis as an endothelium independent source of NO that may be a redundant system for endogenous NO production. Nitrate must first be reduced to nitrite by oral commensal bacteria; nitrite can then be further reduced to NO along the physiological oxygen gradient. But despite decades of rigorous research on sodium nitrate's safety and efficacy as a curing agent, sodium nitrite is still regarded by many as a toxic undesirable food additive. However, research within the biomedical science community has revealed enormous therapeutic benefits of nitrite which are being developed as novel therapies for conditions associated with nitric oxide insufficiency. Thus, this review will highlight the fundamental biochemistry of nitrite in human physiology and provide evidence that nitrite be considered an essential nutrient. Foods or diets enriched with nitrite can have profound positive health benefits.

Keywords: nitrite, nitrate, nitric oxide, curing, nutrition, epidemiology, cardiovascular, cancer, diet, nitrosamines, antioxidants

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/295/547

Pomegranate (*Punica granatum*): a natural source for the development of therapeutic compositions of food supplements with anticancer activities based on electron acceptor molecular characteristics

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ABSTRACT

Background: Numerous in vitro and in vivo studies, in addition to clinical data, demonstrate that pomegranate juice can prevent or slow-down the progression of some types of cancers. Despite the well-documented effect of pomegranate ingredients on neoplastic changes, the molecular mechanism(s) underlying this phenomenon remains elusive.

Methods: For the study of pomegranate ingredients the electron-ion interaction potential (EIIP) and the average quasi valence number (AQVN) were used. These molecular descriptors can be used to describe the long-range intermolecular interactions in biological systems and can identify substances with strong electron-acceptor properties. In this study, candidate human proteins interacting with pomegranate flavonoids have been analyzed by the informational spectrum method (ISM). This represents a virtual spectroscopy method for studying protein molecular interactions.

Results: Our analysis indicates that the anti-cancer properties of pomegranate juice can be ascribed to the strong electron-acceptor properties of its chemical ingredients. This analysis also suggests that pomegranate flavonoids inhibit the “NF-kappaB” (NF-κB) pathway, which plays a critical role in the pathogenesis of cancer.

Conclusion: The results offer a possible explanation for an important molecular mechanism underlying the anticancer activity of pomegranate ingredients, which could also serve as a basis for the development of new therapeutic compositions of food supplements with pomegranate- like anticancer properties.

Key words: cancer, pomegranate, flavonoids, food supplement, informational spectrum method

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/289/558

Evaluation of the effect of the administering of an N-acetyl-glucosamine-containing green tea supplement on biomarkers for cartilage metabolism in healthy individuals without symptoms of arthritis: a randomized double-blind placebo-controlled clinical study

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ABSTRACT

Background: To evaluate the chondroprotective action of an N-acetyl-glucosamine (GlcNAc)-containing supplement on the joint health of healthy individuals without symptoms of arthritis, we conducted a randomized double-blind placebo-controlled clinical trial.

Methods: Subjects (n=100, 51.3 ± 1.0 years (mean ± SE)) without symptoms of arthritis were randomly assigned to receive a 1000 mg GlcNAc-containing diet (GlcNAc group) or a placebo diet (placebo group) once a day for 16 weeks, and the effect on the cartilage metabolism was evaluated by analyzing the ratio of type II collagen degradation to synthesis using type II collagen degradation (C2C) and synthesis (PIICP) markers.

Results: The results indicated that the changes in the C2C/PIICP ratios from the baseline were slightly suppressed in the GlcNAc group compared with those in the placebo group at weeks 16 during the intervention and 4 weeks after the intervention. However, there was no significant difference between the two groups. To make the effect of GlcNAc even more clear, the subjects with joint loading and impaired cartilage metabolism were evaluated. Interestingly, the changes in the C2C/PIICP ratios from the baseline were significantly suppressed in the GlcNAc group compared with the placebo group at weeks 16 during the intervention and 4 weeks after the intervention. Moreover, test supplement-related adverse events were not essentially observed during and after the intervention.

Conclusions: These observations suggest that the oral administration of GlcNAc at a dose of 1000 mg/day exerts a chondroprotective action on the healthy individuals by lowering the C2C/PIICP ratio, which indicates relative reduction of type II collagen degradation and increase of type II collagen synthesis, without apparent adverse effect.

Key words: N-acetyl-glucosamine, biomarker, cartilage metabolism, joint health

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A survey of consumer attitude towards nutrition and health statements on food labels in South Australia

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ABSTRACT

Background: For many decades, Australia has required a Nutrient Information Panel to be included on food packaging, usually on the back of products. Recently, two regulated, voluntary systems were introduced for use on food packaging in Australia: the Health Star Rating system and nutrient content and health claims. Nonetheless, the scope and potential for these new initiatives to achieve their purpose is partly depdendant on their perception by consumers. This report describes the results of a population based survey of South Australian adults about how various elements of food labels are used to inform their purchase decisions.

Methods: A survey was conducted using a random stratified sampling technique in people aged 15 years and older in the Australian state of South Australia. All surveys were administered face- to-face to 3005 people between September 2015 and December 2015. Data was weighted by the inverse of the individual's probability of selection, as well as the response rate in metropolitan and country regions and then reweighted to benchmarks from the June 2014 Estimated Resident Population calculated by the Australian Bureau of Statistics.

Results: The response rate for the survey was 57.3%. Most respondents to the survey rated their own dietary intake as 'healthy' (61.5%) or 'extremely healthy' (9.1%). Aside from price, country of origin was nominated as the most important information on the food label of a food bought for the first time (by 35.0%), followed by the ingredient list (21.6%) and claims about nutrition (20.9%). The response to this question was markedly different by age group, with almost half (48.3%) of those aged 55 years or over considering that country of origin was the most important information to look for. For the youngest age group (15-34 yrs), 28.4% considered the ingredient list was the most important information, 26.5% considered claims about nutrition to be most important, and 22.2% considered country of origin to be the most important information on the food label. The Nutrition Information Panel was used to guide the purchase decision for a new breakfast cereal by more than half of respondents (50.8%), while a statement on the front of the pack about how the food effects health was used to guide the purchase decision of only 8.9%. While only 22.1% disagreed (16.4% disagreed somewhat, 5.7% disagreed completely) with the statement that 'the Nutrient Information Panel on food packaging is a trustworthy source of information,' almost double the amount of subjects at 44.0% disagreed (36.1% disagreed somewhat, 17.9% disagreed completely) that 'statements about health on food packaging are a trustworthy source of information.'

Conclusion: For South Australian adults, statements about health benefits of food on food packaging are viewed with much greater suspicion than the nutrient information panel. Attitudes towards food packaging varied more by age group than by sex of the respondent. For an unfamiliar food, country of origin is considered the most important information on food packaging by more than a third of adults.

Keywords: Food packaging, Nutrition label, Front of Pack, Health Star, South Australia

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Investigation of phytochemical constituents, phenolic profiles and antioxidant activities of ricegrass juice compared to wheatgrass juice

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ABSTRACT

Background: Cereal grass has been brought attention as a new functional food. Wheatgrass juice was known as a super food which provides lots of advantages for human health. However, the young stage of rice sprout has not been made widely known for consumption, though it is in the similar family to wheat (Poaceae). Accordingly, ricegrass juice can and should be introduced, especially in Asian countries, as an economical functional drink. Nevertheless, currently there is none of the apparent evidences which confirm the nutritive values of ricegrass juice compared to wheatgrass juice.

Objective: To investigate the chemical compositions, major phytochemical constituents, bioactive compounds content, specific phenolic profiles, and *in vitro* antioxidant activities of ricegrass juice compared to wheatgrass juice.

Methods: Rice and wheat seeds were germinated and grown hydroponically for 8 days. Both fresh plants were determined for chemical compositions. Next, the grasses were extracted with water, centrifuged, and the supernatants were tested for chlorophyll, carotenoid, and ascorbic acid contents. The left-over supernatant were freeze-dried. The extracts were then screened for the main group of phytochemicals, total extractable phenolic and specific phenolic compounds. Lastly, the extracts were tested for the antioxidant activities using DPPH, ABTS, FRAP, FCA and HRSA.

Results: Data revealed that wheatgrass contained higher levels of protein and fat. Both ricegrass and wheatgrass juice extract exhibited the group of phenol, tannin and saponin but not alkaloid, flavonoid, sterol, terpenoid, courmarin, and cardiac glycoside. Wheatgrass juice can be detected for higher level of ascorbic acid and chlorophyll. Both grass juices were found the similar phenolic acids analyzed by HPLC included pyrogallol, vanilic acid, syringic acid and ferulic acid, however, ricegrass juice contained larger amounts of all phenolic acids excluding syringic acid. Conversely, wheatgrass juice exposed higher antioxidant activities for all methods. This may propose from the synergistic effects of ascorbic acid, chlorophyll, and phenolic compounds in wheatgrass juice, while the main composites exhibited antioxidant activities in ricegrass were phenolic compounds.

Conclusion: Ricegrass juice contained great level of phenolic acid molecules. Even if ricegrass juice gave less statistically ability on antioxidant activities, they still had comparable levels of antioxidant activities. With the reduction in cost of raw materials and contribution of high nutritional values, ricegrass juice could be introduced as an antioxidant boosting drink in competition to wheatgrass juice.

Keywords: Antioxidant, Phytochemical, Phenolic compounds, Ricegrass, Wheatgrass

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/290/564

Influence of hot water blanching process on nutritional content, microstructure, antioxidant activity and phenolic profile of *Cinnamomum porrectum* herbal tea

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ABSTRACT

Background: *Cinnamomum porrectum* leaves, one kind of *Cinnamomum* family, has recently been used to produce a locally herbal tea. Although *C. porrectum* essential oil and aqueous extract have been reported to have some biological activities, including antioxidant, antimicrobial, and anti-inflammatory activities, there is no scientific data using the blanching process for the production of herbal tea. Therefore, this experiment aimed to study the effect of hot water blanching before drying process on microstructure, nutrition content of the tea powder, TPC, TFC, antioxidant activities of infusion, as well as the phenolic profile of the extract.

Objective: To determine effect of hot water blanching process on nutritional value, microstructure, phenolic profile, and antioxidant activity of the *C. porrectum* herbal tea.

Methods: The *C. porrectum* leaves were divided into 2 groups; control (un-treated) and blanched before dried for herbal tea processing. The fresh leaves and the powders of control and blanched leaves were checked for proximate composition and chlorophyll contents, in addition to color value. The powders were determined microstructure by SEM. The infusions were determined to have color value and total extractable phenolic and flavonoid contents, as well as antioxidant activities. The hydrolyzed extracts of freeze dried infusion were subjected to identify phenolic profile by HPLC.

Results: The blanched tea powder yielded a percentage of fat and protein contents higher than un- treated due to easier extraction because of the bigger pore size found in microstructure. Chlorophyll content of blanched was decreased compared with the control sample. However, it was found that blanching could greater maintain green color of both powder and infusion. Additionally, blanching helped increased TPC, TFC extractability, and antioxidant activities in all assays except metal chelating property. Based on retention time and peak profile determined by using HPLC, it was found that both control and treated extracts consisted of similar main phenolic and flavonoid compounds however, only kaempferol was found in un-treated. Moreover, hydrolyzed blanched extract showed a higher intensity of 2 unknown compounds than un-treated. Though un-treated provided a higher intensity of pyrogallol, gallic acid, and cinnamic acid, the blanched exhibited a higher intensity of caffeic acid, protocatechuic acid, *p*-coumaric acid, and rutin.

Conclusion: Blanching before drying expanded pore size of dried leaves, increased yield extractability, maintained color value, chlorophylls and increased TPC and TFC which related to antioxidant activities. Blanched extract provided higher intensity of some phenolic compounds than un-treated.

Keywords: *Cinnamomum porrectum*, blanching process, SEM, HPLC

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DNA methyltransferase 1-targeting miRNA-148a of dairy milk: a potential bioactive modifier of the human epigenome

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ABSTRACT:

Background: The perception of milk has changed from a "simple food" to a more sophisticated bioactive functional signaling system that promotes mTORC1-driven postnatal anabolism, growth, and development of the newborn infant. Accumulating evidence supports the view that milk´s miRNAs significantly contribute to these processes. The most abundant miRNA of milk found in milk fat and milk exosomes is miRNA-148a, which targets DNA methyltransferase 1 (DNMT1), a pivotal epigenetic regulator that suppresses transcription. Furthermore, milk-derived miRNA- 125b, miRNA-30d, and miRNA-25 target TP53, the guardian of the genome that interacts with DNMT1 and regulates metabolism, cell kinetics, and apoptosis. Thus, the question arose whether cow´s milk-derived miRNAs may modify epigenetic regulation of the human milk consumer.

Methods: To understand the potential impact of dairy milk consumption on human epigenetics, we have analyzed all relevant research-based bioinformatics data related to milk, milk miRNAs, epigenetic regulation, and lactation performance with special attention to bovine miRNAs that modify gene expression of DNA methyltransferase 1 (*DNMT1*) and p53 (*TP53*), the two guardians of the mammalian genome. By means of translational research and comparative functional genomics, we investigated the potential impact of cow´s milk miRNAs on epigenetic regulation of human *DNMT1*, *TP53*, *FOXP3*, and *FTO,* which are critically involved in immunologic and metabolic programming respectively. miRNA sequences have been obtained from mirbase.org. miRNA-target site prediction has been performed using TargetScan release 7.0

Results: The most abundant miRNA of cow´s milk is miRNA-148a, which represents more than 10% of all miRNAs of cow´s milk, survives pasteurization and refrigerated storage. The seed sequence of human and bovine miRNA-148a-3p is identical. Furthermore, human and bovine DNMT1 mRNA share 88% identity. The miRNA-148a 7mer seed is conserved in human and bovine DNMT1 mRNA respectively, which may allow for the strong binding of bovine miRNA- 148a to human DNMT1 mRNA. Consequently, we hypothesize that bovine milk miRNA-148a - protected by highly resistant milk exosome membranes - may reach the systemic circulation of the milk consumer targeting and suppressing human *DNMT1* mRNA. Attenuated DNMT1 expression associated with reduced CpG promoter methylation upregulates gene expression of developmental genes such as *FOXP3* and *FTO*. Milk-derived miRNA-125b, miRNA-30d, and miRNA-25 via targeting *TP53* may downregulate p53, which physically interacts with and stabilizes DNMT1. Enhancement of dairy lactation performance is associated with increased expression of bovine milk miRNA-148a, a modification that may further increase the miRNA-148a load of dairy milk.

Conclusion: Translational evidence and comparative functional genomics support our hypothesis that bovine milk

miRNA signaling may suppress human DNMT1-mediated epigenetic regulation and p53 signaling, which closely interacts with the epigenetic and transcriptional regulation of growth, metabolism, cell cycle progression, and apoptosis. Human and bovine milk miRNAs are able to target *DNMT1* and *TP53* mRNAs, share identical seed sequences, and resist pasteurization. Pasteurization and refrigeration of dairy milk conserves the gene regulatory software of milk and allows its unrestricted entry into the human food chain. The continued exposure of modern humans to milk´s epigenetic machinery since the widespread distribution of refrigerators is a novel change of human nutrition which may promote diseases of Western civilization.

Keywords: adipogenesis, dairy, DNA methyltransferase 1, epigenetics, exosome, miRNA-148a, miRNA-125b, milk, obesity, p53, Parkinson disease, prostate cancer

Drought stress affects nutritional and bioactive compounds in potatoes (*Solanum tuberosum* L.) relevant to human health

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ABSTRACT

Background: Potatoes react very sensitively to drought during growth. Thus, appropriate plant stress responses may affect metabolites associated with the health quality of tubers.

Objective: The aim of this study was to determine the effects of drought stress (DS) on soluble sugars, starch, crude protein, minerals, free amino acids (AAs), and fatty acids (FAs).

Design: The experiment was carried out on three potato genotypes during two years with four replications. The plants were grown in pots in a glasshouse with optimal water supply and under drought stress conditions. After harvest, the tubers of these two variants were analyzed for nutritional and bioactive compounds relevant to human health.

Results: Apart from genotypic differences in most parameters, the results revealed that the DS caused a decline in glucose and fructose ($P < 0.05$, all) in both years, while sucrose was increased, especially in the second year with severe stress ($P < 0.01$). Starch was significantly reduced by moderate stress in the first year ($P < 0.01$), but less affected in the second year. Crude proteins and total amounts of free amino acids (AAs) were clearly enhanced by the stress in both years ($P < 0.05$, all). The minerals magnesium (Mg), potassium (K) and phosphorus (P) ($P < 0.05$, all) were similarly enhanced, while calcium (Ca) actually declined ($P < 0.05$). The portion of α-linolenic acid (ALA) on total lipids was elevated in the stress variants ($P < 0.01$), while oleic acid (OLA), its precursor, decreased significantly ($P < 0.05$), but only in the first year. In the second year, ALA was generally higher and not further induced by the stress. Additionally, OLA was less affected in that year, which was similar to all the other FAs in both years. Interestingly, *Myo*-inositol (MI) and lipid acyl hydrolases (LAH) associated with modulation in cell membrane lipids were raised by the drought stress in each year ($P < 0.01$, all). In the second year, MI and LAH data of the drought stressed tubers correlated significantly ($r = 0.90$, $P < 0.01$), suggesting their joined action within plant stress responses.

Conclusions: The biochemical changes induced by DS are not alarming with regards to human health. Decline in glucose, fructose, and starch, in addition to increase in crude proteins, free AAs, ALA, MI, and minerals like Mg, K and P is profitable for the health benefits of tubers. However, a better quality is associated with a decrease in tuber yield.

Keywords: potato, drought stress, bioactive compounds, chronic disease

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Colonic delivery of nutrients for management of blood glucose in type 2 diabetes patients

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ABSTRACT

Background: It is now widely accepted that bariatric surgeries such as Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) can resolve or improve type 2 diabetes mellitus. Post- prandial glucagon-like peptide-1(GLP-1) increases after both RYGB and SG and blockade of the GLP-1 receptor suppresses the hypoglycemic effect post-operatively. The expedited delivery of nutrients, including L-glutamine and butyrate, to the distal small intestine and colon, where most GLP-1–secreting enteroendocrine L-cells are expressed, could explain this increase post-surgery. Pharmacological treatments that target nutrient-sensing receptors on L-cells may mimic the effects of bariatric surgeries and may ameliorate deficiencies in gut hormone responses involved in the regulation of glucose and satiety. In this study, we investigated the effects of the colonic delivery of L-glutamine and butyrate on GLP-1 secretion and glucose homeostasis in both a pre-clinical rodent model and clinical type 2 diabetes mellitus (T2DM).

Results: Infusion of 4.4mg of sodium butyrate, compared to saline, into the colon of Zucker diabetic fatty (ZDF) rats increased GLP-1secretion in response to an intra-duodenal glucose challenge. In a chronic study, oral dosing of 40mg of sodium butyrate twice a day, formulated as colon-targeted sustained-release tablets, preserved glucose tolerance and insulin sensitivity in ZDF rats. In ten T2DM patients requiring oral anti-hyperglycemic agents, infusion of 1g of L-glutamine into the colon, compared to saline, increased plasma GLP-1 ($p=0.017$ at 30 min) and insulin ($p<0.01$ at 90min; $p=0.001$ at 120min; AUC $p<0.005$) after an oral glucose challenge. Similar infusion with butyrate significantly increased only insulin secretion at 120 min, compared to saline ($p<0.05$). Neither agent had an effect on glucose disposal.

Conclusion: Targeted colonic delivery of L-glutamine and butyrate augments secretion of meal- stimulated GLP-1 and insulin; L-glutamine was more efficacious in humans. Such an approach may be valuable for the management of hyperglycemia in T2DM patients. A chronic clinical study with colon-targeted sustained-release L-glutamine is required to validate this hypothesis.

Key words: Diabetes, nutrients, gut hormones, GLP-1, secretagogues, glucose management.

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/283/574

Adding stewed apricot juice to senna improves quality of colon cleansing in preparation for colonoscopy

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ABSTRACT

Background: To achieve optimal colonoscopic examination, the bowel must be sufficiently cleansed. However, none of the currently available colonoscopy preparation regimens is safe, efficient, and comfortable. The aim of this study was to determine whether adding stewed apricot juice to senna increased patient comfort and improved bowel cleansing during colonoscopy preparation.

Methods: Outpatients of both genders who were over 18 years old and were referred for elective colonoscopy were randomly allocated to drink stewed apricot juice with senna or senna by itself. The quality of the colon cleansing was evaluated using the Ottawa scale. Patient tolerance and adverse events were evaluated through the completion of a questionnaire.

Results: The study included a total of 128 patients in the randomization procedure. A significantly greater cleansing effect was observed using stewed apricot juice plus senna in the right and transverse colon ($p = 0.038$, $p = 0.037$ respectively). It was also determined that in the stewed apricot juice plus senna group, overall cleansing was superior ($p < 0.001$), total colonoscopy (17.6 min vs. 22.8 min, $p = 0.048$) and cecal intubation (7.4 min vs. 11.2 min, $p = 0.042$) times were shorter, and the colonoscopy procedure was easier (79.4% vs. 49.2%, $p < 0.001$). No differences were observed between the groups with respect to patient acceptance, compliance, and adverse events. In the stewed apricot juice plus senna group, 91.2% of patients stated their willingness to receive the same regimen in the future compared to 80% of the patients in the senna alone group ($p = 0.037$).

Conclusion: The addition of natural, stewed apricot juice to senna significantly improves cleansing outcomes without additional adverse effects.

Clinical trial registration number is NCT02665624, and the validity date is 24.01.2016.

Keywords: bowel cleansing, colonoscopy, stewed apricot juice, senna.

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Diabesity: an epidemic with its causes, prevention and control with special focus on dietary regime

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ABSTRACT

Diabesity refers to the complicated conditions of diabetes and obesity occurring simultaneously within a single individual. The incidences of diabetes and obesity are growing at a rapid pace throughout the world that are mainly associated with lifestyle and dietary habits, aside from genetic vulnerability. Authors have reviewed the epidemiology and other negative aspects of diabesity followed by some of the management practices recommended. The declining of traditional lifestyles and dietary patterns is leading to a rapid increase in the prevalence of diabesity that is upcoming as a serious cause of concern world over. Diabetes, obesity, and their associated complications are without doubt a principal issue and threat in developing and under-developed nations. Diabesity has emerged as a major threat. This condition has been described as a slow poison, whose influence cannot be controlled or cured. The dietary measures offer the most viable and effective solution to diabetes onset, in addition to the obese state. The designing of a smart diet (i.e. healthy diet) and selecting gut microbiota having probiotic influence on the host can target in the weight reduction/ management, in addition to stabilizing sugar levels in the blood of an individual. Additionally, the regular physical workout can help an individual in controlling body weight and regulate other biochemical conditions which lead to various types of metabolic disorders. All of these issues are discussed in this review article which covers the causes, prevention, and control of diabesity.

Keywords: Diabetes; obesity; diabesity; gut microbiota; probiotics

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Topical applied nutraceutical antioxidant formulation reduces ocular oxidative stress

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ABSTRACT

Oral nutraceutical antioxidants have shown disappointing clinical results in reducing oxidation- induced age-related cataract and other ocular diseases. Based on the hypothesis that nutraceuticals do not adequately reach the lens by oral administration, we have developed a unique topical antioxidant formulation whose active ingredients have the reported ability to reduce oxidative stress through free radical scavenging and chelating activity. This topical nutraceutical formulation was designed to mimic the *in vivo* activity of multifunctional antioxidants, compounds which are being developed in our laboratory to independently scavenge free radicals and selectively bind redox metals.

A comparison of the efficacy of this topical nutraceutical to multifunctional antioxidants in laboratory animal models of oxidation-induced lens changes, retinal changes, and dry eye is reviewed. Although it is less potent than the small molecule multifunctional antioxidants that will require FDA approval, the topical nutraceutical formulation beneficially reduces ocular oxidative stress. These studies suggest that this topical antioxidant may fill an unmet therapeutic need by providing a nutraceutical that beneficially reduces the effects of oxidation on age-related ocular diseases.

Keywords: oxidative stress, nutraceutical antioxidants, age-related ocular diseases, dry eye, cataracts, retinal degeneration

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/297/570

A drink containing amino acids and chromium picolinate improves postprandial glycemia at breakfast in healthy, overweight subjects

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ABSTRACT

Background: Chromium (Cr) and certain amino acids (AA) have been individually shown to improve postprandial glycemia.

Method: The present randomized, controlled, cross-over trial in 19 healthy, overweight subjects (age 51±1y and BMI 27.3±0.3 kg/m^2; mean±SEM) evaluated a combination of leucine, isoleucine, valine, lysine, and threonine (5AA) with Cr. Postprandial glycemia and insulinemia were measured following a bread meal, served with carbonated water (Ref) or carbonated water containing 5AA, Cr-picolinate (CrPic) or a combination (5AA+CrPic).

Results: The 5AA+CrPic and 5AA respectively lowered the incremental glucose peak ($P < 0.001$) by almost 30% compared to Ref. No significant differences in incremental insulin peaks were found. However, during the first 15 minutes 5AA induced a higher insulin response (+112%; $p<0.01$) compared to Ref. Interestingly, 5AA+CrPic reduced the initial AA-induced insulin increase by more than 50%, indicating improved insulin economy.

Conclusions: These observations suggest that a drink containing both 5AA and CrPic attenuate postprandial glycemia in healthy "at risk" subjects.

Keywords: Amino acids, chromium picolinate, postprandial glycemia, insulin economy, drink

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/304/578

Survival rate of *Saccharomyces boulardii* adapted to a functional freeze- dried yogurt: experimental study related to processing, storage and digestion by Wistarrats

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ABSTRACT

Background*: Saccharomyces boulardii* is a probiotic clinically effective in the prevention and treatment of antibiotic induced diarrhea in both children and adults, *Clostridium difficile* infections, inflammatory bowel disease, and other gastrointestinal disorders. However, the microorganisms need to survive the gastrointestinal transit and arrive to their action site alive in order to exert their beneficial effects. Microencapsulation is an alternative to improve the viability of probiotic in foods which can also survive in the gastrointestinal conditions. Freeze-- drying is a method of dehydration that does not affect nutrients and bioactive compounds, such as probiotics contained in foods. All of them will increase the survival rate of *S. boulardii.*

Purpose of this study: This study focused on formulae freeze-dried yogurt containing inulin, vegetable palm oil, and *S. boulardii*, both as free cells and in microencapsulated form. Also, the effect of ampicillin associated *S. boulardii*.

Methods. Yogurts were given to an "in vivo" digestion process, using male Wistar rats. The survival of *S. boulardii* was subsequently evaluated in colon and feces. For this study, six treatments of four of rats were used: i) control rats ii) rats fed with yogurt containing *S. boulardii* as free cells, iii) rats fed with yogurt containing *S. boulardii* in micro-encapsulated form, iv) control rats fed with penicillin, v) rats fed with ampicillin plus yogurt containing *S. boulardii* as free cells, and vi) rats fed with penicillin plus yogurt containing *S. boulardii* in micro-encapsulated form.

Results: The study demonstrated it was feasible to freeze-dry the *S. boulardii* and incorporate it into a yogurt made with skim milk, inulin, and unsaturated vegetable oil. The freeze-drying process not affected the survival of the *S. boulardii* ($p<0.05$). Microencapsulation increased the survival of *S. boulardii* on 1.77-Log CFU/g, and the presence of *S. boulardii* was only detected in colon and feces of those rats which ingested ampicillin, regardless to the formula contained the probiotic.

Conclusion: This study demonstrated that freeze-drying maintains the survival of *S. boulardii* in the evaluated foods and that micro-encapsulation increases the survival of this probiotic. Furthermore, *S. boulardii* was

installed in the gastrointestinal tract when the microbial flora was damaged by ampicillin.

Keywords: Yogurt, probiotic, *Saccharomyces boulardii*, micro-encapsulation, freeze-drying.

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/319/580

Improvement of glucose metabolism via mung bean protein consumption: A clinical trial of GLUCODIA™ isolated mung bean protein in Japan

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ABSTRACT

Background: The main component of mung bean protein, accounting for more than 80%, is 8Sα globulin. Its structure closely resembles that of soybean β-conglycinin. Thereby, the mung bean protein is expected to have similar physiological effects to those of β-conglycinin, but there is no clinical evidence for these effects.

Purpose of this study: The aim of this study was to confirm the positive effects of mung bean protein (GLUCODIA™) on glucose metabolism in clinical trials.

Method: This clinical study was conducted using a double-blind placebo- controlled design with 45 prediabetes patients.

Results: Many of the subjects were pre- diabetes with blood glucose levels exceeding 140 mg/ dl by 2 - hour plasma glucose level. However, the initial mean fasting plasma glucose level was less than 100 mg/ dl. Therefore, mung bean protein did not lower fasting plasma glucose levels. The test period extended from summer to autumn, and increased fasting plasma glucose levels in the placebo group were observed due to seasonal factors. However, this increase was suppressed in the test group. Similarly, the mean insulin level increased in the placebo group, but the increase was also suppressed in the test group. Among obese subjects with a high body mass index, significant increases in fasting plasma glucose and insulin levels in the placebo group were observed. In the comparison between the test and the placebo groups with the average elevation value, there was a significant difference in fasting blood glucose level and significant tendencies in insulin level and homeostatic model assessment for insulin resistance value between the two groups.

Conclusion: Mung bean protein suppresses fasting plasma glucose and insulin levels. Consequently, it may have an inhibitory effect on insulin resistance, a trigger of metabolic syndrome.

Key words: mung bean protein, insulin, obesity, body mass index, randomized clinical trial, seasonal variation.

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/320/587

Health Benefits of Dietary Tree Peony Seed Oil in a High Fat Diet Hamster Model

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ABSTRACT

Background: Tree peony (*Paeonia ostii*) seed oil is rich in different unsaturated fatty acids, including monounsaturated fatty acids (MUFA), n-3, and n-6 polyunsaturated fatty acids (PUFA). Overall, health benefits of this edible plant oil have not been widely explored. In this study, we experimentally investigated benefits of dietary tree peony seed oil (PSO) in dyslipidemia-associated metabolic diseases using a high fat diet hamster model.

Methods: High fat diets (HFD) containing 15 % coconut oil (CO) or PSO were initially developed based on the rodent chow diet. Fatty acid profiles of diets and red blood cells (RBC) from animals fed these diets for 8 weeks were analyzed and compared. Effects of these oil supplements on triglycerides and cholesterol levels were characterized. Benefits on fatty liver progress were also investigated in this animal model.

Results: HFD fortified with 15% PSO was abundant in different unsaturated fatty acids, containing 40% α-linolenic acid, 27% linoleic acid, and 23% oleic acid respectively. Compared to the control group with 15% CO, animals with 15% PSO displayed dramatic alteration of *in vivo* fatty acid profile in RBC, featuring a significant increase in n-3 but no change in n-6 PUFA, thereby resulting in a decreased ratio of n-6 to n-3 PUFA. PSO intervention also remarkably reduced triglyceride levels in both blood and adipose tissues, but did not affect circulating cholesterol. Moreover, benefits on liver health were observed in the PSO group, evidenced with reduced hepatic steatosis and improved hepatic histology.

Conclusion: Altogether, the data demonstrated multifaceted benefits of dietary PSO in reducing important risk factors of dyslipidemia-associated cardiovascular and liver diseases.

Keywords: Peony seed oil, High fat diet, Triglyceride, Cholesterol, Hepatic steatosis

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/313/584

Oxidation and apoptosis are induced by CLA-t10c12 similar to DHA in 3T3 adipocyte cells.

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ABSTRACT

Background: Commercial conjugated linoleic acid (CLA) dietary supplements contain an equal mixture of the C18:2 isomers, cis-9trans-11 and trans-10cis-12. Predominantly, CLA- c9t11 occurs naturally in meat and dairy products at ~ 0.5% of total fat , whereas CLA- t10c12 occurs at > 0.1%. Recent studies show that CLA-c9t11 generally promotes lipid accumulation but CLA-t10c12 may inhibit lipid accumulation and may also promote inflammation. The omega-3 fatty acids α-linolenic acid (C18:3n-3) and docosahexaenoic acid (DHA) have also been observed to inhibit lipid accumulation and effect inflammation; therefore we examined the effects of the two main isomers of CLA and omega -3 fatty acids C18:3n-3 and DHA at the molecular level to determine if they are causing similar oxidative stresses.

Methods: Purified CLA-c9t11 and CLA-t10c12 were added to 3T3 cells induced into mature adipocyte cultures at 100uM concentrations and compared with 100uM C18:3n-3 (α-linolenic acid) and 50uM docosahexaenoic acid (DHA) to observe their effect on growth, gene transcription and general oxidation. The results of multiple separate trials were averaged and compared for significance at levels of $P < 0.05$, using one way ANOVA and *Student's t-test*.

Results: C18:3n-3, DHA and CLA-t10c12 inhibited 3T3 adipose cell growth and caused a significant increase in lipid hydro peroxide activity. CLA-t10c12 and c9t11 increased AFABP, FAS and ACOX1 mRNA gene expression but DHA and C18:3n-3 decreased the same mRNAs. CLA-c9t11 but not the t10c12 stimulated adipoQ expression even though; CLA-c9t11 had only a slightly greater affinity for PPARγ than CLA- t10c12, according to TR-FRET assays. The expression of the xenobiotic metabolism genes, aldo-keto reductase1c1 (akr1c1), superoxide dismutase (SOD) and inflammation chemokine secretions of eotaxin (CCL11), Rantes (CCL5), MIG (CCL9) and MCP-1 were increased by DHA, C18:3n- 3 and CLA-t10c12 but not CLA-c9t11. This correlated with an increase in apoptosis factors, caspase 3, Bcl-2 and BAXs. Apoptosis factors were partially reduced by co-treatment with lipophilic anti-oxidant α-tocopherol.

Conclusions: CLA-t10c12 stimulated the production of more reactive oxygen species (ROS) than CLA-c9t11. In response, cascades of genes are activated in detoxification, inflammation or apoptosis, to deal with the potentially damaging effects of ROS including CCL5 and MCP-
1. This was similar to treatment with the omega- 3 fatty acids but the fat metabolic enzymes were generally inhibited by C18:3n-3 and DHA except CLA-t10c12 which did not stimulate adipoQ.

Keywords: CLA-t10c12, CLA-c9t11, gene expression, adipocyte lipid hydroperoxide, DHA, 3T3 adipocytes, apoptosis.

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Nutritional components of the sea cucumber *Holothuria scabra*

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ABSTRACT

Background: *Holothuria scabra* is one of the most commercially important species found in the Pacific region. The sea cucumber extracts have been widely reported to have beneficial health effects. The aim of this study was to determine the nutritional compositions of *H. scabra*, and compare its important nutritional contents with that of other species.

Methods: The sea cucumbers were dissected, sliced into small pieces, and then freeze-dried. The nutritional compositions, including proximate composition, amino acids, fatty acids, collagen, GABA, Vitamin A, C, and E of the whole body and body wall of *H. scabra*, were analyzed.

Results: *H. scabra* contained a high quantity of protein (22.50% in whole body and 55.18% in body wall) and very low lipids (1.55% in whole body and 1.02% in body wall). The three most abundant amino acids found in both the whole body and body wall were glycine, glutamic acid, and proline. The main fatty acids found in the whole body were stearic acid and nervonic acid, and in the body wall were arachidonic acid and stearic acid. The whole body and body wall also contained high levels of essential amino acids, essential fatty acids, and collagen, in addition to moderate amounts of vitamin E and low amounts of GABA and vitamin C.

Conclusions: The sea cucumber, *H. scabra*, contained high quantity of protein and very low lipid. It contained high essential amino acids, essential fatty acids, nervonic and arachidonic acids, and collagen, which also contained GABA, vitamin C, and vitamin E.

Keywords: sea cucumber; *Holothuria scabra*; nutrition components; functional food

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/303/588

Influence of selenium bio-fortification on nutritional compositions, bioactive compounds content and anti-oxidative properties of young ricegrass (*Oryza sativa* L.)

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ABSTRACT

Background: Young ricegrass (*Oryza sativa* L.) can be introduced as a functional food product, as sprouts have gained significant interest in recent times due to their high nutritional values. Bio- fortification of selenium is one strategy to enhance plant bioactivity. However, the level of selenium used varies among species of plants. Thus, the proper level needs to be explored.

Objective: To investigate the influence of selenium bio-fortification on nutritional compositions, bioactive compounds content, and anti-oxidative properties of young ricegrass.

Methods: Sodium selenite ranging 0, 10, 20, 30, and 40 mg Se/L has been hydroponically bio- fortified into ricegrass, grown for 8 days, and then investigated for changes of growth characteristics, selenium content, accumulation of bioactive compounds, and anti-oxidative properties.

Results: Results revealed that selenium bio-fortified exogenously increased the accumulation of selenium in ricegrass by 529% at 40 mg Se/L treatment without negative changes in the leaves' biomass at the day they were harvested. However, the root part weight slightly decreased when the selenium level increased. Selenium at concentration of 10 and 20 mg Se/L can stimulate the production of phenolic compounds and antioxidant activities in young ricegrass as measured by DPPH, ABTS, FRAP, and chelating assay. Conversely, the higher level of selenium fortification reducing the accumulation of phenolics in ricegrass may due to pro-oxidant expression.

Conclusion: Selenium bio-fortification can be used as a useful technique to improve quality of ricegrass plantation. 10 mg Se/L treatment was an ideal to trigger the synthesis of phenolics which exhibited high antioxidant activities. However, 40 mg Se/L treatment was the most effective for the production of Se plant foods.

Keywords: Antioxidant activities; Bio-fortification; Ricegrass; Selenium

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/321/592

Efficacy of a novel herbal composition licorice flavonoid oil in subject with metabolic syndrome: a randomized double-blind placebo-controlled clinical study

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ABSTRACT

Background: In order to evaluate the effects of licorice flavonoid oil (LFO) on abdominal waist circumference, blood pressure, body weight, body mass index (BMI), lipid profile, body fat composition, and fasting blood glucose in patients with metabolic syndrome, a 12 week randomized double-blind placebo-controlled study was conducted.

Methods: Fifty patients with metabolic syndrome aged between 18-75 years were assigned to either the LFO or placebo group. Abdominal waist circumference, blood pressure, body weight, and BMI were assessed at baseline, week 4, week 8, and week 12. Clinical laboratory examinations, fat composition, and fasting blood glucose level were assessed at baseline (week 0) and final visit (week 12).

Results: A total of 50 subjects (25 subjects in each group) completed the 12-week study. Significant difference in changes from the baseline was observed in body weight, waist circumference, and BMI in the LFO group compared to the placebo group from week 4 or week 8 onwards. No adverse events were noted throughout the study.

Conclusion: The present study suggests that LFO is a promising dietary nutrient for improving metabolic syndrome, particularly through its beneficial effect of normalizing body weight, BMI, and possibly the amount of visceral fat and HDL cholesterol.

Keywords: licorice flavonoid oil; *Glycyrrhiza glabra L.*; metabolic syndrome; body mass index

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Metabolic effects of Gum Arabic (Acacia Senegal) in patients with Type 2 Diabetes Mellitus (T2DM): Randomized, placebo controlled double blind trial

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ABSTRACT

Background: Gum Arabic (GA) is a water-soluble dietary fiber, indigestible to both humans and animals. While GA currently does not have any therapeutic potential, it has nutritional value and some effects on metabolism of glucose and lipids. Thus, the aim of this study is to assess the effect of GA on serum level of glucose, lipids, and the BMI in type 2 diabetic patients.

Methods: A double-blind randomized placebo-controlled trial took place at Academy Charity Teaching Hospital (ACTH) in Sudan between August 2014 to February 2015. The trial was conducted in type 2 diabetic patients who were on regular oral hypoglycemic drugs and had HbA1C ≥ 6.5%. Patients excluded from the study included those on insulin, any patient with a metabolic or gastrointestinal disease, and any patient with history of drug addiction and alcoholism. Other patients excluded were patients who had previous allergic reactions to GA in addition to patients who were pregnant or planned for conception within 6 months. 120 patients were invited to participate in this trial. 100 patients gave consent and were randomized to GA and placebo groups. The GA group was given 30 g of *Acacia Senegal* and the placebo group was given5 g of placebo daily for 3 months. The outcomes assessed were primarily the effect of GA on glucose levels in addition to the effects on levels of lipids and BMI in type 2 diabetic patients.

Results: The GA group showed significant reduction in fasting plasma glucose (FPG) and HbA1c ($P<0.05$) within the GA group. Moreover, GA supplementation improved lipid profiles; decreased LDL-Cholesterol by 5.95%, total Cholesterol by 8.28% and triglyceride by 10.95% from baseline levels. HDL-Cholesterol showed significant increase by 19.89% within GA group ($P<0.05$), BMI was decreased significantly by 2.06% (95% CI: −0.98; −0.16), $P<0.05$).

Conclusions: Gum Arabic is a dietary supplement for improving nutrition of type 2 diabetic patients; it has demonstrated a good effect on improving their poor glycemic control. It has also shown improvement in the levels of the lipids and the BMI. Further studies are needed in obese and pre-diabetic patients to evaluate

GA therapeutic potentials.

Trial registration: PACTR201403000785219.

Keywords: Gum Arabic, Diabetes Mellitus type 2, Lipid profiles, Fasting Plasma Glucose, Dietary Fibers, HbA1c

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Black rice as a functional food in Indonesia

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ABSTRACT

There are many local black rice cultivars in Indonesia, yet only a few of these are formally described in the literature. It has been reported that black rice has many phytochemical variants which may contribute to its use as a functional food, including nutraceuticals and secondary metabolites such as anthocyanin, oryzanol, and more. The purpose of this article was to review literature describing black rice cultivars from Indonesia, with a particular focus on its potential use as a functional food. Our literature search revealed several articles that describe black rice in relation to its nutraceutical properties and its role in reducing non-communicable diseases. Other studies describe the diversity of local pigmented rice and its potential for lowering the risk of hyperlipidemia, hyperglycemia, and for cancer prevention. Black rice has been described as a functional food in several countries; however, there is great diversity among cultivars and further research on Indonesian varieties will determine whether local variants are candidates as well for the development of functional foods.

Keywords: black rice cultivar, functional food, non-communicable diseases, nutraceutical, phytochemical

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A novel protodioscin-enriched fenugreek seed extract (*Trigonella foenum-graecum*, family Fabaceae) improves free testosterone level and sperm profile in healthy volunteers

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ABSTRACT

Background: A novel, patent-pending 20% protodioscin-enriched extract has been developed in our laboratories from fenugreek seeds (Furosap®). We assessed the efficacy of Furosap® in 50 male volunteers (age: 35-65 years) on free and total increased testosterone levels, sperm profile, mental alertness, cardiovascular health, mood, libido, and quality of life.

Methods: Furosap® (500 mg/day/subject) was administered to the 50 male volunteers over a period of 12 weeks in a one-arm, open-labelled study, to determine the efficacy on free and total testosterone levels, sperm profile and sperm morphology, libido and erectile dysfunction, mood and mental alertness and broad spectrum safety parameters. Institution Review Board approval was obtained for this study and the study was registered at the clinicaltrials.gov (NCT02702882).

Results: A statistically significant increase in free testosterone levels were observed in these volunteers following supplementation of Furosap®. Sperm morphology, sperm counts, mental alertness, mood, cardiovascular health, and libido performance were significantly improved. Extensive blood chemistry analyses revealed broad spectrum safety. No significant changes were observed in serum lipid function, cholesterol, triglyceride, HDL and LDL levels, and hemogram.

Conclusions: Results confirmed that this protodioscin-enriched extract from fenugreek seeds (Furosap) is safe and efficacious in boosting serum free testosterone levels, healthy sperm profile, mental alertness, cardiovascular health, and overall performance in male volunteers.

Keywords: Standardized fenugreek seed extract; Protodioscin; Testosterone booster; Sperm profile; Mood alleviation; Safety

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Seaweed fucoxanthin supplementation improves obesity parameters in mildly obese Japanese subjects

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ABSTRACT

Background: Fucoxanthin is a seaweed xanthophyll that has demonstrated an anti-obesity effect in rodents. However, clinical investigations of its influence on mildly obese subjects has not been performed. We conducted a clinical trial of fucoxanthin supplementation in Japanese obese subjects.

Methods: We examined the effect of fucoxanthin (1 or 3 mg daily) in a double-blind placebo- controlled study. Capsules containing fucoxanthin or placebo capsules were administered for 4 weeks to male and female Japanese adults with a body mass index (BMI) of more than 25 kg/m^2. Before and after treatment, the body weight, body composition, abdominal fat area, and the circumferences of the neck, arm, and thigh were evaluated.

Results: There was significant reduction of the relative (ratio versus before treatment) body weight, BMI, and visceral fat area in the 3 mg/day fucoxanthin group compared to the placebo group. Relative values of total fat mass, subcutaneous fat area, waist circumference, and right thigh circumference were also significantly lower in the 1 mg/day fucoxanthin group than the placebo group. A significant decrease of the absolute right thigh circumference was noted in the 1 mg/day fucoxanthin group compared to the placebo group. In the subjects ingesting fucoxanthin, there were no abnormalities of the blood pressure, pulse rate, blood parameters, and urinalysis parameters, which thereby suggests adverse effects.

Conclusions: Fucoxanthin reduced body weight, BMI, and abdominal fat by acting on both visceral and subcutaneous fat. Consequently, Fucoxanthin may be able to improve a moderate overweight state in both men and women.

Keywords: Randomized, double-blind, placebo-controlled crossover trial; fucoxanthin; body mass index; body weight; subcutaneous fat; adipose tissue

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/333/606

Reduction of blood pressure by aronia berries through inhibition of angiotensin- converting enzyme activity in the spontaneously hypertensive rat kidney

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ABSTRACT

Background: Aronia berries contain many important effects on potential health, with previous studies suggesting that aronia juice is useful for the treatment of hypertension.

Objective: To examine whether aronia berries have improvement effects on hypertension through the inhibition of angiotensin- converting enzyme (ACE) activity.

Method: The normal diet containing 10 % freeze- dried aronia berries was administered to five spontaneously hypertensive rats (SHRs) in each group for 28 days, with their body weight, food intake, and systolic blood pressure being measured. At 28 days after administration of aronia berry- containing diets, the serum, lungs, and kidneys were isolated and used for measurement of ACE activity.

Results: In this study, we found that blood pressure in SHRs fed freeze- dried aronia berries- containing diet decreased compared with the blood pressure in SHRs fed normal diet. We also discovered that the catalytic activity of ACE was reduced in the kidney of SHRs fed freeze- dried aronia berries- containing diet but not in the lungs of aronia berries- administered rats.

Conclusion: Aronia berries have beneficial effects on the amelioration of hypertension through inhibition of the kidney renin- angiotensin system.

Key word: aronia, hypertension improvement, kidney renin- angiotensin system, ACE.

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Omega 3 fatty acids intake versus diclofenac in osteoarthritis induced in experimental rats

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ABSTRACT

Background: Osteoarthritis (OA) is a degenerative joint disease, characterized by abnormal remodeling pattern of joints driven by inflammatory mediators within the affected joints. Its symptoms are many like pain, stiffness, and decreased function.

Objective: The present study mainly focused on the anti-inflammatory effect of omega 3 fatty acids (F.As) versus diclofenac, non-steroidal anti-inflammatory drug in OA induced in rats

Design: Intraarticular injection of monosodiumiodoacetate (MIA) 24.6 mg/kg in 0.6 ml saline was used to induce OA. Diclofenacand omega-3 F. These were administered orally, daily for 21 days and after 24 hours of OA induction.

Results: Osteoarthritis induction resulted in an increase in serum levels of IL-6 (479.5%), TNF- α(545.5%), and CRP (754.2%) along with IL-10 level decrease (70.3%) as compared to normal group. Diclofenac intake demonstrated significant increase of IL-6 (24.9%), CRP (88.6%), and TNF-α (25.2%) compared to the OA control group. Omega 3 FAs intake showed significant reduction in inflammatory markers along with IL-10 increase, in comparison to OA group. Both treatment demonstrated a significant increase in TIMP2 along with decreased MMP2 and MPO in comparison with OA control. Positive correlation of IL-6 with MPO ($r = 0.7$, $P=0.002$), and negative one with IL-10 ($r = 0.9$, $p<0.0001$) and TIMP2 ($r = -0.5$, $p<0.008$) was observed. Interleukin-10 was negatively correlated with MMP2 ($r = -0.5$, $p<0.007$) and MPO ($r = -0.8$, $p<0.0001$).

Conclusion: Data derived from biochemical and histopathological results, indicated that omega3 FAs may be expressed as a natural anti-inflammatory agent of a significant potential in OA with evident remarkable effect.

Keywords: OA; omega3FAs; diclofenac; MMP2; TIMP2; MPO

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Selenium bio-fortification: an alternative to improve phytochemicals and bioactivities of plant foods

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ABSTRACT

Plants are major food sources which possess marvelous health benefits to human beings. To the present age, the effort to improve composites in plants using a bio-fortification technique is expedient to obtain super plant foods. Selenium (Se) is an essential trace element that works on antioxidant system in living beings. Plants have been bio-fortified with Se worldwide to increase Se content in addition to improving the bioactive compounds and biological properties. However, restricted documents were elucidated on the summary and underlying mechanisms which provide beneficial effects on plant phytochemicals and bioactivities improvement. Accordingly, this review article attempts to study available literature on Se bio-fortified plants while also clarifying possible routes through which Se may affect plants biochemical process. Increasing the content of Se bio-fortified in plants resulted in both positive and negative effects. The appropriate exogenous concentration of Se bio-fortification varies among the individual plants as different species have the ability to accumulate and tolerate different levels of Se. The concentration of Se which can support growth or induce them to the early stage of stress are strategic to provide desired effects on an improvement of phytochemicals. Moreover, Se bio-fortified molecules acts as a protectant against drought, cold, UV, heavy metals, and salt strains. The greater antioxidant, anti-cancer, and prebiotic properties were also reported from an increased amount of phytochemical and the synergistic effects of Se and plant phytochemicals. However, higher doses of Se fortified were toxic to plants at specific levels. Consequently, Se bio-fortification can be claimed as a unique strategy to improve plant treasures.

Keywords: Selenium, Bio-fortification, Phytochemicals, Bioactivities

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Allomeric Scaling: Theory and Applications

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ABSTRACT

The history and bases for selectedallometric energy relationships are reviewed in this article, specifically those related to quarter-power scaling as described by M. Kleiber, i.e. interspecies metabolic rates scaleas a function of mass to the three-quarters power (metabolic body size). Interspecies requirements for essential factors are also noted (e.g., vitamins and minerals). A case is made thatinterspecies vitamin and mineral requirements are similar when expressed per unit of metabolizable energy consumed or metabolic body size. Furthermore, it is emphasized that: 1) these relationships may be applied broadly and allow for the scaling of energy-related and nutrient needs in animals as small as screws to as large as elephants, and 2) application of appropriate allometric scaling methods to nutritional questions allows one to make stronger inferences when extrapolating results derived from experimental animal models to humans.

Key words: Nutrient requirements, basal metabolism, metabolic body size, allometric scaling

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Lost in Translation: Allometric scaling of bioactive dietary n-3 and n-6 fatty acids

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ABSTRACT

Experimental animal models are the primary tool to test nutritional intervention strategies for health promotion and prevention and/or treatment of human diseases. These kinds of experiments test hypotheses that otherwise could not be done in humans. These models generate data important for pre-clinical screening purposes. However, their ability to predict human responses has been disappointing, particularly when it comes to dietary n-3 and n-6 polyunsaturated fatty acids (PUFA). Many times, it is difficult to recapitulate the data as a result of diet between pre-clinical experiments and clinical trials, in part because we lack the fundamental understanding of how to effectively translate diets between species. The diets in experiments using rodent models are preferentially designed to generate positive results (i.e., perform a dose response and pick the dose that works) with little thought on their applicability to humans. Accordingly, the levels of n-3 and n-6 PUFA used in rodent diets are typically on the extreme and rarely justified. A search of the literature reveals no guidelines establishing appropriate levels for the use of PUFA in rodent diets, although extrapolation to human conditions is quite common despite being inappropriate. The goal of this paper is to examine allometric scaling models between species for dietary PUFA using similar endpoints with the hypothesis that equivalent physiological changes in rodents and humans support the mathematical model.

Keywords: alpha-linolenic acid, allometric scaling, arachidonic acid, docosahexaenoic acid, eicosapentaenoic acid, linoleic acid, n-6, n-3, plasma fatty acids, polyunsaturated fatty acids

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Improving laboratory mice diets to increase relevance to human populations

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ABSTRACT

Mouse models have been an invaluable resource for biomedical research and have been instrumental for advances in our understanding of biology and human disease. However, in using these models there is the inherent issue of the translatability of research findings to human populations. Some differences between humans and rodents can never be reconciled due to key differences in physiology. However, mice models have evolved over time through innovations in genetics and standardized diets, resulting in reduced variability across experiments. Developing mice diets that more closely emulate what humans eat will help increase the translational fidelity of mouse models to human populations. This review will focus on the role of basal laboratory diets for improving mouse models.

Keywords: laboratory mouse diets, total Western Diet, allometric scaling, nutrient density scaling

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Allometric scaling models: history, use, and misuse in translating resveratrol from basic science to human clinical applications

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ABSTRACT

Determination of the first-in-human and pharmacologically active dosage for drugs and nutraceutical compounds is a critical step in study design and product development. Allometric scaling is a form of mathematic modeling commonly used to convert dosages between species. While allometric scaling allows for quick and straightforward conversions between species, it is often misunderstood and misused in translational clinical applications. This is readily demonstrated in the case of resveratrol – a polyphenol which is found in red wine. In the past decade, a considerable amount of research has emerged regarding the health benefits of the resveratrol supplementation. Although data from rodent models suggests that resveratrol can have major effects on cardiometabolic and neurologic health, human clinical trials have had mixed results. While some human clinical trials have yielded encouraging results, a few noteworthy trials have reported that seemingly appropriate allometry-derived dosages of resveratrol did not provide the expected health benefits reported in animal models. In this article, we discuss the history of various models within allometry, including their advantages, disadvantages, and nuances from a clinical perspective. This historical information will provide some insight into why dosages recommended from allometric scaling are appropriate in some circumstances and inappropriate in others. We will then demonstrate how allometric models have been utilized to translate dosages of resveratrol from rodent models into the dosages recommended for human clinical trials. Pharmacokinetic data from various human clinical trials were summarized and compared to data predicted from allometric models. Data from selected human clinical trials were then synthesized to demonstrate the dosage-dependent effects of resveratrol and to provide further insight into the appropriate use of allometric models for selecting resveratrol dosage. Altogether, this information will promote a greater understanding of the role of allometric scaling in dose selection and provide an explanation for some of the apparent inconsistencies in translational research regarding resveratrol.

Keywords: allometric scaling, dose conversion, bioavailability, pharmacokinetics, resveratrol

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A randomized, double-blind, placebo-controlled study evaluating the effects of quercetin-rich onions on cognitive function in elderly subjects

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ABSTRACT

Background: Quercetin, a phenolic compound, exhibits various functional effects that include anti-oxidant, anti-dyslipidemic, and anti-dysglycemic activities, in addition to beneficial effects on cognitive function. We evaluated the effects of a powder made from quercetin-rich onions ('Quergold' and 'Sarasara-gold') on cognitive function.

Methods: In this randomized, double-blind, placebo-controlled study, we randomized 50 adults (25 males and 25 females, aged 65–84 years) and made them consume products made from quercetin-rich (active test food group) or quercetin-free (placebo food group) onions. Cognitive function, hematological, and biological examinations were performed at the beginning (week 0) of the study and at weeks 12 and 24 after the start of the study.

Results: There were no differences in the Mini-Mental State Examination (MMSE) and cognitive impairment rating scale scores between the two groups. However, in younger subjects, the MMSE scores were significantly higher in the active test food group than in the placebo food group at week 24 ($p = 0.019$).

Conclusion: These results suggest that the ingestion of quercetin-rich onions improves cognitive function and reduce cognitive decline in elderly people.

Clinical trial registration: UMIN000015940

Keywords: clinical trial; cognitive function; mild cognitive impairment; Mini Mental, State Examination; onion; quercetin

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Demonstrating the relationship between the phytochemical profile of different teas with relative antioxidant and anti-inflammatory capacities

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ABSTRACT

Background: Indigenous or traditional aqueous plant extracts are commonly used by nearly 80% of the world's population for primary health needs. Accordingly, teas such as *Camellia sinensis* and herbal teas were characterized for their phytochemical content and potential to offer specific bioactivities that could benefit human health by mitigating oxidative stress and inflammation.

Methods: In the present study, we compared the phytochemical profiles, antioxidant, and anti- inflammatory activities of four *Camellia sinensis* teas, including white, green, oolong, black, and two herbal teas. These two herbal teas, Rooibos and Yerba mate, are produced and consumed by different populations worldwide. We also studied the impact of the Rooibos tea on the production of inflammatory mediators, including nitric oxide (NO), inducible nitric oxide synthase (iNOS), cyclooxygenase 2 (COX-2), and different cytokines in Raw 264.7 cells, both with or without interferon γ (IFN-γ) and lipopolysaccharide (LPS) stimulation.

Results: White tea had the highest total phenolic content (TPC) and antioxidant activity among the six teas that were examined. In contrast, Rooibos tea had the lowest TPC, antioxidant, and anti- inflammatory activities. Yerba mate tea exhibited the greatest potential to inhibit NO production in IFN-γ and LPS-induced Raw 264.7 cells. The anti-inflammatory activity of teas was discovered to be correlated with antioxidant activity and phytochemical composition. Among the six teas examined, only Rooibos tea was found to induce NO in unstimulated Raw 264.7 cells. Under basal conditions, Rooibos tea induced interleukin-1α (IL-1α), IL-1β, IL-6, IL-10, granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage colony-stimulating factor (GM-CSF), tumor necrosis factor-alpha (TNF-α), iNOS, and COX-2 production. However, Rooibos tea also demonstrated a dose-dependent inhibition of IL-6, IL-10, iNOS, and COX-2 expression in stimulated Raw 264.7 cells. Although a high concentration of Rooibos tea was effective in inhibiting induced IL-1α, G-CSF, and GM-CSF, lower concentrations also up-regulated the expression of these cytokines. No inhibitory effects of Rooibos tea examined were discovered with the mitigation of IL-1β and TNF-α.

Conclusion: Rooibos tea possesses dual functions on inflammation, either by promoting an inflammatory response to cytokine induction or alternatively inhibiting inflammation during tissue injury or a pathogen infection via a mechanism involving the inhibition of pro-inflammatory cytokines and mediators such as iNOS and COX-2. The potential of Rooibos tea to induce NO production is also noteworthy in mitigating disease states including hypertension and cardiovascular diseases.

Keywords: *Camellia sinensis,* Rooibos tea, herbal tea, inflammation, cytokine, antioxidant

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/342/618

Antioxidant activity and phenolic contents of Ajwa date and their effect on lipo-protein profile

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ABSTRACT

Background: Dates (*Phoenix dactylifera L.*) are well known as both a food and economic crop for many years worldwide due to its substantial nutritional, health, and economic benefits besides its appeal and environmental value. However, although Date pits are rich in phenolic and antioxidant contents, they are generally neglected and treated as a waste product. Ethnobotanical records indicate the potential of Ajwa dates pits and flesh having phenolics, antioxidants, and some other nutrients.

Objective: The purpose of the study was to extract the phenolic contents and to determine the antioxidant scavenging activity of Ajwa date flesh and pits in comparison to local date varieties in three different solvents with three different concentrations, and to observe their effect on the high lipo-protein profile of albino mice.

Materials and Methods: Three solvents viz**.** Methanol, Ethanol, and Acetone were used at concentrations of 70%, 80%, and 90% to make nutraceutical extracts. These extracts were characterized for numerous nutritional parameters. Correlation of flavonoid with phenolic, DPPH, ABTS, and other parameters were studied. The above extracted Ajwa flesh and pits extracts were then administrated to high cholesterol induced albino mice under three different treatments (10%, 20% and 30%) in four different groups where one group was studied as control

Results: Pits appeared to be the richest source for total phenols and total flavonoid contents. Such extracts from pits were high in DPPH and ABTS activity compared to that of the flesh in all date cultivars, which were the highest in Ajwa pits (3932.3 mg GAE/100g, 2956.2 mg QEC/100g, 96.3% and 86.2% respectively). In the comparative analysis of solvents, 80% ethanol extracted the highest antioxidant activity for both DPPH and ABTS assay in all date varieties and their parts. Behaviour of solvent for polyphenol (Total phenols and total flavonoids) extraction was highly variable so that a single solvent cannot be recommended for extraction. Highly significant correlation of flavonoids with DPPH was observed in pits part. Phenolic contents positively correlated with flavonoids, DPPH, and ABTS. DPPH and ABTS also revealed a strongly positive correlation. In PCA analysis phenolic contents, flavonoid contents and antioxidant activity showed a strong relation among pits, while demonstrating a weak relation in flesh parts. Furthermore, results also depicted that 30% extracts of Ajwa pits have a higher effect on the percent reduction of total protein, total triglycerides, total cholesterol, and LDL-C levels, in addition to a significant percent increase in HDL-C levels in treated albino mice

Conclusion: The work identifies variability among the flesh and pits of Ajwa date and local date varieties for their polyphenols contents, antioxidant activity, and their health beneficial effect against a high Lipo-protein profile that can be used as an active ingredient against different maladies in food products and supplements.

Keywords: PCA, Ajwa, lipo-protein, phenolics

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Functional quality, sensorial and shelf-life characteristics of Agathi (*Sesbania grandiflora* (L). Poir leaves enriched breads

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ABSTRACT

Background: In our modern life, the burdens of non-communicable diseases such as obesity, cancer, cardiovascular disease, and type-2 diabetes have increased. By contrast, life expectancy and also cost of health care has increased. Therefore, individuals search other ways to improve or maintain their well-being. In this regard, food and pharmaceutical industries offer functional foods (FFs) with health promoting and disease-preventing properties. *Sesbania grandiflora* L.Poir is a small, loosely branching tree also known as the local name, Agathi. Agathi belongs to the Fabaceae family, and is one of the most popular green vegetables and traditional medicinal plants of India. The chemical analysis *of Sesbania grandiflora* leaves reveal it to be a rich source of nutrients and beneficial bioactive compounds, such as antioxidants and polyphenols. Bread has been regarded as one of the most popular food for centuries, as a good source of calories and other nutrients. Bread is traditionally made from wheat flour. The addition of Agathi leaves led to the enhancement of functionality of common bread.

Objective: Against the background of this information, the present investigation was undertaken with a clear objective of evaluating the effects of the addition of Agathi leaves on the sensory, textural, and baking characteristics, by examining their microbial quality on a 5- day storage period, at an ambient temperature, in different packaging materials, and assessing the improvement, if any, in their antioxidant content.

Methods: Shade dried Agathi leaf powder was analysed for proximate, mineral, and phytochemical composition. Bread samples were prepared with ingredients such as yeast, salt, sugar, water, shortening, baking time, temperature using straight dough process, and varying levels of shade dried Agathi leaves. Physical parameters such as loaf weight, loaf volume, and color values were recorded. Breads were subjected to a sensory evaluation, and *in vitro* anti- oxidant capacity was evaluated.

Results: Addition of leaves to the plain bread is a means of fortification of bread. The leaves of the Agathi plant are rich in nutrients, antioxidants and, dietary fiber. Incorporation of dried leaves to wheat flour shows that the supplemented breads have, in general, enhanced moisture retention capacity, slower staling rate, richer antioxidant content, better baking characteristics, and improved sensory properties in terms of color, texture, mouth feel, and flavor. Shade dried leaves at 10% level of addition on wheat flour were found to be the optimum level that offered the highest acceptability of the fortified bread.

Conclusion: Results show that the addition of the Agathi leaf powder bettered the crumb moisture content with only a little increase in crumb firmness. A substantial improvement in sensory characteristics was observed with the Agathi supplemented breads. A sharp increase in antioxidant content was an important beneficial fortification

effect observed in the fortified breads. Agathi leaf content of 10 gm was found to be the optimum level that offered the best compromise for the highest acceptability of the fortified breads.

Keywords: Functional food, bioactive compounds, *In vitro* Anti-oxidant capacity

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The anti-atherosclerotic effects of tomatoes

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ABSTRACT

Tomatoes are rich in lycopene, which causes the red coloring of tomatoes. Several reports have suggested lycopene plays a role in the prevention of cardiovascular diseases. In this study, we systematically reviewed the interventional studies using tomatoes or tomato products to understand the anti-atherosclerotic effects of the tomato as a functional food. We found that a significant number of interventional studies reported the anti-atherosclerotic effects of tomatoes, including anti-obesity effects, hypotensive effects, improvement of lipid/glucose metabolism and endothelial function, anti-oxidative and anti-inflammatory effect, and anti-platelet effect; however, the anti- platelet effect was disagreed upon by some studies. Furthermore, we discovered cooking methods significantly affect anti-atherosclerotic effects of tomatoes.

Keywords: anti-oxidative effect, atherosclerosis, body weight, tomatoes, serum lipids

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Managing hypertension: relevant biomarkers and combating bioactive compounds

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ABSTRACT

Hypertension is one of the most common chronic diseases affecting many people of a higher age group. The standard definition that is offered to the general public has a minimum age of 18 years to be diagnosed with hypertension. Many studies have been conducted in the hopes of finding consistent data that provides information on the biomarkers of hypertension and effective forms of treatment. However, there is a tendency for skewed data due to the ineffectiveness of diagnosing hypertension, because of the reasons of variability in technique or even negligence. Interestingly, research has indicated that there are connections to certain biomarkers of hypertension, however the results have been deemed inconclusive. Moreover, the results provide promising data for future studies with an emphasis on biomarkers. The biomarkers that have been consistently brought to researchers' attention are: circulating C-reactive protein (CRP), plasminogen activator inhibitor-1 (PAI-1), urinary albumin:creatinine ratio (UACR), and aldosterone:renin ratio (ARR). These four biomarkers have become the foundation of multiple hypertension studies, yet the only formal conclusion that could be drawn is that there is a wide range of variables that have some kind of influence on hypertension. More recently, treatment options for hypertension have increasingly become an emphasis of studies; and research has predicted that nutrition plays a key role in the managing of diseases. Furthermore, the role of bioactive compounds has gained traction in hypertension research, as it has been loosely correlated to managing specific biomarkers. Ultimately, these correlations to bioactive compounds like, antioxidants, would demonstrate that certain functional foods have the capacity to help treat hypertension. The modality is to find an alternative option for managing or treating hypertension through natural sources of food or food products fortified with ingredients to combat the known biomarkers. This is why the research of functional foods will provide hypertensive patients with an opportunity to affordably manage their chronic disease.

Keywords: hypertension, bioactive compounds, functional foods, vitamins

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Maitake mushrooms (*Grifola frondosa*) enhances antibody production in response to influenza vaccination in healthy adult volunteers concurrent with alleviation of common cold symptoms

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ABSTRACT

Background: The prevention of influenza virus infection is a critical public health challenge. Thus new, safe, and effective strategies are needed to reduce the risk of infection. Maitake mushrooms (*Grifola frondosa*) are popular in Asia for their flavor and immune-stimulating properties. In this study, we examined whether the dietary consumption of Maitake was effective in boosting the potency of influenza virus vaccination.

Methods: We set up a double-blind, placebo-controlled clinical trial (n=50 subjects for Maitake consumption; n=50 for placebo) and analyzed hemagglutination inhibition (HI) antibody titers in response to trivalent influenza vaccine (type A H1N1, H3N2, and type B BX-51B) for a 12-week period of daily Maitake intake (6.825g), beginning 4 weeks before and continuing 8 weeks after vaccination. We also evaluated the efficacy of Maitake for suppression of common cold symptoms by questionnaire.

Results: We found that continuous Maitake intake raised HI titers against influenza type A virus H1N1 and type B virus, and significantly increased the seroconversion rate for older adults (>60 years of age). Additionally, severe cold symptoms including rhinorrhea and headache were significantly improved by Maitake intake.

Conclusion: In this clinical trial, we demonstrated that Maitake intake enhanced antibody production in response to influenza vaccination while simultaneously suppressing multiple common cold symptoms. The current results suggest that Maitake may activate both innate and adaptive immune responses for the prevention of virus infection. In conclusion, we expect that Maitake intake potentiates host defense systems and has a protective effect against influenza virus and other pathogenic viruses and bacteria.

Keywords: clinical trial, *Grifola frondosa*, influenza, Maitake, vaccine

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Beneficial effects on fasting insulin and postprandial responses through 7- day intake of New Zealand blackcurrant powder

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ABSTRACT

Background: Blood glucose and insulin are elevated after intake of carbohydrate, with levels returning to normal in about 2-3 hours after ingestion. We examined the effects of daily New Zealand blackcurrant intake over 7 days on fasting glucose and insulin levels and the responses of glucose and insulin during an oral glucose tolerance test (i.e. OGTT).

Methods: Seventeen healthy participants (9 males, 8 females, age: 24±8 years, body mass: 75.4±16.4 kg, height 172±11 cm, body mass index: 25.3±3.3) consumed 6 g·day^{-1} New Zealand blackcurrant (NZBC) powder for 7 days. Every 6 g of the serving contained 138.6 mg anthocyanins, 49 mg vitamin C, and 5.2 g of carbohydrates with total phenolic content 271.6 mg. A cross-over design was used. Participants completed one OGTT before starting the supplementation (day 0) and another OGTT after 7 days of the supplementation (day 7). For the OGTT, participants were seated and consumed 75 g of glucose dissolved in 250 mL water. Finger prick capillary samples were taken before and every 30 minutes for a total of 120 minutes after consuming the glucose drink. Following duplicate glucose analysis, blood samples were centrifuged and then plasma was separated and frozen (-20°C) for triplicate insulin analysis using a human 96-well insulin enzyme-linked immunosorbent assay (IBL international, Hamburg, Germany).

Results: NZBC had no effect on fasting glucose (control: 4.46±0.45; NZBC: 4.41±0.44 mmol·L^{-1}, P=0.657), although there was a trend for fasting insulin to be 14.3% lower (control: 66.5±28.2; NZBC: 57.0±29.5 pmol·L^{-1}) (P=0.091). HOMA-IR was not different between the control and NZBC (1.81±0.73 vs 1.58±0.83) (P=0.126). With NZBC during the OGTT, plasma glucose at 60 min was 8.1% lower (control: 6.68±1.13; NZBC: 6.14±1.41 mmol·L^{-1}; P=0.016), insulin at 30
min was 18.4% lower (control: 337.1±228.3; NZBC: 275.0±136.4 pmol·L^{-1}; P= 0.021), and insulin at 60 min was 39.2% lower (control: 297.8±154.3; NZBC: 181.2±97.4 pmol·L^{-1}; P= 0.002). With NZBC during the OGTTs, areas-under-the-curve for plasma glucose (control: 752.6±79.4, NZBC: 709.8±93.3 mmol·L^{-1}·120 min) and insulin (control: 28443±12816, NZBC: 20406±7985, pmol·L^{-1}·120 min) were 5.7% (P=0.051) and 31.1% lower (P<0.001) respectively.

Conclusion: A trend for lower fasting insulin with normal glucose and lower areas under the curve for glucose and insulin suggests that repeated intake of New Zealand blackcurrant powder increases insulin sensitivity. This is the first observation of a high-anthocyanin containing berry powder to increase insulin sensitivity. Regular intake of New Zealand blackcurrant powder may be beneficial for the postprandial responses in people with type 2 diabetes or metabolic syndrome.

Keywords: Anthocyanins, Glycaemia, Insulinaemia, Berries, Blood Glucose, Diabetes, Metabolic Syndrome

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Quantitative Analysis of Sugar Ingredients in Beverages and Food Crops by an Effective Method Combining Naphthimidazole Derivatization and ^{1}H- NMR Spectrometry

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ABSTRACT

Background: Though carbohydrates are needed for health, excessive uptake of sugar may induce obesity, decayed teeth, and chronic diseases. The Taiwan Food & Drug Administration has recently proposed to regulate common sugars, a list that includes glucose, galactose, fructose, lactose, maltose, and sucrose in beverages and dietary foods. Accordingly, rapid and effective methods are needed for the quantitative analysis of sugar ingredients in beverages and foods.

Objective: To establish a convenient method of quantifying sugar ingredients in beverages and foods by using one-dimensional ^{1}H-NMR spectroscopy via a simple treatment with naphthimidazole (NAIM) labeling kit.

Methods: The sample of beverages or the hydrolysate of food crops were treated with an NAIM labeling kit that contains 2,3-naphthalenediamine and iodine in acetic acid solution. After the complete conversion of the reducing sugars to sugar-NAIM derivatives, the mixture solution was subjected to rotary evaporation under reduced pressure, and the residue was dissolved in D2O solution with dimethylsulfoxide (DMSO) as an internal standard for the ^{1}H-NMR spectrometric analysis.

Results: An aldose existing in two anomeric isomers is completely converted to the corresponding NAIM derivative that shows a single characteristic vinyl proton at a distinct position to facilitate the quantitative analysis by NMR spectrometry. Even 10 µmol of common sugar ingredients in 50 µL of beverage or in the hydrolysate prepared from 1 mg of food crop can be quantified.

Conclusion: The results suggest that a simple treatment of beverage with the NAIM labeling kit provides a convenient method for the quantification of sugar ingredients by ^{1}H-NMR spectrometry. This method combining NAIM derivatization and ^{1}H-NMR analysis is also useful for the profiling and fingerprinting of food crops.

Keywords: sugar, beverage, food crop, naphthimidazole, ^{1}H-NMR spectrometry, quantitative analysis.

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Changes in the rate of PSA progression and the level of alkaline phosphatase during high dose vitamin C treatment of patients with prostate cancer

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ABSTRACT

Introduction: Intravenously administered vitamin C (IVC) may have anti-cancer and anti- inflammatory properties. Many studies demonstrated evidence of a good safety profile of IVC treatments and improvement of the quality of life in cancer patients. IVC has been proposed as a treatment for cancer as an adjuvant in conjunction with other therapies. To investigate high dose ascorbic acid potential in treating prostate cancer, a retrospective study was conducted using clinical data from the Riordan Clinic database (1994-2015).

Methods: We collected data, when available, on the following patient characteristics at diagnosis and during the courses of IVC therapy: age, tumor stage, Gleason score, serum prostate specific antigen (PSA) and alkaline phosphatase (ALP) levels, and location of metastases. In particular, PSA, ALP, and C-reactive protein (CRP) levels are analyzed in prostate cancer patients given IVC therapy during several years.

Results: We found that PSA, CRP, and ALP correlate with tumor staging as measured by Gleason scores. Moreover, peak plasma ascorbate levels attained during the patients first IVC infusions are reduced in patients with elevated PSA and CRP levels. Tracking the changes in PSA and ALP with time in patients for whom data are available indicates that the rate of increase in these variables over time can be reduced by incorporating IVC therapy and by increasing the frequency of IVC treatments.

Conclusion: There appeared to be a relation between the frequency of IVC treatments and the rate of PSA change, with PSA rate of growth decreasing as the frequency of IVC increases. Further research into the use of IVC in prostate cancer patients is warranted.

Key words: High dose vitamin C, prostate cancer, prostate specific antigen, alkaline phosphatase, C-reactive protein.

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/360/634

Phenolic and Flavonoid Compounds in Aqueous Extracts of *Thunbergia laurifolia* Leaves and Their Effect on the Toxicity of the Carbamate Insecticide Methomyl to Murine Macrophage Cells

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ABSTRACT

Background: *Thunbergia laurifolia* is a Thai herb and has been used in Thai folklore medicine for centuries. Generally, Thais consume *T. laurifolia* as a herbal tea because of its beneficial properties as an antidote for chemical toxins, drug-, arsenic-, strychnine-, alcohol- and food- poisoning. However, its effectively against some insecticide compounds, e.g. methomyl, has not yet been determined.

Objective: To examine the protective effect of aqueous extract from leaves of *T. laurifolia* on methomyl (MT) poisoning of murine macrophage cells (anti-MT effect) and to identify phenolic and flavonoid compounds in the extract.

Methods: *T. laurifolia* was extracted with water and stored in freeze-dried form. The extract was investigated for its antioxidant activity and some phenolic and flavonoid compounds were identified using liquid chromatography–mass spectrometry (LC-MS). To study anti-MT effects in RAW264.7 murine macrophage cells, these were treated with leaf extract either before (pre- treatment), concomitantly (combined) or after (post-treatment) exposure to MT and cell viability determined in an MTT test (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide).

Results: The extract exhibited strong antioxidant properties based on total extractable phenolic content (TPC), total extractable flavonoid content (TFC), 2,2'-azino-bis(3-ethylbenzothiazoline-6- sulphonic acid) (ABTS) radical scavenging, 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging and Ferric ion reducing antioxidant power (FRAP) activity. The LC-MS analyses of phenolic compounds indicated the presence of caffeic acid, rosmarinic acid, catechin, rutin, isoquercetin, quercetin and apigenin as bioactive compounds. Viability of RAW 264.7 murine macrophage cells treated with MT was increased significantly by post-treatment with leaf extract but not by combined or pre-treatments.

Conclusion: The aqueous extract of *T. laurifolia* leaves contained abundant antioxidant activity. Flavonoids present were catechin, rutin, isoquercetin, quercetin and apigenin. The aqueous leaf extract was able to help cells recover from the effects of exposure to MT.

Keywords: *Thunbergia laurifolia*, phenolics, flavonoids, methomyl, RAW264.7 murine macrophages, insecticide

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/336/630

Suppressive activity of enzymatically-educed soy protein hydrolysates on degranulation in IgE-antigen complex-stimulated RBL-2H3 cells

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ABSTRACT

Background: Soy protein isolate (SPI) is increasingly used in foods because it is a high quality non-dairy protein with excellent functional properties. However, soy allergy is one of the world's major eight food allergies.

Objective: To investigate the anti-allergic activity of soy protein hydrolysates (SPHs) produced with alcalase and pepsin proteases.

Methods: SPI was enzymatically hydrolysed using the proteases, while evaluating the reaction conditions which include E/S (enzyme to substrate ratio) of 0.5%, 1.0% and 1.5% (250 u/mg and 5 u/g of pepsin and alcalase respectively); and hydrolysis time (0 min, 30 min, 1h, 2h, 4h and 8h). Afterwards, rat basophilic leukaemia (RBL)-2H3 cells activated by the IgE-antigen complex were used to assess mast cell degranulation inhibitory activity of the SPHs by the release of *β*- hexosaminidase. RBL-2H3 cells were sensitized with monoclonal anti-dinitrophenol (DNP) specific IgE and challenged with the antigen DNP-bovine serum albumin in the presence or absence of SPHs.

Results: It was observed that 0.1 mg/mL concentration of the 0.5% E/S SPHs prepared in the first 4h significantly ($P < 0.05$) inhibited *β*-hexosaminidase release in an IgE-antigen complex- stimulated RBL-2H3 cells compared to those produced at other time intervals, E/S, and concentrations.

Conclusion: This is the first report of its kind that shows the ability of SPHs to suppress degranulation of RBL-2H3 cells. Consequently, SPHs have good prospects to be used as potential sources of low cost hypo or anti-allergic protein.

Keywords: Soy Protein Isolate, Soy Protein Hydrolysates, RBL-2H3 Cells, *β*-Hexosaminidase, Anti-allergy

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Astaxanthin attenuates neurotoxicity in a mouse model of Parkinson's disease

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ABSTRACT

Background: Astaxanthin (AXT) is a natural carotenoid with diverse biological activities. Although it is best known as a potent antioxidant, recent work suggests additional mechanisms of action that have the potential to oppose the ongoing pathophysiology of Parkinson's disease (PD). For example, AXT has a putative role in modulating microglial activity and preserving mitochondrial function, thereby implicating this compound as a neuroprotective agent. Both oxidative stress and inflammation are involved in the progression of many neurodegenerative diseases. Therefore, we examined the efficacy for AXT to reduced neurotoxicity in a toxic model of PD in mice.

Methods: In this study, we used a 4-week dietary supplementation of algae derived AXT to reduce 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induced dopaminergic cell death.

Results: AXT treated mice were protected against the loss of tyrosine hydroxylase (TH) staining in the substantia nigra (SN) after MPTP exposure compared to the control diet. This effect of preserved TH immunoreactivity was also observed in the striatum. Furthermore, AXT administration was able to interrupt the neuroinflammatory process known to contribute to neurodegeneration in this model.

Conclusion: We demonstrate that AXT neuroprotection was associated with attenuated microglial activation as indicated by reduced immunohistochemical detection of IBA-1 in the SN and striatum of AXT treated mice. Altogether, these studies suggest that AXT has neuroprotective property in the central nervous system against MPTP neurodegeneration.

Keywords: Astaxanthin, Neuroprotection, Neurodegeneration, Neuroinflammation, Parkinson's disease

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Evaluation of the effect of N-acetyl-glucosamine administration on biomarkers for cartilage metabolism in healthy individuals: a randomized double-blind placebo-controlled clinical study

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ABSTRACT

Background: A randomized double-blind placebo-controlled clinical study was conducted to evaluate the chondroprotective action of N-acetyl-glucosamine (GlcNAc) supplement on healthy individuals without arthritis.

Methods: Healthy subjects (n=120, 54.3 ± 8.1 years (mean ± SD)) without arthritis were randomly assigned to receive 500 mg GlcNAc (n=60, GlcNAc group) or a placebo (n=60, placebo group) once a day for 16 weeks, and cartilage metabolism was evaluated by analyzing type II collagen degradation (C2C) and type II collagen synthesis (PIICP) markers, and the ratio of type II collagen degradation to type II collagen synthesis (C2C/PIICP).

Results: Among 120 eligible subjects, 114 subjects completed the study. First, all the subjects with a body mass index of ≥25 kg/m^2 and Kellgren and Lawrence grade of ≥1 were analyzed. However, the changes in the C2C and PIICP levels and the C2C/PIICP ratios from the baseline were not significantly different between the placebo and GlcNAc groups during 16 weeks and 8 weeks after the intervention. Next, to make the effect of GlcNAc even clearer, the subjects with body mass index of <25 kg/m^2 and Kellgren and Lawrence grade of 0 were analyzed. The changes in the C2C levels from the baseline were significantly decreased in the GlcNAc group compared with the placebo group at 8 and 12 weeks during the intervention. In contrast, the changes in the PIICP levels from the baseline levels were almost constant during and after the intervention in both groups. Based on these findings, the changes in the C2C/CIICP ratios from the baseline slightly decreased in the GlcNAc group compared to the placebo group at 8 and 12 weeks during the intervention. Furthermore, no test supplement-related adverse events were observed during and after the intervention.

Conclusion: These observations suggest that oral administration of GlcNAc at a dose of 500 mg/day exerts a chondroprotective effect in subjects without arthritis. This effect was achieved by improving cartilage metabolism (reducing type II collagen degradation), without causing apparent adverse effects.

Keywords: N-acetyl-glucosamine, biomarker, cartilage metabolism, joint health, randomized clinical study
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Influence of an elevated nutrition risk score in patients suffering from esophageal cancer following tumor resection

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ABSTRACT

Background: Patients who suffer from malignant tumors of the esophagus and esophagogastric junction have 5-year survival rates of up to 83%, something that is documented in the early stages of cancer. Too often, weight loss is an underestimated sign for patients suffering from cancer on the upper gastrointestinal tract. Weight loss is associated with different adverse outcomes. Even after tumor resection, malnutrition remains a severe problem that still affects long-term disease free survivors.

Material and methods: This study included the clinical courses of 205 patients suffering from cancer of the esophagus or the esophagogastric junction who were operated on between July 2007 and December 2009. On admission, the nutrition risk score was evaluated. Follow-up data were collected routinely. The aim of the underlying study was to show the prevalence of an elevated nutrition risk score (NRS) and to demonstrate its influence on perioperative mortality and morbidity. Furthermore, the relevance of an elevated nutrition risk score on the postoperative survival was analyzed.

Results: More than a third (35.8%) of the patients included in this study had a nutrition risk score of at least three. A preoperative elevated nutrition risk score did not have a significant influence on perioperative morbidity or on 30-days mortality rate. In patients with early tumor stage UICC stage I a/b, an elevated risk score of 3 or more had a significant influence on postoperative survival. In contrast, in advanced tumor stages an increased NRS did not have a significant negative influence on survival within both UICC II a/b and UICC III a/b.

Conclusion: Further studies are required to demonstrate whether a nutritional intervention can improve the survival rates of patients suffering from malignant tumors within the esophagus and in whom an operation has to be performed.

Keywords: Weight loss, esophageal cancer, NRS

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A randomized, double-blind, placebo-controlled study to examine the effects of high-isoflavone soybeans "Yukipirika" in climacteric women

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ABSTRACT

Background: Soy isoflavones belong to a class of plant-based compounds known as phytoestrogens and effect menopausal symptoms and bone metabolism. We evaluated the effects of high-isoflavone soybeans ("Yukipirika") in climacteric women.

Methods: In this randomized, double-blind, placebo-controlled study, we randomly selected 64 female subjects (aged 46–60 years) to consume products made from high-isoflavone soybeans (active test), low-isoflavone soybeans (Placebo 2), or wheat (Placebo 1). The simplified menopausal index (SMI) test, visual analog scale (VAS) of skin and hair conditions, joints functions, and bowel movements, blood examination, and urinalysis were performed at weeks 0, 4, and 8 during the study period.

Results: Intake of high-isoflavone soybeans did not change bone metabolism parameters. However, a subsection of the SMI score was improved in the active test food group compared to the Placebo 2 food group. Additionally, VAS of skin conditions, joints functions, and bowel movements improved in the active test group compared to the Placebo 1 or Placebo 2 groups.

Conclusion: These results suggest that the ingestion of high-isoflavone soybeans "Yukipirika" can improve skin conditions, joints functions, and bowel movements, in addition to menopausal symptoms.

Clinical trial registration: UMIN000019450

Keywords: bone metabolism, clinical trial, isoflavone, soybeans, menopausal symptoms, Yukipirika

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Elemental content profiles in propolis from several cities of Turkey

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ABSTRACT

Background: Macro-element content profiles in propolis that have been previously used in traditional folk medicine have provided enough information to develop a classification of the geological origin of propolis. Within this study, we aim to contribute our research to existing literatüre, particularly through our use of EDXRF spectroscopy, which has not been used to study propolis before. The results of the study led us to conclude that the residues of heavy metals were a limited concentration in Turkish propolis samples.

Objective: The purpose of this study was to investigate the macro-element profiles in Turkish propolis from 18 different cities of Turkey.

Methods: The macro-element of 22 raw propolis samples were investigated using Energy- Dispersive X-ray fluorescence spectrometry.

Results: Turkish Propolis was discovered to be rich with minerals of potassium, sodium which could be more beneficial in human nutrition. Potassium content was at a relatively higher level than other elements in these samples, while calcium content was at alower level in those samples from various regions of Turkey.

Conclusion: The elements of propolis that we studied were distinctive enough to make the discrimination of propolis from different locations in Turkey possible. The quantification by energy-dispersive X-ray fluorescence spectrometry procedures provided good resolution of multi- element analysis in propolis samples.

Keywords: Propolis; element analysis; energy-dispersive X-ray fluorescence spectrometer

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Natural product inhibitors of acetyl-lysine erasers in the prevention and treatment of heart failure

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ABSTRACT
Heart failure (HF) is a major public health concern, with five-year mortality rates following first admission for HF being approximately 50%, thereby stressing the need for novel therapeutic approaches. Histone deacetylases (HDACs) govern lysine acetylation of histone tails that regulates nucleosmal DNA. HDAC inhibitors have emerged as efficacious therapies in pre-clinical models of HF. Interest in diet-gene interactions has given rise to the study of 'food bioactives' as epigenetic regulators of gene expression that control human health and disease. These reports demonstrate that bioactive food compounds regulate epigenetic marks that link diet to gene regulation. In fact, others have also shown that bioactive compounds can target HDACs for inhibition; accordingly, bioactive food compounds offer unique opportunities for therapeutic intervention and prevention of heart failure. Lastly, there is emerging interest into how these food bioactives function together or as additives within foods 'functional foods' to regulate epigenetic disease. This review will highlight bioactive compound HDAC inhibitors and their role in the heart.

Keywords: acetylation, bioactive compounds, dietary HDAC inhibitors, HDACs, histone deacetylases

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DNA methyltransferase 1-targeting miRNA-148a of dairy milk: a potential bioactive modifier of the human epigenome

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ABSTRACT

Background: The perception of milk has changed from a "simple food" to a more sophisticated bioactive functional signaling system that promotes mTORC1-driven postnatal anabolism, growth, and development of the newborn infant. Accumulating evidence supports the view that milk´s miRNAs significantly contribute to these processes. The most abundant miRNA of milk found in milk fat and milk exosomes is miRNA-148a, which targets DNA methyltransferase 1 (DNMT1), a pivotal epigenetic regulator that suppresses transcription. Furthermore, milk-derived miRNA- 125b, miRNA-30d, and miRNA-25 target TP53, the guardian of the genome that interacts with DNMT1 and regulates metabolism, cell kinetics, and apoptosis. Thus, the question arose whether cow´s milk-derived miRNAs may modify epigenetic regulation of the human milk consumer.

Methods: To understand the potential impact of dairy milk consumption on human epigenetics, we have analyzed all relevant research-based bioinformatics data related to milk, milk miRNAs, epigenetic regulation, and lactation performance with special attention to bovine miRNAs that modify gene expression of DNA methyltransferase 1 (*DNMT1*) and p53 (*TP53*), the two guardians of the mammalian genome. By means of translational research and comparative functional genomics, we investigated the potential impact of cow´s milk miRNAs on epigenetic regulation of human *DNMT1*, *TP53*, *FOXP3*, and *FTO,* which are critically involved in immunologic and metabolic programming respectively. miRNA sequences have been obtained from mirbase.org. miRNA-target site prediction has been performed using TargetScan release 7.0.

Results: The most abundant miRNA of cow´s milk is miRNA-148a, which represents more than 10% of all miRNAs of cow´s milk, survives pasteurization and refrigerated storage. The seed sequence of human and bovine miRNA-148a-3p is identical. Furthermore, human and bovine DNMT1 mRNA share 88% identity. The miRNA-148a 7mer seed is conserved in human and bovine DNMT1 mRNA respectively, which may allow for the strong binding of bovine miRNA- 148a to human DNMT1 mRNA. Consequently, we hypothesize that bovine milk miRNA-148a - protected by highly resistant milk exosome membranes - may reach the systemic circulation of the milk consumer targeting and suppressing human *DNMT1* mRNA. Attenuated DNMT1 expression associated with reduced CpG promoter methylation upregulates gene expression of developmental genes such as *FOXP3* and *FTO*. Milk-derived miRNA-125b, miRNA-30d, and miRNA-25 via targeting *TP53* may downregulate p53, which physically interacts with and stabilizes DNMT1. Enhancement of dairy lactation performance is associated with increased expression of bovine milk miRNA-148a, a modification that may further increase the miRNA-148a load of dairy milk.

Conclusion: Translational evidence and comparative functional genomics support our hypothesis that bovine milk miRNA signaling may suppress human DNMT1-mediated epigenetic regulation and p53 signaling, which closely interacts with the epigenetic and transcriptional regulation of growth, metabolism, cell cycle progression, and

apoptosis. Human and bovine milk miRNAs are able to target *DNMT1* and *TP53* mRNAs, share identical seed sequences, and resist pasteurization. Pasteurization and refrigeration of dairy milk conserves the gene regulatory software of milk and allows its unrestricted entry into the human food chain. The continued exposure of modern humans to milk´s epigenetic machinery since the widespread distribution of refrigerators is a novel change of human nutrition which may promote diseases of Western civilization.

Keywords: adipogenesis, dairy, DNA methyltransferase 1, epigenetics, exosome, miRNA-148a, miRNA-125b, milk, obesity, p53, Parkinson disease, prostate cancer

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Evaluation of bioactivity of fucoidan from laminaria with *in vitro* human cell cultures (THP-1).

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ABSTRACT

Background: Seaweeds represent one of the few remaining food sources available globally which are not being fully utilized or even over utilized. Kelps (*Laminaria spp.*) are one of the numerous species of brown seaweeds, a popular marine vegetable, which has been used as a source of iodine and minerals for centuries. Kelps contain anionic polysaccharides called fucoidans heteroglycans with L – fucose units. Their monosaccharide composition, physicochemical and bioactive properties vary between seaweed species. The objective of this work was to evaluate the bioactive properties of laminaria fucoidan (*L. digitata* and *L. hyperborea*) toward THP–1 macrophages, a human macrophage like cell line, and investigate its potential antioxidant and immunomodulatory characteristics.

Methods: THP-1 macrophages were incubated with five fucoidan concentrations. The Oxygen Radical Absorbance Capacity (ORAC) assay was determined for cell lysates and for the fucoidan extract, in addition to Total Polyphenol Content (TPC). Cytotoxicity of fucoidan was assessed by light microscopy, followed by XTT proliferation assay. Enzyme–linked immunosorbant assays (ELISA) were performed to determine concentrations of the secreted tumor necrosis factor α (TNF-α), interleukin 6 (IL–6), and interleukin 10 (IL–10).

Results: Fucoidan did not affect macrophage ability to scavenge oxygen radicals (ORAC) confirming its antioxidant properties toward activated macrophages. The laminaria fucoidan extract at 100 µg/ml concentration lowered macrophage viability. Lower concentrations of laminaria fucoidan did not have impact on cell viability. Very low concentration of fucoidan at 0.1 µg/ml triggered secretion of TNF-α. However, IL–6 and interleukin IL–10 were expressed when concentration of applied fucoidan was 10 µg/ml indicating bioactivity of laminaria fucoidan through immunomodulatory actions.

Conclusion: The study demonstrated how laminaria fucoidan may have bioactive properties towards THP–1 macrophages. Changes in cytokine secretion between pro–inflammatory (TNF–α, and IL–6) and anti–inflammatory (IL–10) cytokines confirmed bioactivity of the laminaria fucoidan extracts.

Keywords: Seaweeds, Kelps, Laminaria, fucoidan, bioactivity, macrophages

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Curcumin protects liver inflammation by suppressing expression of inducible nitric oxide synthase in primary cultured rat hepatocytes

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Running title: Curcumin inhibits hepatic iNOS induction

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ABSTRACT

Background: Curcumin has beneficial effects on organ metabolism. However, there is little evidence that curcumin affects inflammatory mediators, such as tumor necrosis factor (TNF)-α and nitric oxide (NO). In an inflamed liver, proinflammatory cytokines stimulate liver cells, followed by the induction of inducible NO synthase (iNOS). Excessive NO produced by iNOS is one of the factors in liver injury. Therefore, inhibiting iNOS induction for preventing liver injury is important.

Objective: This study aimed to investigate liver protective effects of curcumin by examining interleukin (IL)-1β-stimulated hepatocytes.

Methods: Primary cultured rat hepatocytes were treated with IL-1β in the presence or absence of curcumin. Induction of NO production and iNOS, and the signaling pathway of iNOS were analyzed.

Results: Simultaneous addition of IL-1β and curcumin decreased expression levels of iNOS protein and mRNA, resulting in inhibition of NO production. Curcumin also reduced mRNA expression of TNF-α and IL-6. Curcumin inhibited two essential signaling pathways for iNOS induction, NF-κB activation and type I IL-1 receptor upregulation. Transfection experiments revealed that curcumin reduced iNOS mRNA levels at the promoter activation and mRNA stabilization steps. Delayed administration of curcumin after IL-1β addition also inhibited iNOS induction.

Conclusions: Curcumin affects induction of inflammatory mediators, such as iNOS and TNF-α, in part through the inhibition of NF-κB activation in hepatocytes. Curcumin may have therapeutic potential for organ injuries, including the liver.

Key words: curcumin, inducible nitric oxide synthase, liver injury, primary cultured hepatocytes, nuclear factor-κB, type I interleukin-1 receptor, tumor necrosis factor-α.

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Improvement of defecation in healthy individuals with infrequent bowel movements through the ingestion of dried Mozuku powder: a randomized, double-blind, parallel-group study

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ABSTRACT

Background: Okinawa mozuku (*Cladosiphon okamuranu*) is a type of edible seaweed of the family *Chordariaceae* that typically contains the polysaccharide fucoidan as a functional ingredient. In Okinawa, raw mozuku is eaten as vinegared mozuku together with vinegar or as tempura (deep-fried in batter). Polysaccharides such as fucoidan are generally known to regulate intestinal function, which is why we have used Okinawa mozuku to investigate this intestinal regulatory effect.

Methods: The study was designed as a randomized, double-blind, parallel group study. Dried Okinawa mozuku powder at a dose of 2.4 g/day (1.0 g/day of fucoidan) and a placebo not containing any dried Okinawa mozuku powder were each made into capsules and given to healthy men and women with infrequent weekly bowel movements (2–4 movements a week) to ingest for eight weeks. We then investigated changes in the defecation situation, blood tests, and adverse events.

Results: In the group that ingested the capsules containing dried Okinawa mozuku powder, the number of days with a bowel movement significantly increased compared with the placebo group after four weeks of ingestion ($p < 0.05$). Furthermore, after eight weeks of ingestion, the same increasing trend was seen compared with the placebo group ($p = 0.0964$). The volume of stool also increased significantly in the dried Okinawa mozuku powder group after eight weeks compared with the placebo group. In terms of blood tests and adverse events, no adverse events occurred that were the result of the test food.

Conclusion: Ingestion of Okinawa mozuku was found to have a regulatory effect on intestinal function by promoting defecation in healthy individuals with a tendency for constipation. This demonstrated that Okinawa mozuku is a functional food capable of making defecation smoother and increasing the volume of stool.

Keywords: Okinawa mozuku, *Cladosiphon okamuranus*, fucoidan, dry powder, bowel movement, constipation

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Functional Foods in fad diets: A review

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ABSTRACT

Fad diets can be defined as any diet making claims that are unrealistic and not supported by evidence-based data. Having been developed since the early 19th century, fad diets promise drastic weight loss and/or other unsubstantiated health claims while often omitting entire food groups. Their popularity with the public makes them an important topic for nutritionists and clinicians, especially in the framework of the obesity epidemic. Additionally, it is conceivable that components of fad diets can indeed facilitate weight loss, even if the diet overall is without merit. The grapefruit diet, the cabbage soup diet, and the human chorionic gonadotropin (hCG) diet are among the most popular fad diets and are reviewed within this study not only in terms of the diet plan itself, but also in terms of possible and known weight loss and health benefits provided by the foods on which the diets are based. Bioflavonoids in grapefruit, including naringin, hesperidin, and bergamottin, may benefit glucose homeostasis. Cabbage contains lutein, zeaxanthin, kaempferol, quercetin, and apigenin, which have anti-inflammatory properties and improve both glucose homeostasis and fat metabolism. The hCG diet is frequently supplemented with non-hCG preparations often containing African mangoes, which has been shown to enhance weight loss by an unspecified mechanism; astragalus root, which has antioxidant, anti-inflammatory, and peroxisome proliferator-activated receptor-gamma receptor agonistic properties; arginine, which stimulates lipolysis; glutamine, which has been shown to enhance weight loss, perhaps by altering the gut microbiome; carnitine, which appears to facilitate weight loss; B12, which improves insulin resistance; and niacin, which improves the dyslipidemia associated with being overweight/obese. Presently, high-quality clinical trials suggest that fad diets reduce weight in the short term due to drastic caloric restriction rather than functional food properties. However, the proof of principle has been demonstrated, and clinical trials of the functional foods utilized in fad diets are much needed.

Keywords: functional foods, fad diet, weight loss, naringin, hesperidin, and bergamottin

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/346/656

Double-blind, parallel group, placebo-controlled study of *Kjellmaniella crassifolia* Miyabe (Gagome) in human: The potential of Gagome to activate the immune system

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ABSTRACT

Background: Marine brown algae, *Kjellmaniella crassifolia* Miyabe (Gagome) is extensively harvested in Northern Japan and is known to help improve the immune system and prevent lifestyle diseases by its functional constituents, particularly the polysaccharide fucoidan. However, since most scientific findings come from animal studies, we examined its potential effectiveness in humans to raise immune functions, using small amounts of Gagome to avoid overconsumption of iodide.

Methods: We set up a double-blind, placebo-controlled clinical trial (n=30 subjects for Gagome consumption; n=30 for placebo), in which 0.8 gram/day of Gagome containing 200 mg as dietary fiber (ca. 80 mg as fucoidan) was ingested for 8 weeks. The primary end-point was natural killer (NK) cell activity while other immune-related biomarkers, such as immunoglobulins (IgM and IgA) and cytokines (IL-12 and IFN-□) were secondary end-points.
Results: No adverse effects were observed during the course of the clinical trial. We found that 8-week daily Gagome intake raised NK cell activities for the group with a relatively higher baseline number of NK cells (p=0.03). We also demonstrated that Gagome intake exerted a tendency to stimulate IgA secretion. These results indicate the possibility that Gagome intake may potentiate host defense systems in human as seen in animal studies.

Conclusion: In this study, we used small amounts of Gagome (0.8 g daily) as an active test sample to avoid overconsumption of iodide, and found that this amount could enhance NK cell activities, particularly in the subclass with initially higher NK cell numbers. We also found an appreciable increment of IgA. With all of these facts, it seems that Gagome intake activates immune responses that contribute to the promotion of health through stimulation of the immune system.

Keywords: clinical trial, dietary fiber, fucoidan, Gagome, natural killer cells

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Lentinula edodes and *Pleurotus ostreatus*: functional food with antioxidant - antimicrobial activity and an important source of Vitamin D and medicinal compounds

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ABSTRACT

Background: Mushrooms produce a large amount of medicinal compounds, and are also an optimal source of fibres, proteins, vitamins (like groups B and D), and other micronutrients including potassium, magnesium, etc. Consequently, mushrooms are commonly considered to be functional foods. Many works report the high biological potentials of medicinal mushrooms involving their antibacterial, hypoglycaemic, anticholesterolemic, radical scavenging, and anti- inflammatory effects.

Context and purpose of this study: First off, this work aimed to find strains of *Lentinula edodes* and *Pleurotus ostreatus* from a bank of edible mushrooms bought from international strain banks (Table I) that could possess health benefit related properties, such as a radical scavenging activity (antioxidant effect), antibacterial effects against common pathogenic bacteria, and being able to produce interesting nutrients and secondary metabolites. As the fungal bank comprises of 20 strains of *L. edodes* and 20 strains of *P. ostreatus,* a first screening was made by the selection of 13 strains for each mushroom able to grow in multiple wood types or that were particularly productive and had proved good growth reproducibility over the last 5 years. This work also studied the correlation between culture conditions and mushroom quality in terms of the previously reported properties. Comparison among the selected strains was operated by the assessment of antioxidant and antimicrobial activities after different sample treatments. Furthermore, an initial optimization of the analytic techniques was produced for the direct estimation of important secondary metabolites and nutrients by means of HPLC-MS/MS technique. Further research will encompass an evaluation of transformation processes (drying, freezing, rehydration, cooking, etc.) impact on radical scavenging, antibacterial activity, and possible degradation/loss of nutraceutically important substances such as vitamin D2, ergothioneine, eritadenine, lovastatin, lentinan, and lenthionine.

Results: 13 strains of each mushroom species have been cultivated on different wood logs. Seven strains of shiitake and six strains of oyster mushroom were able to produce sporocarps. Antioxidant levels in water extracts from dried mushrooms produced significatively different results on the basis of strains and of wood. Both mushrooms demonstrated higher radical scavenging activity in log cultivation than substrates cultivation, which was subsequently used as reference. Furthermore, all strains of *P. ostreatus* demonstrated the lowest level of antioxidant activity at 4°C, a significant increase towards 50°C and a limited decrease towards 80°C. The same trend was observed for shiitake extracts. Concerning the shiitake mushroom only, crude water extracts showed an interesting

antibacterial activity against the model microorganisms *Pseudomonas aeruginosa* and *Staphylococcus aureus*. A comparison was also performed between the best performing strain extract and the commercial antibiotic Ceftriaxone against *P. aeruginosa*, assessing that 20 mg of crude extract corresponds to 0.2 mg of the pure antibiotic when studied by means of disk diffusion assay.

Conclusion: The results suggested that the cultivation of both shiitake and oyster mushrooms on logs could enhance the content of antioxidant and antibacterial activities, compared to the cultivation of mushrooms on sawdust substrates. Radical scavenging and antibacterial activity depends both on *L. edodes* strain and the log type. The bacteriostatic/bactericidal activity of the best performer strain may depend on a pH and solvent treatment sensitive substance. Secondary metabolites such as ergothioneine and vitamin D2 from both shiitake and oyster were released just after water extraction: this suggests that the transformation/cooking processes may produce a loss of characteristic mushroom biological properties in water. Further evaluation of biologically relevant compounds content and loss during different food transformation and cooking processes will be assessed.

Keywords: Shiitake, Oyster, *Pleurotus ostreatus, Lentinula edodes, Pseudomonas aeruginosa, Staphylococcus aureus*, Log grown mushroom, antioxidant, radical scavenging, total phenolic content, DPPH, ABTS, Folin-Ciocalteu, antibacterial, fruitbodies, sporocarps.

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The modified amino sugar N-Butyryl Glucosamine fed to ovariectomized rats preserves bone mineral through increased early mineralization, but does not affect body composition

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ABSTRACT

Background: The toxicities of pharmaceuticals for chronic arthritis and osteoporosis should be of concern to consumers. This partially accounts for the popularity of consumption of the amino sugar glucosamine, in-spite of controversy about its efficacy. We chemically synthesized N- butyryl glucosamine (GlcNBu), which we discovered protected bone and cartilage in an inflammatory arthritis rat model when used as a feed supplement. GlcNBu can also be potentially synthesized biochemically, since we recently demonstrated that human acetyl-CoA: glucosamine-6-phosphate N-acetyltransferase 1 has a relaxed donor specificity and transfers acyl groups of up to four carbons in length, i.e. the butyryl moiety. Oral GlcNBu had no detectable toxicity and also protected against bone loss in ovariectomized (OVX) rats as a model for osteoporosis. However, we demonstrated this only for bones excised at 6 months. Thus, the current study aims to determine when bone mineralization is maximized during daily GlcNBu supplementation, in both OVX and Sham-OVX rats, in addition to the relationship of bone mineralization to body composition.

Methods: Female Sprague-Dawley rats were randomized into 4 groups, containing 8 rats each. The groups consisted of OVX or Sham-OVX rats whose diets were supplemented with either 200 mg/kg/day of GlcNBu or an equimolar amount of glucose. We performed sequential bone density and body composition measurements, by dual-energy X-ray absorptiometry in the live, anesthetised rats, over a 6-month experimental period, starting at the age of 8 weeks. Results were analyzed by descriptive statistics and 2-way ANOVA.

Results: The major increases in the mineral content and density of the spine and the femur in GlcNBu-supplemented rats occurred early, from the baseline to week 8. Ovariectomy resulted in a number of significant differences in body composition, while feeding GlcNBu had no significant effects on body composition. The significant effects of ovariectomy on body composition initially appeared at 8 weeks, while the GlcNBu effects on increased bone mineral initially appeared at 2 weeks. An interaction between OVX and GlcNBu was seen only at 16 weeks for the bone mineral density of the femoral head.

Conclusions: Supplementation of the diet by GlcNBu in both OVX and Sham-OVX rats increases bone mineral as

early as 2 weeks. Ovariectomy but not GlcNBu supplementation had a significant effect on body composition. The effect of GlcNBu occurs independently of changes in body composition, probably as a direct effect of stimulation of bone matrix synthesis which continues to be mineralized. This work represents an important step in the development and commercialization of GlcNBu for the prevention and treatment osteoporosis, where there is now an increasing demand for safe, long term agents.

Keywords: osteoporosis, ovariectomy, N-butyryl glucosamine, bone, mineralization, body composition, dual-energy X-ray absorptiometry

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/377/673

Effects of vitamin E and its derivatives on diabetic nephropathy in Rats and identification of diacylglycerol kinase subtype involved in the improvement of diabetic nephropathy

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ABSTRACT

Background: Diabetes is a significant social issue. Controlling diabetic complications such as nephropathy is very important for QOL of diabetic patients. One of the mechanisms which causes diabetic complications is the abnormal activation of protein kinase C (PKC) by increased diacylglycerol (DG) from hyperglycemia. Diacylglycerol kinase (DGK) can attenuate PKC activity by converting DG to phosphatidic acid. Thus far, d-α-tocopherol (VtE) treatment has been shown to prevent early changes of diabetic renal dysfunctions by activating DGK. However, it is still unknown whether VtE derivatives improve diabetic nephropathy similarly to VtE, and which DGK subtype is activated by VtE and/or the derivatives.

Objective: The purpose of the study was to investigate effects of VtE and its derivatives on diabetic nephropathy in rats, in addition to identifying the DGK subtype involved in the improvement of nephropathy in vivo.

Methods: To induce diabetes in rats, six weeks old male Sprague-Dawley rats were intraperitonealy administrated 65 mg/kg streptozocin (STZ) in 20 mM citrate buffer. For two or eight weeks, 40 mg/kg VtE, 44 mg/kg acetate VtE (aVtE) or 49.3 mg/kg succinate VtE (sVtE) was intraperitonealy administrated every other day after STZ administration. The blood glucose level, body weight, and kidney weight, in addition to urinary volume, albumin, and BUN were measured every week after STZ administration. Additionally, in order to identify the DGK subtype activated by VtE and aVtE, the DGK subtype expressed in the rat glomerulus was checked by RT-PCR and western blotting, and the activity in the glomerulus from the rats before and after the VtE and aVtE treatments were measured in the presence or absence of EGTA.

Results: Averages of kidney weight and BUN of rats treated with VtE, aVtE and sVtE for 8 weeks were reduced, compared to the control. However, the intraperitoneal administration of sVtE was toxic. Additionally, the amount of urine volume and urinary albumin significantly improved by the two-weeks treatment of VtE and aVtE. mRNA of DGKα, γ, δ, ε, and ζ were detected in the glomerulus, but only the protein of DGKα and DGKδ were detected as

calcium-dependent and independent subtype respectively. Both VtE and aVtE activated DGK in the glomerulus. However, the calcium dependent DGK subtype was mainly activated by aVtE, with not only the calcium- dependent subtype but also the calcium-independent subtype being activated in the case of VtE. In other words, DGKα was activated by aVtE and DGKδ was additionally enhanced in the case of VtE.

Conclusion: These results clearly indicated that aVtE as well as VtE improved diabetic nephropathy, with the activation of DGKα and/or δ being potentially involved with this improvement.

Key words: diabetic nephropathy, diacylglycerol kinase, vitamin E

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In vitro investigation of orange fleshed sweet potato prebiotic potential and its implication on human gut health

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ABSTRACT

Background: Some food ingredients (prebiotics) have been shown to promote a healthy gut by selectively stimulating growth/activity of beneficial gastrointestinal microbes and metabolites such as short chain fatty acids (SCFA) while inhibiting pathogens. Orange fleshed sweet potato (*Ipomoea batatas* Lam; OFSP) root tuber is a starchy tropical crop and highly nutritious in terms of pro- vitamin A (beta carotene), dietary fibre, and natural sugars, with negligible amount of fats and cholesterol. The aim of the study was to investigate using simulated human gut system whether OFSP may have prebiotic activity derived from their fibre, resistant starch, and/or the sugars.

Methods*: In vitro* pH controlled stirred batch culture fermentation system was used to compare the effect on human gut microbiota of four substrates: two varieties of OFSP (SPK 004 and Tainung), FOS and sucrose known for positive prebiotic and non-selective change respectively. The system was inoculated with faecal slurry from six different human healthy donors from different ethical backgrounds, age, and the effectual change recorded over 24 hours by monitoring bacterial counts (total bacteria, *Bacteroides* and *Bifidobacterium*) using qPCR molecular technique and SCFA profiles by gas chromatography.

Results: The total bacteria count increased by (0.92-1.7 log10) and *Bacteroides* genus (1.03-1.8 log10) throughout the experimental period but with no significant differences ($p<0.05$) between the four substrates. However, there were significant differences ($p<0.05$) in the beneficial *Bifidobacterium* (1.66-2.66 log10) between the 2 varieties of OFSP and the two controls (FOS and sucrose). The levels of SCFA increased, with acetate as the predominant acid and lactic acid being the least. The OFSP purees elicited high butyric acid levels, which were comparable to those of positive control FOS.

Conclusion: The study demonstrated that OFSP purees may have prebiotic potential that can positively modulate gut microbiota by promoting growth of beneficial bacteria, *bifidobacterium* genus, and stimulating production of SCFA especially butyric acid which is the favourable in human gut health. However, further research using more probiotic and pathogenic microbes in addition to *in vivo* clinical studies and compositional analysis of OFSP is needed to confirm prebiotic activity.

Keywords: Orange fleshed sweet potato, prebiotic, human gut microbiota

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Dietary interventions as a neuroprotective therapy for the delay of the onset of cognitive decline in older adults: Evaluation of the evidence

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ABSTRACT

Background: The relationship between nutrition and cognitive functioning is unclear, especially in elderly populations as many elderly people with cognitive impairment have low blood levels of some nutrients even in the absence of malnourishment. The objective of this review was to assess the evidence from systematic reviews of human studies on the effectiveness of dietary interventions as monotherapies in delaying the onset of cognitive decline in older adults.

Scope and approach: Evidence-based methodologies were used to gather and assess the highest levels of evidence that evaluated the effects of administration of any dose of the individual dietary interventions as neuroprotective agents for any duration. The search strategy was designed to identify systematic reviews and meta-analyses published from 1990 to December 2015. There were no language restrictions as part of the inclusion criteria.

Key Findings and Conclusions: This review provides the current state of knowledge from systematic reviews on the effects on cognition of acetyl-L-carnitine, alpha-lipoic acid, choline, inositol compounds, omega-3 polyunsaturated fatty acids, and polyphenols, which are all commonly studied nutrients for neurocognitive effects. A critical evaluation of the current evidence from systematic reviews indicated that there are no clinically-relevant effects from supplementation with these nutrients on delaying the onset of cognitive decline in older adults.

Keywords: diet, cognition, Alzheimer's disease, dementia, nutrient

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/370/664

The influence of probiotics on individual fecal secondary bile acid levels: a two-case study of schizophrenic patients receiving an atypical antipsychotic drug

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ABSTRACT

Background: Probiotics is used as a promising approach in the prevention and treatment of hypercholesterolemia. Modification of bile acid metabolism through the deconjugation of bile salts by microbial bile salt hydrolase (BSH) is considered to be the core mechanism of the hypocholesterolemic effects of probiotics. Nevertheless, BSH activity is reported to be detrimental to the human host due to the generation of toxic secondary bile acids. Thus, the influence of probiotic intake on bile acid metabolism needs to be elucidated. We analyzed the bile acid levels and microbiota in human fecal samples after probiotic supplementation to assess the influence of probiotic intake on fecal bile acid levels. Two patients hospitalized for schizophrenia and dyslipidemia, receiving an atypical antipsychotic drug, were enrolled in this study (Subjects A and B). Both subjects received *Lactobacillus rhamnosus* GG (LGG) for 4 weeks, and no probiotics for the following 4 weeks. Fecal samples were collected at baseline and after 4 and 8 weeks.

Results: Conjugated bile acids may be modified by indigenous intestinal bacteria into unconjugated bile acids and secondary bile acids through deconjugation reactions by BSH activity and the subsequent 7□-dehydroxylation pathway, respectively. In the fecal microbiota from Subject A, the relative abundance of *Bifidobacterium* increased after LGG supplementation (30%– 49%). Most *Bifidobacterium* and *Lactobacillus* strains that colonize mammalian intestines may report BSH activity, and in general bifidobacteria reveals a higher BSH activity than lactobacilli. The fecal unconjugated bile acid and secondary bile acid levels in Subject A increased after the LGG supplementation (0.36–1.79 and 1.82–16.19 □mol/g respectively). Although the LGG supplementation appears to promote bile acid deconjugation, most of the unconjugated bile acids in Subject A appear to have been modified into secondary bile acids. Alternatively, in Subject B there were no significant changes throughout the study.

Conclusion: We observed a significant increase in the fecal secondary bile acid levels after probiotic administration in one of our cases. Further studies are needed to elucidate the factors affecting 7□-dehydroxylation of bile acids to confirm the safety of using probiotics.

Keywords: bile salt hydrolase; BSH; dihydroxylation; *Bifidobacterium*

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High light bio-fortification stimulates *de novo* synthesis of resveratrol in *Diplotaxis tenuifolia* (wild rocket) micro-greens

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ABSTRACT

Background: Brassica vegetables and leafy greens are consumed globally due to their health promoting phytochemicals. *Diplotaxis tenuifolia* (wild rocket or arugula) is a popular Brassica leafy green, with a diverse range of phytochemicals (in mature plants). Immature plants (micro-greens, 2-4 true leaves) accumulate phytochemicals up to 10 times more than plants grown to maturity. Although plants accumulate phytochemicals ubiquitously, environmental stimuli can further enhance this phenomenon of accumulation, which is part of a global stress mechanism in plants. In this study, we describe a simple method toward the bio-fortification of a wild rocket micro-green system, *via* environmental manipulation (using high light).

Objective: To establish a high light-induced bio-fortification strategy to augment the accumulation of bio-active compounds in Brassica micro-greens (wild rocket), with the purpose of developing a 'designer' micro-green melange (functional food product) containing a diverse range of bio-active (disease preventative) compounds.

Results: High light stimulated wild rocket micro-greens to achieve a significant increase of known phytochemicals (documented in relevant Brassica leafy greens). Furthermore, undocumented phytochemicals (resveratrol, catechin, epicatechin, and kaempferol, among others) also accumulated to adequate concentrations. Plant extracts from bio-fortified micro-greens displayed increased antioxidant capacity (up to 3-fold, when compared to the control), a key component in future cancer cell research.

Conclusion: The use of high light resulted in successful bio-fortification of wild rocket micro-greens, evidenced by the accumulation of previously undocumented polyphenols (such as resveratrol, catechin and epicatechin) and improved antioxidant capacity.

Keywords: antioxidant, high light, micro-greens, resveratrol, wild rocket

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/380/681

Effects and safety of daily ingestion of plum extract on blood pressure: randomized, double-blinded, placebo-controlled parallel group comparison study

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ABSTRACT

Background: Hypertension is an increasing health issue in Japan. Plums are widely consumed in Japan and are reported to have various health benefits, including improvements to blood flow. However, clinical trials investigating the effects of plum extract on blood pressure have not yet been conducted. Therefore, we evaluated the effects and safety of plum extract on blood pressure in this randomized, double-blinded, and placebo-controlled parallel group comparison study.

Methods: Seventy-four healthy Japanese subjects with systolic blood pressure (SBP) ≥130 and <160 mmHg were randomly divided into test and placebo groups. Subjects were given either plum extract-processed food (3.0 g of plum extract, containing 30 mg of mumefural and 1.119 g of citric acid) or placebo food daily for 12 weeks. Physical examinations, blood measurements, and medical interviews were performed at weeks 0, 4, 8, and 12 and at 2 weeks after the intake period.

Results: SBP and diastolic blood pressure (DBP) did not significantly differ between the groups. However, in subjects with grade I hypertension, DBP was significantly lower in the active test food group than in the placebo food group at week 12 and at 2 weeks after the intake period. An exploratory subgroup analysis revealed that plum extract improved DBP in subjects with normal to high obesity/class I obesity at week 12. Moreover, plum extract had positive effects on fatigue and bowel movements as determined by visual analog scale questionnaire evaluation. No abnormal changes or severe adverse events were observed in the physical examinations, blood measurements, or medical interviews in this trial.

Conclusion: These results suggest that plum extract is safe for long-term intake and improves DBP in subjects with grade I hypertension.

Keywords: blood pressure, clinical trial, mild hypertension, plum extract

Clinical trial registration: UMIN000023184

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Immunomodulatory effects of pepsin-educed soy protein hydrolysate in rats and murine cells

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ABSTRACT

Background: There has been an increase in demand for soy and its products, with soy protein having a huge market in particular. Several reports have established how soy protein hydrolysates (SPHs) yield better physiological properties and play essential functional roles than the crude soy protein.

Objective: To investigate the immunomodulatory and acute toxicity of soy protein hydrolysate (SPH) produced with pepsin protease in mice and rats.

Methods: Soy protein hydrolysate was enzymatically produced using pepsin, with E/S (enzyme to substrate ratio) of 0.5% (250 u/mg) and hydrolysis time of 4h. Afterwards, the SPH effects on murine spleen lymphocyte proliferation, and peritoneal macrophage phagocytosis were investigated in vitro. Confirmation studies were explored in rats' sera IgG and IgA, and the acute toxic effect of SPH was observed in mice subjects.

Results: The hydrolysate increased the levels of splenocytes (stimulative index of 10.141 – 10.811) and peritoneal macrophages (phagocytic index of 1.285 – 1.721). Furthermore, the concentrations of sera IgG and IgA obtained from SPH-fed rats ranged from 0.198 – 0.345 mg/ml and 0.0184 – 0.0194 mg/ml, respectively in comparison with the soy protein isolate (SPI) -fed rats (0.208 – 0.322 mg/ml and 0.0188 – 0.0189 mg/ml, respectively). Additionally, 10 mg dose of SPH stably elicited serum IgG in contrast to other doses, while there was a general decrease in the amounts of IgA obtained in the rat subjects. Moreover, there was no acute toxic effect recorded in the mice subjects.

Conclusion: In light of the results, it is possible that SPH prepared with pepsin has the potential of improving the immune system, and may therefore be used as immunomodulatory or functional food product.

Keywords: Soy protein hydrolysates, splenocyte proliferation, immunomodulatory, phagocytosis and pepsin

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Seaberry extract with ursolic acid improves anxiety about urinary dysfunction in Japanese adults

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ABSTRACT

Background: The seaberry is a yellow berry cultivated in China, Northern Europe, and West Asian countries. Numerous biological activities of seaberries have been reported, and we recently found that ursolic acid and a flavonoid in seaberry extract (SBE) suppressed the contraction of bladder muscle specimens and collagen gel containing bladder smooth muscle cells. However, the influence of SBE on urinary problems of Japanese adults has not been investigated. Therefore, we conducted a clinical trial of SBE supplementation in Japanese subjects with mild urinary dysfunction.

Methods: We examined the effect of SBE (200 or 400 mg daily) containing ursolic acid (0.18 or 0.36 mg) in a randomized double-blind placebo-controlled study. Capsules containing SBE or placebo were administered for 8 weeks to Japanese men and women with mild urinary dysfunction. After 4 and 8 weeks of treatment, urinary symptoms were evaluated by using the King's Health Questionnaire (KHQ) and the overactive bladder syndrome score (OABSS).

Results: There was significant improvement of the KHQ emotion domain score after intake of 400 mg/day of SBE for 8 weeks compared with placebo. The answers to "Does your bladder problem make you depressed?" and "Does your bladder problem make you feel bad about yourself?" were significantly improved by SBE (400 mg/day) at 8 weeks. In the OABSS, the item "How often do you have a sudden desire to urinate, which is difficult to defer?" was significantly improved by SBE compared with placebo. Laboratory tests did not reveal any abnormalities suggesting adverse effects SBE.

Conclusion: Intake of SBE (400 mg/day for 8 weeks) improved several emotional parameters related to urinary dysfunction. SBE may be useful for reducing moderate urinary symptoms.

Keywords: King's health questionnaire, overactive bladder syndrome score, seaberry, ursolic acid, overactive bladder, urination, micturition

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/385/686

Nephroprotective effect of ethanolic leaf extract of *Thaumatococcus danielli* (benth.) in streptozotocin induced diabetic rats

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ABSTRACT

Background: The leaves of *Thaumatococcus danielli* (Benth.) have been traditionally used in folk medicine to treat malaria in Nigeria. However, there is no report on whether these leaves contain Nephroprotective activity. Thus, the ethanol leaf extract was investigated for Nephron- protective activity in Streptozotocin induced diabetic rats.

Methods: First, the LD50 of the leaf was determined using standard procedure. Rats were assigned to 5 groups (A-E) of five rats. Except for the control group, each group was made diabetic using Streptozotocin (65 mg/kg/b.wt. i p). The treated groups received 0.5 ml of glibenclamide (25 mg/kg/b.wt, o.p), 250 and 500 mg/kg/b.wt, o.p of *Thaumatococcus danielli* respectively. After 14 days of treatment, animals were sacrificed under light anaesthesia. Data expressed as Means ± S.D (n=5) and was analyzed using one-way ANOVA followed by Dunnet's test. Values were considered significant at $p<0.05$.

Results: The plant showed a LD50 greater than 5000 mg/kg/b.wt in albino rats observed for 72 hours. A significant ($p<0.05$) decrease in serum Na^+, Cl^-, HCO^-3, total protein, and an insignificant increase in K^+, urea and creatinine level were observed in the diabetic group when compared with the normal group. Oral administration of plant extract and glibenclamide significantly ($p<0.05$) restored the electrolytes to near normal. Histological alterations such as glomerulonephritis and tubules infiltration by inflammatory cells observed in diabetic control were also reversed.

Conclusion: This study suggests renal protective ability of the plant against impairment due to hyperglycemia.

Keywords: Streptozotocin, *Thaumatococcus danielli*, Nephroprotective, Glibenclamide, serum electrolytes.

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Reduction of safrole content of *Cinnamomum porrectum* leaves by blanching and the effect on the antioxidant and anti-inflammatory activities of its herbal tea

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ABSTRACT

Background: *Cinnamomum porrectum* (*C. porrectum*) is an aromatic medicinal plant from southern Thailand. While many *Cinnamomum* species demonstrate medicinal properties such as anti-inflammatory effects, some species are known to contain safrole, a group 2B carcinogen. Although the leaves of *C. porrectum* are used to produce herbal tea, there is no scientific data to support its properties as a functional food or any guarantee of its safety.

Objective: To determine the effect of blanching before drying of *C. porrectum* leaves on their safrole content, phenolic profile, total phenolic content (TPC), and total flavonoid content (TFC), antioxidant and anti-inflammatory activities were compared to leaves dried with hot air.

Methods: In the first part of the study, the leaves were dried in three conditions: freeze dried (F), hot air dried at 60 °C (C), and blanched for 60 seconds at 100 °C (B) before being dried at 60 °C until the moisture content reached 5-7% and then were ground and sieved to make powders. The F, C, and B were extracted by methanol and redefined as FM, CM, and BM, for the determination of their chemical constituents by GC-MS using *C. porrectum* wood oil (CWO) as the safrole standard. In the second part of the study, the C and B powders were analyzed for their proximate composition and were also used to make herbal tea infusions (CT and BT respectively) which were analyzed for their phenolic profile, TPC, TFC, antioxidant activities, cytotoxicity, and anti-inflammatory activity in RAW 264.7 cells.

Results: Significantly decreased safrole contents of 89% and 82% were found in the BM sample when compared with CM and FM respectively. The CT and BT had similar phenolic profiles but different contents. The TPC, TFC, ABTS, and FRAP activities, in addition to cell viability and the nitric oxide inhibition of BT were higher than that of CT.

Conclusion: The results demonstrate how blanching *C. porrectum* leaves before drying can decrease the safrole content when compared to freeze dried and hot air-dried leaves, thereby leading to a decrease of cytotoxicity in RAW 264.7 cells. Additionally, BT demonstrated a more intense phenolic profile, TPC, ABTS, and FRAP compared with the un-blanched control sample.

Keywords: *C. porrectum*, freeze drying, hot air drying, blanching before drying, safrole, RAW 264.7 cells.

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Enzymatic hydrolysis on protein and β-glucan content of Sang-yod rice bran hydrolysates and their anti-inflammatory activity on RAW 264.7 cells

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ABSTRACT

Background: Research focusing on the improvement of the utilization of rice bran is increasing due to its nutritional properties. Several biological activities of rice bran hydrolysates and its constituents have been reported. Sang-yod rice, a local rice variety in Southern Thailand, is a pigmented rice. Furthermore, its bran has high nutritive value and health beneficial components. Accordingly, there is growing interest in transforming this by-product into a functional food ingredient.

Objective: To investigate the effect of enzymatic hydrolysis processes on the digestion of protein and β-glucan and evaluate anti-proinflammatory properties of selected hydrolysates on RAW 264.7 macrophage cells.

Method: Sang-yod rice bran hydrolysates were obtained using a single or co-enzymatic hydrolysis process and sequential hydrolysis process using amyloglucosidase and protease G6. Effects of enzyme concentration (3-5% v/w) and hydrolysis duration (30, 60, and 120 min) on soluble protein and β-glucan contents of obtained rice bran hydrolysates were evaluated. The selected rice bran hydrolysates were evaluated for their cell viability and inhibition against NO and pro-inflammatory cytokines generation on RAW 264.7 mouse macrophage cell lines.

Results: Protein content (0.59-3.37 %) of the rice bran hydrolysates (RBHs) was increased by increasing of enzyme concentration (3-5% v/w) and hydrolysis time (60-120 min). However, the β- glucan content (0.88-4.63%) of RBHs decreased with the increase of those parameters. The RBHs derived by the sequential process using 5% v/w enzyme concentration and 60 min hydrolysis time gave high protein (3.23%) and high β-glucan (4.02%) contents. The hydrolysates with high amount of protein and/or β-glucan contents demonstrated no cytotoxicity against RAW 264.7 cells at a concentration range of 100-2,000 µg/ml. Additionally, they demonstrated NO inhibition and pro-inflammatory inhibition ranges of 49.09-71.63% and 9.37-71.96% respectively. Generation of TNF- α, IL-6, and IL-1β cytokines was inhibited differently by the selected RBHs.

Conclusion: Pre-digestion of Sang-yod rice bran with amyloglucosidase followed with co-hydrolysis of amyloglucosidase and protease G6 of the sequential hydrolysis process was the most effective process to release β-glucan and protein from the rice bran. The hydrolysate obtained from the process using an enzyme concentration at 5% v/w and 60 min hydrolysis duration of each stage had the highest soluble β-glucan and protein content. Moreover, the process provided the hydrolysates with potential anti-inflammatory properties on nitric oxide inhibition and pro-inflammatory cytokine inhibition on RAW 264.7 macrophage cell lines.

Keywords: Sang-yod rice, Rice bran hydrolysate, β-glucan, Enzymatic hydrolysis, Anti- inflammatory activity

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Aegeline vs Statin in the treatment of Hypercholesterolemia: A comprehensive study in rat model of liver steatosis

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ABSTRACT

Background: Aegeline (AG) is a natural hydroxyamide which has not been explored in depth for its potential applications in food, pharmaceutical, and cosmetic industries. Accordingly, in this study, the property of AG as antioxidant, anti-hypercholesterolemic, and an anti-aging component was explored. The hepatoprotective effect of AG on hypercholesterolemic rats was investigated for health care benefits as a hypocholesterolemic drug vs Atorvastatin (AV) for the first time.

Objective: The objective was to delineate the mechanism of action of AG in impeding high cholesterol diet (HCD) induced hepatic steatosis in a rat model with special reference to antioxidant status and expression of Nuclear Factor Kappa B (NF-κB) mediated cell adhesion molecules.

Methods: Thirty-six Wistar rats were divided into six groups. The pathology group rats were fed with HCD for 16 weeks and treatment groups rats were fed with HCD for 12 weeks and further supplemented with AG/AV for another 4 weeks. *In vivo* and *in vitro* experiments were carried out to find out the relative markers of the pathological condition likely Malondialdehyde (MDA), Oxidized LDL (Ox-LDL), and CRP levels were determined. Standard biochemical parameters were carried out. The expression profile by Western blot analysis was performed to assess the levels of NF-κB, Interleukin 6(IL6) and vascular cell adhesion molecule1 (VCAM1), in the hepatic tissues of various experimental groups. Additionally, histopathological examination of liver tissue sections was carried out.

Results: AG administration effectively decreased the oxidative stress induced by HCD as evidenced by MDA levels. Furthermore, the lowered levels of Ox-LDL and CRP in AG administered rats deem it to be a potent anti-inflammatory agent. Compared to AV, AG had a pronounced effect in down-regulating the expression of cell adhesion molecules.

Conclusion: Thus, this study validates AG to be an effective stratagem in bringing down the oxidative stress induced by HCD and can be deemed as an anti-hypercholesterolemic and anti- steatotic agent.

Keywords: Aegeline, Atorvastatin, liver, hypercholesterolemia, aging

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Anti-aging effects of black raspberry extract on cataract, alopecia, skin whitening, and weight loss

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ABSTRACT

Background: To maintain good health, it is important to eliminate extra reactive oxygen generated in the body. Furthermore, ingesting foods containing antioxidants is beneficial. The oxygen radical absorbance capacity (ORAC) values for black raspberry extract (BRE), blueberry extract (BBE), and raspberry extract (RBE) are 62, 66, and 49 µM Trolox equivalents (TE)/g respectively. These values are higher than those for typical antioxidant foods that have been discovered so far (3–30 µM TE/g). Our aim was to find new functionality from the food with the high ORAC value. Therefore, we have prepared these four berry extracts and examined whether they have anti-aging effects and if those effects correlate with their antioxidant activities.

Methods: We studied the following effects of 4 berry extracts: 1) lens cell protective effects; 2) effects against alopecia; 3) induction of uncoupling protein-1 (UCP1), a regulator of fat and energy consumption in adipocytes, and stimulation of irisin secretion from skeletal muscle cells; and 4) inhibitory effects on melanocyte tyrosinase activity. The evaluation method was based on below; 1) a-*crystallin*, *type 17 collagen, heat shock protein 47 (HSP47), UCP1 and Irisin* - mRNA by qRT-PCR, 2) the amount of the *UCP1 and Irisin* protein by ELISA. 3) Inhibition of tyrosinase activity was measured by dopachrome production using L-tyrosine.

Results: In lens cells, a-*crystallin* mRNA expression was induced 1 hour after treatment of the cell with Blabina (a powdered formulation containing BRE) and BRE. The extracts of all four berry species promoted the growth of follicle dermal papilla cells by 3-20% in a concentration-dependent manner. These berry extracts were also discovered to markedly induce the expression of mRNAs of *type 17 collagen* and *HSP47* in the hair follicle stem cell and elevate the expression levels of *UCP1* mRNA and its protein in adipocytes in a concentration-dependent manner. BRE and Blabina inhibited 5a-reductase in follicle dermal papilla cells and tyrosinase activity in melanocytes at the concentrations which inhibited dopachrome production by at least 50%. Finally, Blabina was discovered to stimulate the irisin secretion from skeletal muscles.

Conclusion: These results suggest that berry extracts, particularly BRE, have anti-aging effects through their higher antioxidant activities.

Keywords: Anti-aging, antioxidant, alopecia, black raspberry, weight loss, oxygen radical, absorbance capacity, skin whitening

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Glucosinolates and isothiocyanates from broccoli seed extract suppress protein glycation and carbonylation

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ABSTRACT

Background: Glucosinolates from brassica plants are hydrolyzed by internal or salivary myrosinase to produce isothiocyanates. Glucoraphanin, a major glucosinolate in broccoli, is hydrolyzed to sulforaphane (SFN), which exhibits antitumor and detoxification activities. Regarding the influence of broccoli and its constituents on the skin, a few studies have reported anti-inflammatory and antioxidant effects. Recently, advanced glycation end products (AGEs) and carbonyl proteins have been reported to accelerate skin aging.

Objective: To evaluate the effects of broccoli seed extract (BSE) and glucosinolates on protein glycation and carbonylation *in vitro*.

Methods: To evaluate the effects of BSE and its constituents, protein glycation and carbonylation were induced by mixing fructose with bovine serum albumin (BSA) and then measuring production of AGEs, fructosamine, and carbonyl proteins (CP). Production of CP after mixing fatty acids with BSA was also assessed. Furthermore, the effect of BSE and its constituents on CP production by human fibroblasts (TIG103) was examined.

Results: BSE suppressed the production of AGEs, fructosamine, and CP after mixing fructose and BSA. BSE also suppressed production of CP when oxidized linoleic acid was mixed with BSA. Isothiocyanates, including SFN and iberin, suppressed fructose-based CP production, but SFN had no effect on CP production stimulated by oxidized linoleic acid. In contrast, glucosinolates from BSE did not suppress fructose-based CP production, but suppressed CP production due to oxidized linoleic acid. Among the glucosinolates in BSE, glucoberteroin showed the strongest suppression of CP production. CP production in fibroblasts was also suppressed by glucosinolates, including glucoiberin and glucoberteroin.

Conclusion: BSE demonstrated anti-glycation and anti-carbonylation effects on protein reactions with fructose and oxidized fatty acids. Isothiocyanates suppressed protein carbonylation induced by fructose, but not those induced by oxidized lipids. On the other hand, glucosinolates (precursors of isothiocyanates) did not suppress protein carbonylation induced by fructose, but suppressed carbonylation due to oxidized lipids. Moreover, glucoberteroin and glucoiberin suppressed CP production in a cell-based assay. These results suggest that glucosinolates in BSE could suppress protein carbonylation leading to aging of the skin.

Keywords: Broccoli, glucosinolate, sulforaphane, carbonylation, glycation, glucoberteroin, glucoiberin

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Comparative study of the antioxidant and immunomodulant activities between yeast and lab fermented papaya

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ABSTRACT

Background: Dietary supplements of *Carica papaya Linn* fermented with yeast using a biotechnological process have well recognized positive effects on immunological, hematological, inflammatory, and oxidative stress parameters, utilized as biomarkers of chronic and degenerative diseases. Although many natural products fermented with lactic acid bacteria (LAB) have shown beneficial effects on the immune system and on antioxidant defenses, formulations of papaya fermented with LAB have not yet been studied.

Aims: The aims of this study were to investigate the immunomodulatory activity linked to the type of papaya fermentation (yeast *vs* LAB) in macrophages and to evaluate whether the type of fermentation differently modulates oxidative stress both in cell free system and in a model of embryonic brain cells.

Methods: Cytotoxicity was evaluated through cell proliferation kinetic and lactate dehydrogenase release assays; immunomodulatory activity through the transcriptional activation of inducible nitric oxide synthase (iNOS) and Tumor Necrosis Factor α (TNFα) by qRT-PCR in RAW 264.7 macrophages; antioxidant capacity was assessed, in cell free system and in pheochromocytoma cells embryonic brain cells, by measuring the intracellular ROS levels through a fluorescent dye.

Results: Our data showed that all the formulations studied are safe at low concentrations (3-6 mg/ml); the LAB-fermented formulations promoted the expression of iNOS and TNFα more efficiently than yeast-fermented papaya preparation ($p < 0.001$). In a cell free system, the LAB- fermented formulation acted as mild scavengers of ROS

while, in cells, both formulations didn't show any significant effect.

Conclusion: This study corroborates previous reports showing the efficacy of yeast fermented papaya as a potent immunostimulant and highlights the beneficial contribution of lactic bacteria fermentation.

Keywords: papaya, lactic fermentation, immunostimulant activity, antioxidant activity

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Magnesium Chloride increases apoptosis and decreases prostate cancer cells migration

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ABSTRACT

Background: Reduced levels of magnesium can cause several diseases and increase cancer risk. Motivated by magnesium chloride's ($MgCl_2$) non-toxicity, physiological importance, and beneficial clinical applications. This study aims to study its action mechanism and possible mechanical, molecular, and physiological effects in prostate cancer with different metastatic potentials.

Methods: We examined the effects of $MgCl_2$, after 24 and 48 hours, on apoptosis, cell migration, expression of epithelial mesenchymal transition (EMT) markers, and V-H^+-ATPase, myosin II (NMII) and the transcription factor NF Kappa B (NFkB) expressions.

Results: $MgCl_2$ induces apoptosis, and significantly decreases migration speed in cancer cells with different metastatic potentials. $MgCl_2$ reduces the expression of V-H^+-ATPase and myosin II that facilitates invasion and metastasis, suppresses the expression of vimentin and increases expression of E-cadherin, suggesting a role of $MgCl_2$ in reversing the EMT. $MgCl_2$ also significantly increases the chromatin condensation and decreases NFkB expression.

Conclusions: These results suggest a promising preventive and therapeutic role of $MgCl_2$ for prostate cancer. Further studies should explore extending $MgCl_2$ therapy to in vivo studies and other cancer types.

Keywords: Magnesium chloride, prostate cancer, migration speed, V-H^+-ATPase, EMT

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Late introduction of low dose resveratrol and grape powder after estradiol depletion does not restore glucose tolerance in the ovariectomized rat

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ABSTRACT

Background: Estrogen (E2) loss is associated with insulin resistance. Natural compounds such as resveratrol (RESV) have potential insulin sensitizing effects. Grape pomace powder (GP) also contains RESV and other antioxidants. However, the ability of realistic, attainable concentrations of RESV and GP to reverse glucose intolerance in E2 deficient rats has not yet been explored.

Purpose: The aim of the current study was to determine whether RESV and GP, in realistic amounts that could be achieved with supplementation, would be effective in restoring glucose tolerance in the ovariectomized (OVX) rat. Furthermore, there appears to be a critical time window following the loss of E2 when hormonal replacement is effective, with delayed treatment being ineffective and potentially detrimental. Therefore, we were particularly interested in examining the effectiveness of RESV and GP as a delayed treatment (i.e. after the establishment of glucose intolerance) rather than administering at the onset of E2 loss.

Results: In the present study, rats demonstrated impaired glucose tolerance, as determined by an intraperitoneal glucose tolerance test, 12 weeks after bilateral ovary removal. Subsequently, OVX animals were randomly placed into a sham or one of 3 treatment groups. The treatments were either i) a physiological oral dose of E2 (28µg/kg body mass), ii) RESV (5mg/kg body mass), or iii) GP (1.5g/100g of diet) for another 6 weeks. OVX animals were significantly heavier than non- OVX rats at the onset of glucose intolerance and this did not change throughout the treatment. None of the treatments restored glucose tolerance within the 6 weeks. Insulin tolerance did not worsen in OVX rats and was unaffected by treatment. Adipocyte size was generally increased in OVX animals and was not decreased with treatment.

Conclusion: In conclusion, delayed E2, RESV and GP treatment do not restore glucose tolerance in OVX rats. Low dose RESV and GP supplementation may not be effective alternatives to HRT to restore compromised glucose tolerance.

Keywords: ovariectomy, estrogen, resveratrol, grape pomace, glucose tolerance, insulin tolerance, delayed treatment

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Experimental Comparative Study of potential anxiolytic effect of Vitamin C and Buspirone in rats

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ABSTRACT

Background: Anxiety disorders are the most common of all mental health problems. They are more prevalent among women than among men, and they affect children as well as adults. The aim of the current study is to evaluate this problem via an experimental animal model and try to explore its possible mechanisms by studying the effect of Vitamin C compared to Buspirone on anxiety in rats induced by Monosodium Glutamate (MSG).

Materials and Methods: 56 healthy adult male albino rats (*Sprague-Dawley*) weighing 200-250 gm were used and divided into 7 groups (8 rats each). The first and the second groups were provided with normal saline and MSG at a dose of 2 mg/g p.o. respectively. The other five groups were given MSG and treated daily in the following ways: The third and fourth groups were treated with Vitamin C (100, 200 mg/kg p.o) respectively. The fifth group was treated with only Buspirone (10 mg/kg p.o.), while the sixth and seventh groups were given a combination of Buspirone and Vitamin C with (100, 200 mg/kg) respectively. After 3 weeks, the open field and successive alleys tests were used to assess behavioral changes. The percentage change of systolic blood pressure (SBP) was measured. Additionally, glutathione reductase (GR), malondialdehyde (MDA), and corticosterone levels were determined biochemically.

Results: The results after 3 weeks revealed that the MSG group showed significant anxiogenic effects in both behavioral tests, with an increased percentage change of SBP in addition to increased malondialdehyde and corticosterone levels measured statistically. While the results of the treated groups revealed that the Vitamin C (100mg/kg) treated group demonstrated significant improvement in anxiety levels in the open field test, there were no significant changes in the biochemical assessment. However, the vitamin C (200mg/kg) treated group revealed a significant anxiolytic effect in behavioral tests, improved glutathione and malondialdehyde with low corticosterone level. Administration of buspirone revealed significant anxiolytic effects, which is lower than that of vitamin C (200mg/kg). However, it caused significant increase in the oxidative stress and corticosterone levels. A combination of buspirone with Vitamin C (200mg/kg) only demonstrated significant anxiolytic effect in both tests and a significant decrease of corticosterone.

Conclusion: MSG has neurotoxic effect leading to anxiogenic behaviors in rats which are opposed by Vitamin C. Furthermore, as an antioxidant, vitamin C protects against the oxidative stress induced by MSG. Moreover, it lowers the high corticosterone level associated with MSG or buspirone administration.

Keywords: MSG, vitamin C, buspirone, glutathione reductase, malondialdehyde, open field, successive alleys

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Daily consumption of fermented soymilk helps to improve facial wrinkles in healthy postmenopausal women in a randomized, parallel-group, open-label trial

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ABSTRACT

Background: Soymilk fermented by lactobacilli and/or bifidobacteria is attracting attention due to the excellent bioavailability of its isoflavones. This study aims to investigate the effects of fermented soymilk containing high amounts of isoflavone aglycones on facial wrinkles and urinary isoflavones in postmenopausal women in a randomized, parallel-group, open-label trial.

Methods: Healthy Japanese women were randomly divided into active (n = 44, mean age 56.3 ± 0.5) or control (n = 44, mean age 56.1 ± 0.5) groups, who consumed or did not consume a bottle of soymilk fermented by *Bifidobacterium breve* strain Yakult and *Lactobacillus mali* for 8 weeks. Maximum depth of wrinkles around the crow's feet area and other wrinkle parameters were evaluated as primary and secondary endpoints respectively at weeks 0, 4, and 8 during the consumption period. Urinary isoflavone levels were determined by liquid chromatography-mass spectrometry.

Results: The active group demonstrated significant improvements in the maximum depth ($p=0.015$) and average depth ($p=0.04$) of wrinkles, and significantly elevated urinary isoflavones (daidzein, genistein, and glycitein; each $p < 0.001$) compared with the control during the consumption period. No serious adverse effects were recorded.

Conclusion: These findings suggest that fermented soymilk taken daily may improve facial wrinkles and elevate urinary isoflavones in healthy postmenopausal women.

Key words: postmenopausal women; isoflavone; fermented soymilk; phytoestrogen; facial wrinkle

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/412/1177

Beneficial effects of a Fermented Papaya Preparation for the treatment of electrohypersensitivity self-reporting patients: results of a phase I-II clinical trial with special reference to cerebral pulsation measurement and oxidative stress analysis

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ABSTRACT

Background: Electromagnetic Field Intolerance Syndrome (EMFIS), also termed Idiopathic Environmental Intolerance (IEI) attributed to Electromagnetic Fields (IEI-EMF) by WHO, is a newly identified pathological disorder occurring in electrohypersensitivity (EHS) self-reporting patients. To date, there has been no recognized treatment of this disorder. We have shown that EHS self-reporting patients experience some degree of oxidative stress, inflammation, and autoimmune response. Additionally, Fermented Papaya Preparation (FPP) has some antioxidant, anti-inflammation, and immuno-modulating properties. The objective of this phase I-II clinical trial was thus to test whether FPP treatment is well tolerated, can improve clinical outcomes, and can normalize biological abnormalities.

Methods: 32 EMFIS-bearing patients were serially included in this trial, among which 26 and 16 of them were evaluable after 3 and 6 months of FPP treatment, respectively. Clinical assessment was conducted during a specific face to face interview by using a validated pre-established questionnaire. Biological assessment consisted of measuring intracerebral tissue pulsometric index (PI) in the temporal lobes with ultrasonic cerebral tomosphygmography (UCTS), in addition to oxidative stress and inflammation with a battery of oxidative stress and inflammation-related peripheral blood tests.

Results: Overall, clinical improvement was obtained in 50-60% of the cases, among which 20- 35% presented major improvement that mainly consisted of the regression of cognitive symptoms such as loss of short term memory, concentration, attention deficiencies, insomnia, and fatigue. This clinical improvement was objectively supported by a statistically significant normal recovery of mean PI in the temporal lobes and by a FPP-related antioxidative effect, evidenced by a statistically significant decrease in malondialdehyde levels in the plasma ($p<0.0001$) and increase in the Glutathione peroxidase activity in red blood cells ($p<0.01$) in patients experiencing oxidative stress. Moreover, this trial evidenced some degree of FPP-related anti-inflammatory effects by demonstrating a statistically significant decrease in histamine ($p=0.049$) and HSP27/HSP70 chaperone proteins ($p=0.007$) in the peripheral blood of patients

with initial increased values of these inflammation-related biomarkers.

Conclusion: The results suggest a beneficial clinical and biological therapeutic effect of FPP in EHS self-reporting patients. However, the precise underlying mechanism has not yet been elucidated.

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Cytotoxic activity and anti-cancer potential of Ontario grown onion extracts against breast cancer cell lines

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ABSTRACT

Background: Breast cancer is the most commonly diagnosed cancer and the second leading cause of cancer deaths among Canadian women. Cancer management through changes in lifestyle, such as increased intake of foods rich in dietary flavonoids, have been shown to decrease the risk associated with breast, liver, colorectal, and upper-digestive cancers in epidemiologic studies. Onions are high in flavonoid content and one of the most common vegetables. Additionally, onions are used in most Canadian cuisines. This study aimed to investigate the extracts synthesized from Ontario-grown onion varieties in inducing anti-migratory, cytostatic, and cytotoxic activities in two sub-types of human breast cancer cell lines.

Methods: We investigated the effect of five prominent Ontario grown onion (Stanley, Ruby Ring, LaSalle, Fortress, and Safrane) extracts on two subtypes of breast cancer cell lines: a triple negative breast cancer line MDA-MB-231 and an ER+ breast cancer line MCF-7.

Results: These onion extracts elicited strong anti-proliferative, anti-migratory, and cytotoxic activities on both the cancer cell lines. Flavonoids present in these onion extracts induced apoptosis, cell cycle arrest in the G2/M phase, and a reduction in mitochondrial membrane potential at dose-dependent concentrations. Onion extracts were more effective against MDA-MB- 231 compared to the MCF-7 cell line.

Conclusion: Anti-tumor activity of these extracts depends upon the varietal and can be formulated into nutraceuticals and functional foods for the wellbeing of cancer patients. Overall, the results suggest that onion extracts are a good source of flavonoids with anti-cancerous properties.

Keywords: onion extracts, flavonoids, anti-proliferative, breast cancer, cytotoxic activity

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Metformin inhibits expression of the proinflammatory biomarker inducible nitric oxide synthase in hepatocytes

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ABSTRACT

Background: Metformin is used to treat patients with type II diabetes. However, there are few scientific reports on its anti-inflammatory effects. In the inflamed liver, proinflammatory cytokines stimulate liver cells, followed by inducible nitric oxide synthase (iNOS) expression. Excessive NO levels produced by iNOS have been implicated as a factor in liver injury. As a result, it is essential to inhibit iNOS induction to prevent liver injury.

Objective: This study aimed to investigate liver protective effects of metformin by examining interleukin (IL)-1β-stimulated hepatocytes.

Methods: Primary cultured rat hepatocytes were treated with interleukin (IL)-1β in the presence or absence of metformin. iNOS induction and its signaling pathway were analyzed.

Results: Metformin decreased iNOS protein and mRNA expression, resulting in the inhibition of hepatic NO production. Metformin also reduced tumor necrosis factor (TNF)-α and IL-6 mRNA expression. Metformin inhibited an essential signaling pathway for iNOS induction, type I IL-1 receptor upregulation. Transfection experiments revealed that metformin reduced iNOS mRNA levels through both promoter transactivation and mRNA stabilization. Delayed metformin administration after IL-1β addition also inhibited iNOS induction.

Conclusion: Metformin affects the induction of inflammatory mediators including iNOS and TNF-α, demonstrating its therapeutic potential for organ injuries, including the liver.

Keywords: metformin, inducible nitric oxide synthase, liver injury, primary cultured hepatocytes, type I interleukin-1 receptor, tumor necrosis factor-α

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Polyphenols of leaves of *Apium graveolens* inhibit in vitro protein glycation and protect RINm5F cells against methylglyoxal-induced cytotoxicity

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ABSTRACT

Background: The health benefits of edible plants have been widely investigated and disseminated. However, only polyphenols have been found to have sufficient therapeutic potential to be considered in clinical trials. Fewer manuscripts have other applications such as prospective health benefits and disease treatment. Other components of edible plants are responsible for a range of other benefits including antimalarial, burns, flu, cancer, inflammation, diabetes, glycation, antimicrobial, prevention of neurodegeneration, analgesic, antimigraine activity, sedative activities, etc. Accordingly, the public needs to be informed of the potential edible plants have to act on different targets and maintain better control over diabetes compared to commercial drugs which can be toxic, have side effects, do not have the capacity to maintain blood glucose at normal levels, and do not protect the patient from the complications of diabetes over time. Consequently, edible plants, such as *Apium graveolen*, which have therapeutic targets on AGEs formation, are potentially a better alternative treatment for diabetes.

Aim: To demonstrate if CM is capable of suppressing the formation of AGEs and protein oxidation *in vitro*. Also to investigate if *A. graveolens* is a potential functional food that can be used to prevent the development of diabetic complications.

Methods: The leaves of celery were extracted with methanol (CM). Polyphenols contents in CM were investigated by liquid chromatography-electrospray ionization mass. The ability of the compounds to inhibit formation of AGEs was evaluated in vitro models using formation of AGE fluorescence intensity, level of fructosamine, Nε-(carboxymethyl)lysine (CML), methylglyoxal (MG)-derived protein, and formation of amyloid cross β structure. Protein-oxidation was determined by thiol group and protein carbonyl content. Inhibition of MG-derived AGEs and

MG- trapping ability were also measured. Additionally, insulin production was determined in methylglyoxal-treated pancreatic RINm5F cells assay.

Results: Apigenin, kaempferol, apiin, rutin, caffeic acid, ferulic acid, chlorogenic acid, coumaroylquinic acid, and p-coumaric acid were the major polyphenols contained in CM. In all the model tests CM displayed potent AGE inhibitory activity, suggesting that CM delayed the three stages of glycation. Accordingly, the mechanisms of action of celery involving dicarbonyl trapping and breaking the crosslink structure in the AGEs formed may contribute to the protection of pancreatic RINm5F cells against MG conditions.

Conclusion: These findings indicate that CM have an excellent anti-glycation effect which may be beneficial for future development of antiglycating agents for the treatment of diabetes.

Keywords: *Apium graveolens*, anti-glycation, polyphenols methylglyoxal, insulin, pancreatic cells

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L-Carnitine has a liver-protective effect through inhibition of inducible nitric oxide synthase induction in primary cultured rat hepatocytes

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ABSTRACT

Background: L-Carnitine has protective effects on various injured organs. However, it has not been reported whether L-carnitine influences the induction of inducible nitric oxide synthase (iNOS) expression during inflammation. Nitric oxide (NO) produced by iNOS is an inflammatory indicator in organs which become inflamed, including the liver.

Objective: This study aimed to examine whether L-carnitine influences the induction of iNOS gene expression in inflammatory cytokine-stimulated hepatocytes and the mechanisms involved in the action.

Methods: L-Carnitine was added into the primary cultures of rat hepatocytes stimulated by interleukin-1β (an *in vitro* liver injury model). The production of NO and induction of iNOS and its signaling pathway were analyzed.

Results: Transfection experiments with iNOS promoter-luciferase constructs revealed how L- carnitine inhibited iNOS mRNA synthesis activity and reduced its stability. In support of this observation, L-carnitine reduced iNOS mRNA and iNOS protein expression levels, resulting in reduced NO production. L-Carnitine blocked two essential pathways for iNOS induction: IκB kinase (IκB degradation/NF-κB activation) and phosphatidylinositol 3-kinase/Akt (type I IL-1 receptor upregulation).

Conclusions: L-Carnitine inhibited the induction of inflammatory mediator iNOS, partially through inhibition of NF-κB activation, which demonstrated L-carnitine has protective effects in an *in vitro* liver injury model. L-Carnitine may have therapeutic potential for organ injuries, including the liver.

Keywords: L-carnitine, hepatic encephalopathy, inducible nitric oxide synthase, liver injury, primary cultured hepatocytes, nuclear factor-κB, type I interleukin-1 receptor

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Tomato juice saponin, esculeoside B ameliorates mice experimental dermatitis

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ABSTRACT

Background: Allergic diseases like atopic dermatitis have recently increased. A naturally occurring glycoside, Esculeoside B, has been identified as a major component in tomato juice from the can. Accordingly, the present study investigated the effects of esculeoside B on experimental dermatitis mice.

Results: Oral treatment with 10 mg/kg of esculeoside B on the experimental dermatitis mice for 4 weeks significantly decreased the skin clinical score of 2.0 compared to the control score of 5.0. Furthermore, the scratch frequency of mice treated with esculeoside B was lower compared to the control group. Overall, the administration of esculeoside B significantly inhibited T lymphocyte proliferation and demonstrated a tendency to decrease in IL-4 production. For example, the 121.2 pg/ml in the control group decreased to 96.1 pg/ml. There was also a decrease in serum IgE levels from 928.0 ng/ml in the control group to 687.8 ng/ml.

Conclusion: Our study is the first to demonstrate how tomato juice saponin or esculeoside B may ameliorate mice experimental dermatitis by the inhibition of T cell proliferation.

Keywords: tomato juice; experimental atopic dermatitis; IgE; cytokine; tomato saponin; esculeoside B

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/420/1173

Induction of apoptosis by fucoidan isolated from a traditional food, *Saccharina longissima*, in U937 human leukemia cells

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ABSTRACT

Background: A brown seaweed, *Saccharina longissima* (*Laminaria angustata var. longissima*) has been consumed in Okinawa for 300 years. It is native to the southernmost part of Japan, in Okinawa, but grows on the Pacific coast (Kushiro and Nemuro) in Hokkaido in the northernmost part of Japan. Previously, we reported the structural characteristics from *S. longissima*. The fucoidan consisted of L-fucose, D-galactose, D-glucose, D-xylose, D-glucuronic acid, and sulfuric acid. This fucoidan activated the RAW 264.7 murine macrophage cell line. The aim of this study was to investigate the effects of a fucoidan isolated from *Saccharina longissima* on cell anti- proliferation and apoptosis in the U937 human leukemia monocyte lymphoma cell line.

Methods: U937 cells were incubated with four fucoidan concentrations. The degree of apoptosis was determined using the APOPercentage APOPtosis assay, caspaer-3 activity assay and Western blotting analysis assay.

Results: The treatment of cell with a fucoidan highly substituted with sulfate, in addition to L- fucose residues, inhibited cell growth. Apoptosis increased in U937 cells in a dose-dependent manner following the addition of fucoidan. However, the fucoidan did not induce apoptosis in the presence of caspase inhibitor (z-VAD-FMK).

Conclusion: The fucoidan from *Saccharina longissima* induced apoptosis in U937 cells. Accordingly, the kelp containing this fucoidan may contribute to the observed longevity of the Okinawan population.

Keywords: fucoidan, *Saccharina longissimi,* brown seaweed, traditional food, human leukemia cells, apoptosis

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/411/1107

Protective effects by co-administration of eicosapentaenoic acid, capsaicin, and dextrin against obesity-related metabolic dysregulation in ob/ob mice

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ABSTRACT

Background: Obesity and its related metabolic syndrome are closely associated with major risk factors for chronic diseases, including dyslipidemia and insulin resistance. This study aimed to investigate whether a combination of eicosapentaenoic acid (EPA), capsaicin **(**Cap), and indigestible dextrin (Dx) could protect mice against obesity and its related metabolic disorders.

Methods: We fed male C57BL/6J and genetically obese ob/ob mice various diets for 10 weeks. The normal group was standard chow (SC; 5.3% fat content)-fed C57BL/6J mice. The control group was SC-fed ob/ob mice. The experimental groups were SC-fed ob/ob mice whose diets were supplemented with either 4% (w/w) EPA (EPA group), a combination of 4% (w/w) EPA and 0.01% (w/w) Cap (EPA+Cap group), or 4% (w/w) EPA, 0.01% (w/w) Cap, and Dx (EPA+Cap+Dx group).

Results: We discovered that the weight of body and fat tissue, levels of serum glucose, insulin, total cholesterol, high-density lipoprotein cholesterol, aspartate aminotransferase and alanine aminotransferase, and the homeostasis model assessment of insulin resistance (HOMA-IR) index were significantly higher in the control group than in the normal group ($P < 0.05$ for all parameters). However, the weight of body and fat tissue, the serum glucose, total cholesterol, alanine aminotransferase levels, and the HOMA-IR index were lower in the EPA+Cap+Dx group than in the EPA and EPA+Cap groups.

Conclusions: Our findings suggest that the co-administration of EPA, Cap, and Dx may suppress the progression of obesity-related metabolic dysregulation and subsequent complications.

Keywords: eicosapentaenoic acid, capsaicin, dextrin, mice, obesity

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/512/1174

Effects of 4-week continuous ingestion of champignon extract on bowel movements and intestinal putrefaction products: A randomized, placebo-controlled, double-blinded, parallel-group comparative trial

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ABSTRACT

Background: The aim of this study was to analyze the putrefaction products in the feces of subjects from a previous study (age range 50–79 years) which assessed the improvement of breath, body, and fecal odor after ingesting champignon extract.

Methods: The study was designed as a randomized, placebo-controlled, double-blinded, and parallel-group comparative trial. Subjects were divided into four groups, including the placebo (n=20), champignon extract at 50 mg/day (n=20), champignon extract at 500 mg/day (n=20), and champignon extract at 1000 mg/day (n=20) for 4 weeks.

Results: The results revealed significant reduction in ammonia and p-cresol levels (both of which are intestinal putrefaction products) among subjects who ingested 50, 500, and 1000 mg of champignon extract per day compared with subjects in the placebo group. Additionally, a significant difference was observed in indole levels in the group that consumed 500 mg/day of the extract compared to the placebo group.

Conclusions: The re-analysis of bowel movement in each test group revealed that the extract improved the number of days with bowel movement, number of bowel movements, and stool volume, which suggests the intestinal environment was improved.

Clinical trial registration: UMIN000014256

Keywords: ammonia, champignon, fecal odor, p-cresol, putrefaction

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/517/1105

Mango (*Mangifera indica* Linn*)* and Anti-Inflammatory Benefits: Versatile Applications in Mitochondrial Bio-Energetics and Exercise Physiology

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ABSTRACT

Background: Mangoes are a popular fruit enjoyed worldwide. The mango is known for its pleasing aroma in addition to its refreshing and soothing taste. Researchers around the globe have demonstrated the diverse beneficial effects of *Mangifera indica* Linn in human health and disease prevention. Additionally, we should acknowledge how Ayurvedic medicine uses different parts of the mango tree. This branch of medicine has used the leaves, twigs, bark, seeds, flowers, raw and ripe fruits of mango to treat diverse degenerative diseases for thousands of years. This study is aimed to investigate diverse health benefits of Mango and mangiferin.

Ethnobotany: The mango (*Mangifera* indica) originally came from India about 4,000 years ago. Since then, the mango has slowly spread across the world. The mango belongs to the family "Anacardiaceae" under the genus "*Mangifera*" and species "*indica*". The mango is also referred to as "Asia's King of Fruits" or a Royal fruit. The color of the mango fruit varies from green, yellowish green, yellow, yellowish red, orange red and red. The smell and taste of the mango fruit varies based on its state of maturity in addition to place of origin and climate. Different parts of a mango tree and mango fruit are rich in vitamins and antioxidants including vitamins B, C, E and beta-carotene, alkaloids, flavonoids, and polyphenolic compounds which include mangiferin, anthocyanins and anthocyanidins, micronutrients and essential minerals, structurally diverse carbohydrates, dietary fibers, fat, and protein.

Health Benefits: Previous and current research demonstrate that the mango fruit and leaf extract, which is enriched in mangiferin and contains structurally diverse chemical constituents, are beneficial. The mango fruit and leaf extract have been shown to boost vitality, vigor, and endurance, leading to extensive application in exercise physiology. Furthermore, these constitutes ameliorate diverse degenerative disease related to metabolic syndrome, bacterial infections, gastrointestinal, and immunomodulatory disorders.

Conclusions: Mango and mangiferin exhibit diverse health benefits including energy boosting, exercise performance, and human health.

Keywords: Mango (*Mangifera indica)*, mangiferin, vitamins and anthocyanins, anti- inflammatory, endurance, energy homeostasis, exercise

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/526/1172

Targeting biofilm inhibition using Quercetin – Interaction with bacterial cell membrane and ROS mediated biofilm control

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ABSTRACT

Background: Quercetin is an active nutraceutical ingredient widely distributed in foods, vegetables, fruits, and more. Quercetin is a versatile functional food with extensive protective effects against many infectious and degenerative diseases due to their antioxidant activities. *Apsergillus niger* is a filamentous fungus and the most abundant mold found in the environment. This fungus has been the source of several bioactive compounds and industrial enzymes through biotransformation.

Aim: In this report we emphasized the potential of *Aspergillus* species for the selective conversion of rutin to quercetin, which involved stereoselective and regiospecific reactions with enhanced production and minimization of the formation of toxic wastes. This fungal microbe was able to transform the complex structure of rutin to quercetin with remarkable catalytic activity for the reaction with high product yield. The quercetin produced demonstrated the ability to inhibit biofilm formation and eradicate established biofilm involving the production of reactive oxygen species (ROS) indicative of membrane activity. These results suggest quercetin may have implications in biofilm control targeting reactive oxygen species as a novel therapeutic strategy.

Methods: Quercetin was synthesized by microbial biotransformation recruiting *Aspergillus niger*. The synthesis of quercetin was compared with the chemical process. Furthermore, the quercetin produced by the biotransformation process was characterized by high performance thin layer liquid chromatography. The quercetin produced was assessed for biological activities. The antimicrobial activity, hemolytic activity, inhibition of biofilm by crystal violet staining, and cell viability by confocal laser scanning microscope was assessed. The membrane interaction effect and oxidant scavenging effect by DPPH, Intracellular ROS release, and lipid peroxidation was measured.

Results: Quercetin produced by microbial transformation demonstrated antimicrobial activity against *S. aureus* by effectively inhibiting the growth and dispersion of preformed biofilms. Quercetin demonstrated a significant free radical scavenging activity and significant inhibition of lipid peroxidation. Significant release of reactive oxygen species was observed in bacterial cells.

Conclusion: In conclusion, the bio transformed quercetin exhibited disruptive potential of biofilm formation by preventing cell surface attachment and biofilm growth. Therefore, it can be suggested that the major public health benefits could be achieved by substantially increasing the consumption of quercetin rich foods.

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Effects of six-week consumption of lard or palm oil on blood pressure and blood vessel H2S in middle-aged male rats

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ABSTRACT

Background: Cardiovascular disease is the leading cause of death. The etiology of this disease is multifactorial, with unhealthy nutrition being one of the main risk factors. Diets high in animal fats and saturated fatty acid have been associated with an increased risk for cardiovascular diseases. However, the results of investigations on the effects of lard (LO)- and palm oil (PO) on cardiovascular risk are still controversial due to the dosages used and the age of the animals investigated.

Objective: We investigated whether LO or PO consumption led to different effects on blood pressure, vascular functions, and lipid profiles within middle-aged rats.

Methods: The study was performed in middle-aged male rats, *n* = 6 for each group. LO, PO, or distilled water (control) 1 or 3 ml/kg were orally gavaged once a day for 6 weeks. Basal blood pressure and heart rate were measured in anesthetized rats. Fasting serum lipids were measured by enzymatic methods. The vascular functions of isolated thoracic aorta were studied using pharmacological techniques in the absence or presence of N-nitro-L-arginine, a nitric oxide synthase (eNOS) inhibitor and or DL-propargylglycine (PAG), a cystothionine-γ-lyase(CSE) inhibitor. Additionally, the aortic wall eNOS and CSE protein expression were measured by Western blotting.

Results: In comparison to the control group (distilled water, DW), no differences were observed in any of the parameters studied after the rats took 1 ml/kg of LO or PO. However, PO caused an increase in neutrophil/lymphocyte ratio and body fat. At 3 ml/kg dosage, LO caused increased basal blood pressure (LO, 153.4 ± 3.2; DW, 131.4 ± 3.2 mm Hg for systolic blood pressure and LO, 130.9 ± 2.5; DW, 107.9 ± 5.8 mmHg for diastolic blood pressure) body and liver cell lipid accumulation, while PO led to increased body fat and fasting serum triglyceride (PO, 131.5 ± 13.2; DW, 91.8 ± 4.8 mg %). Neither LO nor PO treatment had any effect on vascular contraction to phenylephrine, except in the presence of PAG which led to an increased contractile response to

phenylephrine. PO but not LO treatment caused increased vascular wall CSE protein expression.

Conclusion: The results document how both LO and PO at a dose of 3 ml/kg (corresponding to three servings of Thai fast food) cause increased cardiovascular risk factors. However, the blood vessel H2S production increased while the lower dose had a minimal effect.

Keywords: Lard oil, Palm oil, blood vessel, liver lipid, NO, H2S

Animal Ethic Number: Ref. 065/7

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Fucoidan inhibits vascular remodeling in transplant vasculopathy in rat

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ABSTRACT

Background: Fucoidan is a natural sulfated polysaccharide which exists mainly in the cell wall matrix of various species of brown seaweed. Various forms of fucoidan have also been recognized in some marine invertebrates such as sea urchins and sea cucumbers.

Fucoidan inhibits the spread of cancerous cells by preventing the adhesion of tumor cells to the extracellular matrix in addition to inducing apoptosis, or programmed self-destruction, in human T-cells infected by T-cells leukemia virus type I (HTLV-1) which causes adult T-cell leukemia. The polysaccharide has also been shown to stimulate the phagocytic action of macrophages and synthesis of several immune cell types, which increases protection against infection. Fucoidan gives the immune system a big boost by enhancing phagocytosis. Additionally, it increases the number of mature white blood cells which are circulating in the body, thereby bolstering the first line of defense against infections and diseases. Fucoidan has anti-coagulant, anti-thrombotic, anti-inflammatory, antioxidant, anti-allergic, anti-tumor properties and also many others.

The aims of our study were to investigate the ability of fucoidan to alleviate vascular remodeling triggered by immunological stimuli in allogenic aorta transplantation within rats and to evaluate potential mechanisms of this action.

Methods: In this study, we investigated whether fucoidan is able to alleviate the vascular remodeling process triggered by immunological stimuli in rat allogenic aorta transplantation model, in addition to the evaluated potential mechanisms responsible for the observed effects. Our rat aorta transplantation model was subjected to intraperitoneal or oral treatment with fucoidan or placebo.

Results: Our study demonstrated that fucoidan inhibits endointimal hyperplasia formation and vascular modulation. In particular, intraperitoneal and oral administration of fucoidan reduced neointima formation in allografts retrieved 8 weeks after transplantation. Moreover, both treatments with fucoidan reduced the number of smooth muscle (SM) -actin positive cells in intima and adventitia, decreased percentage of macrophages in intima and media, and increased the number of leukocytes in media of the allografts. Fucoidan treatments have also caused reduction in apoptosis in allograft intima and media.

Conclusion: Through our study, we demonstrated the inhibitory effect of fucoidan on vascular remodeling in

transplant vasculopathy within rats. Our study is the first report of the beneficial effects of fucoidan oral administration on this process, which may have important clinical implications and result in a better understanding of vascular remodeling.

Keywords*:* fucoidan, transplant vasculopathy, vascular remodeling

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/525/1171

Anti-obesity and haematological effects of Malaysia *Hibiscus sabdariffa* L. aqueous extract on obese Sprague Dawley rats

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ABSTRACT

Background: *Hibiscus sabdariffa* L. (Hs; Malvaceae) is commonly known as roselle or red sorrel in English or karkadè in Arabic. It is a tropical plant native to India and Malaysia. Roselle extracts have been widely reported to have beneficial health effects. The aim of this study was to determine the effective dose of Hs aqueous extract, which is a possible reducing agent in diet-induced obese rats, and monitoring any toxicological effect.

Methods: Male Sprague Dawley rats (n= 24) aged 6-7 weeks and weighing 210 ± 3.5 g (mean ± S.E.M) were used. The rats were fed a high fat diet (HFD) for 8 consecutive weeks to induce obesity. The animals were then randomly assigned to one of five groups based on the concentration of Hs aqueous extract. The normal group (NG) received a normal diet (commercial chow) throughout the study. The obese group (ObG) included obese rats administered with tap water ad libitum. Groups 1 (150 mg/kg), 2 (200 mg/kg), 3 (250 mg/kg), and 4 (300 mg/kg) were obese rats continuously fed with HFD in combination with the Hs extract for 10 weeks. The effect of Hs on some haematological and blood biochemical parameters were also evaluated.

Results: Hs aqueous extract is a rich source of anthocyanins. The main compounds detected are delphinidin-3-*O*-sambubioside and delphinidin-3-*O*-sambubioside. The extract also possesses high antioxidant properties which may be caused by these anthocyanins. The anti-obesity effect of Hs aqueous extract was demonstrated by the significant reduction in the weight gain and abdominal weight ($p < 0.05$) between treated and non-treated groups, which was dose-dependent. Overall, our study demonstrated that oral administration of Hs at doses of 150, 200, 250, and 300 mg/kg for ten weeks did not cause any toxicity effect within the obese rats.

Conclusion: The results of the study implied Hs aqueous extract at 300 mg/kg is the dose which can the most weight reduction effect with no severe haematological and biochemical changes in all experimental animals.

Keywords: *Hibiscus sabdariffa*, obese rats, roselle, aqueous extract, and body weight

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/407/1101

Daily consumption of monoglucosyl-rutin prevents high-fat diet-induced obesity by suppressing gastric inhibitory polypeptide secretion in mice

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ABSTRACT

Background: Alpha monoglucosyl-rutin (4^G-α-D-glucopyranosyl rutin, αMR) has been shown to stimulate antioxidant defenses and anti-glycation. We evaluated the effects of αMR on body weight gain in mice. This study aimed to investigate the effects of αMR supplementation on diet-induced excess weight gain in mice. Also assessed alterations in insulin, leptin, interleukin 6 (IL-6), resistin, tumor necrosis factor α (TNFα), gastric inhibitory polypeptide (GIP), ghrelin, and glucagon to elucidate the mechanism underlying anti-obesity effects.

Methods: Male C57BL/6J mice were divided into four groups: Control low-fat diet, low-fat diet + 0.5% αMR, high-fat diet, and high-fat diet + 0.5% αMR. Blood chemistry, hepatic lipids, and serum metabolic hormones and cytokines were evaluated after 4 and 13 weeks.

Results: After 6 weeks, the high-fat diet group gained more weight than the low-fat diet group. Supplementing the high-fat diet with αMR suppressed weight gain by week 13. Visceral fat weight was higher in the high-fat diet group on weeks 4 and 13, while αMR supplementation inhibited increase on week 13 but not on week 4. Serum levels of gastric inhibitory polypeptide were higher in the high-fat-diet group than in the low-fat-diet group. αMR supplementation inhibited this elevation and regulated levels of serum leptin and hepatic triglycerides.

Conclusion: For the first time, we demonstrated how daily consumption of αMR inhibits diet- induced visceral fat accumulation by regulating the secretion of gastric inhibitory polypeptide, which thereby prevents excess weight gain. Therefore, αMR may be a promising potential functional food.

Keywords: Anti-obesity, gastric inhibitory polypeptide, mouse, alpha monoglucosyl-rutin; quercetin

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Variations of β-carotene retention in a staple produced from yellow fleshed cassava roots through different drying methods

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ABSTRACT

Background: New yellow cassava fresh roots biofortified with β-carotene are becoming popular in Sub-Saharan Africa in the making of traditional products for households. However, β- carotene is susceptible to rapid depletion during processing. This study aimed to investigate the impact of using different drying methods in processing these fresh Cassava roots and in attempting to increase pro-vitamin A content.

Methods: We processed four newly released yellow fleshed cassava varieties (01/1371, 07/593, 07/539, and 07/0220) into fermented cassava chips, flour, and corresponding dough with sun, oven, and flash drying methods respectively. The β-carotene contents were analyzed using High Performance Liquid Chromatography (HPLC). Percentage true retention (%TR) was computed.

Results: The results demonstrated that %TR in chips (13.7%), flour (11.7%), and dough (5.48%) from sun drying method had the highest level of β-carotene retention compared to oven (11.3%, 7.30%, and 3.47%) and flash (8.8%, 3.33%, and 1.24%) drying methods. The duration, intensity of heat used for drying, and variety had a significant effect on β-carotene retention. Variety 07/0220 with the highest β-carotene concentration (7.81±0.13µ/g) in the fresh roots did not necessarily have the highest concentration after processing. These results suggest that β-carotene retention is not only variety specific but also depends on the method of processing.

Conclusion: These results will support ongoing breeding efforts aimed at increasing pro-vitamin A content in Cassava. The information may also be significant to solutions considering fermented cassava flour and dough in Vitamin A deficient populations.

Keywords: Cassava, drying, fermented flour, carotenoids, retention, Lafun

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FFC's Advancement of Functional Food Definition

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BACKGROUND

To create functional food products based on scientific evidence, we must first define functional foods. Previous definitions describe how functional foods improve health and mitigate disease. However, more refined definitions provide a reason for their efficacy – through the activity of bioactive compounds and the measurement of biomarkers, which are the essential tools for gauging the effectiveness of functional foods.

Functional foods are generally linked to health promotion. The physiological effects of functional food or bioactive compounds may vary, but their categories of action include physical performance, cognitive, behavioral, and psychological function, organ or system function, and combating chronic disease [1, 2].

Therefore, establishing a formal definition for these foods will help bring legitimate functional foods to the market. The addition of bioactive compounds, or biochemical molecules that improve health through the physiological mechanisms, improves the definition of functional foods. As a result, the advancement of the functional food definition by the Functional Food Center (FFC) has developed to provide clarity and a more comprehensive understanding of its meaning

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An *in vitro* study on the regulation of oxidative protective genes in human gingival and intestinal epithelial cells after treatment with salmon protein hydrolysate peptides

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ABSTRACT

Background: Under physiological conditions, molecular oxygen generates reactive oxygen species (ROS) as metabolic by-products. In the absence of an adequate defense mechanism, the accumulation of ROS leads to cell membrane and DNA damage, in addition to tissue degeneration. The up/down regulation of one or more oxidative stress-related genes is one mechanism which confers cytoprotection to tissues exposed to oxidative injury.

Objective: To measure the up/down regulation of 84 oxidative protective NRF2 genes within primary human gingival epithelial cells (HGEPp) and human intestinal epithelial cells (HIEC-6) when treated with varying concentrations of salmon protein hydrolysate (SPH) solution.

Methods: We measured up/down regulation of 84 oxidative protective genes in primary human gingival epithelial pooled cells and human intestinal epithelial cells after pretreatment with 25, 50, and 100 µM/ml of salmon protein hydrolysate solution. A human RT2 Profiler PCR array was used to evaluate the relative change in the expression of these common oxidative protective genes. The salmon protein hydrolysate contains a mixture of bioactive peptides, resulting from enzyme hydrolysis of salmon head and backbones.

Results: Treatment with salmon protein hydrolysate peptides demonstrated up-regulation for 16 human oxidative protective genes and down-regulation for 9 human oxidative stress-related genes. Three genes (ferritin heavy polypeptide-1 (FTH1), heme oxygenase-1 (HMOX1), and arachidonate 12-lipoxygenase (ALOX12)) showed regulation changes at physiologically applicable levels.

Conclusion: The improved oxidation protection observed after SPH treatment conferred by HMOX1 / ALOX12 regulation to HGEPp and HIEC-6 cells may find ultimate utility for these bioactive peptides in the modulation of gastrointestinal stress in irritable bowel syndrome and enterocolitis.

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Immunological effects of Kefir produced from Kefir grains versus starter cultures when fed to mice

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ABSTRACT

Background: Natural kefir grains have a unique microbiota. The structure contains lactic acid bacteria (LAB), acetic acid bacteria and yeast in specific ratios in a polysaccharide matrix. Authentic kefir is produced by a traditional method using kefir grains cultured in milk. In contrast, starter cultures are used instead of kefir grains in the industry. The commercial kefir starter cultures used are limited and often very different from the kefir grain microbiota. The resultant commercial "kefir" is just a fermented drink containing some probiotic microorganisms and does not possess the same microbial population or chemical and physical characteristics of authentic kefir. The aim of this project was to determine and compare the effects on the mouse immune system of kefir produced using natural kefir grain versus commercial kefir produced by starter culture.

Methods: Kefir produced with different cultures was fed to Balb/c mice (6-8 weeks, 20-25 grams, male) by gavage for two weeks at 300 µl/day. Intestinal tissues were collected from sacrificed mice at the end of the trial. The control group of mice (CNI group) were fed with phosphate buffered saline (PBS). The experimental treatments were mice fed mice fed authentic kefir produced using kefir grains (KGI group) and mice fed kefir produced using starter culture (STI group). Immunoglobulin (Ig) A, Immunoglubulin G, Interleukin (IL)-4, Interleukin-10, Interleukin-12, Toll Like Receptor (TLR)-4 were analyzed immunologically in intestinal fluid samples.

Results: Results indicated that IgA values were 60.87, 72.78 and 55.31 ng/mL; IgG values were 26.59, 38.90 and 29.44 ng/mL; IL-4 values were 84, 40.28 and 53.28 pg/mL; IL-10 values were110.98, 175.91 and 134.77 pg/mL; IL-12 values were 53.90, 22.93 and 24.75 pg/mL; TLR-4 values were 0.53, 0.43 and 1.37 ng/mL, for the CNI, KGI and STI groups, respectively.

Conclusion: The high probiotic content of grain kefir had the ability to modulate many immunological mechanisms.

Keywords: immune system, *in vivo*, kefir grain, probiotic, starter kefir culture

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Effects of *Namya Kanom Jeen* powder extracts on antioxidative and anti-inflammatory properties

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ABSTRACT

Background: Spices and herbs are known to have antioxidant and anti-inflammatory properties. We studied their properties of *Namya Kanom Jeen (NKJ)*, a spicy soup (Southern Thailand recipe) with water and ethanol (50% and 95%) extracts.

Aim: To assess functional properties, antioxidant, α-amylase inhibition, and anti-inflammatory properties, of *NKJ* powder extract using *in vitro* model

Methods: Antioxidant activities were determined using free radical scavenging activity (DPPH) and Ferric Reducing Antioxidant Power (FRAP). Anti-inflammation effect was studied by measuring nitric oxide (NO) production inhibition on RAW264.7 macrophage cells after being exposed to lipopolysaccharide (LPS).

Results: Water extract of *NKJ* powder demonstrated the highest activity in anti-inflammatory and antioxidant property by DPPH radical scavenging activity when compared with ethanol extract.

Conclusion: The combined effect of several bioactive compounds within *NKJ* powder extracts may ameliorate the oxidation and inflammation.

Keywords: Antioxidant, Anti-inflammation, Phenolic compound, *Namya Kanom Jeen* powder

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Effects of blueberry leaf and stem extracts on hepatic lipid levels in rats consuming a high-sucrose diet

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ABSTRACT

Background: Blueberry stems, a by-product of blueberry leaf tea production, are typically discarded. We evaluated the effects of hot-water extracts of rabbiteye blueberry (*Vaccinium virgatum* Aiton; RB species) leaves and stems on hepatic lipid levels in rats consuming a high- sucrose diet.

Aim: This study focused on the stems of rabbiteye blueberry (*Vaccinium virgatum* Aiton; RB species), a major blueberry species, and evaluated the effects of daily consumption of blueberry stems on hepatic lipid levels and hepatic lipogenic enzyme activity in rats consuming a high- sucrose diet.

Methods: Male Sprague-Dawley rats were divided into groups that received a control high- sucrose diet alone or supplementation with 2.0% blueberry leaf extract or 0.5% or 2.0% blueberry stem extract. Blood and hepatic lipid levels, hepatic lipogenic enzyme activity, and hepatic quercetin metabolites were evaluated after 28 days of *ad libitum* consumption.

Results: Supplementation with the extracts did not affect body weight gain, food intake, liver and white adipose tissue weights, or serum lipid levels. Hepatic triglyceride and total cholesterol levels were reduced in the groups that received 2.0% supplementation of either extract. Hepatic malic enzyme activity was also reduced in those groups. Quercetin and its glycosides, the major polyphenols identified in the extracts, accumulated in the liver as quercetin aglycone and quercetin metabolites.

Conclusion: We demonstrated how daily consumption of blueberry leaf and stem extracts can decrease hepatic lipid levels, potentially downregulating malic enzyme activity. These effects were intensive in leaf extracts. The active compounds existed in both extracts may be quercetin and its glycosides. Therefore, blueberry stems and leaves may be an attractive candidate novel functional food.

Keywords: Blueberry leaf; blueberry stem; quercetin; hepatic lipid; rat; functional food

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Retention of pro-vitamin A carotenoid in composite bread baked with high quality cassava flour from yellow-fleshed cassava root

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ABSTRACT

Background: As one of the most widely consumed foods, bread is one of the most important agricultural products. Bread made from high-quality cassava flour is consumed in some parts of Sub-Sahara Africa (SSA). The bread has no pro-vitamin S carotenoids (pVAC) due to the use of artificial colorants. Consequently, there is a need for the use of pVAC rich foods for bread production. Foods that are rich with pro-vitamin A carotenoids can be converted into retinol in the human body and whose bioconversion contributes to the reduction of vitamin A deficiency diseases (VAD). VAD has caused annual loss of life in SSA, especially in Nigeria. The yellow- fleshed cassava root might contribute to the reduction of this disease. The high quality yellow cassava flour (YHQCF) produced from yellow-fleshed cassava root may contribute to the pVAC composition of bread. As a result, there is a need for the evaluation of the retention of pVAC in composite bread baked with high quality cassava flour from yellow-fleshed cassava roots.

Aim: To evaluated the retention of pro-vitamin A carotenoid in composite bread baked with high quality cassava flour from yellow-fleshed cassava roots.

Methods: The YHQCF was produced from TMS01/1368 cassava variety. The bread loaves consisted of 20% and 100% YHQCF and were produced by mixing the sugar, margarine, yeast, improver, and salt with the composite flour and YHQCF respectively, after which water was added and mixed to get the homogenous dough. The dough was proofed for 2.5 hours, kneaded, cut into shape, placed in a lubricated baking pan, and baked at 200°C for 30 min. Analyses of the pro- vitamin A (cis and trans-β carotene) and dry matter content were carried out on all the samples, including samples from the YHQCF production steps using standard methods. The samples from the YHQCF production steps were chosen and analyzed for pVAC in order to check the levels of degradation of the pVAC from the raw cassava root to using the root for flour production and the quantity of pVAC retained when 100% of the YHQCF is used for bread production compared to 20% composite. The β-carotene nutrient retention of the bread was also calculated.

Results: The results demonstrated how the total pVAC content of the raw yellow-fleshed cassava root was 16.83 µg/g dry basis with 29% dry matter (DM) content. Subsequent processing by peeling, washing, grating, and

dewatering into granules (56% DM) caused 48% reduction in the pVAC content which was reduced to 40% after drying and milling the dried grits into YHQCF (97% DM). Preparation of recipe for bread demonstrated how the 20% composite flour dough (61% DM) contained 0.29 µg/g db pVAC representing 1.72% retention, which was later reduced to 0.25 µg/g db pVAC or 1.49% retention after baking (62%DM). On the other hand, bread loaves baked from 100% YHQCF (67% DM) retained 0.74 µg/g db pVAC representing 4.40% of the 16.83 µg/g db pVAC in the starting raw material.

Conclusions: The bread produced from 100% YHQCF may contribute to the pro-vitamin A status of bread consumers in SSA more than the 20% YHQCF composite. However, both bread samples are low in pVAC. In order to attain the required retinol equivalent level after bioconversion in the human body, consumption of other foods rich in vitamin A would be required to attain the required retinol equivalent level after bioconversion in the human body but can be enhanced if consumed with other foods rich in vitamin A.

Keywords: High quality cassava flour; composite flour; Bread; Pro-vitamin A carotenoid; Nutrition

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Effects of *Saccharomyces cerevisiae* NK-1 on stool frequency and volume in healthy individuals with infrequent bowel movements: a randomized, placebo, placebo controlled, double-blind study

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ABSTRACT

Background: Constipation and other symptoms of gastrointestinal discomfort, such as abdominal swelling, are common among healthy individuals and have a significant impact on quality of life. Despite the known contribution of gut microbiomes to this pathology, little is known regarding which groups of microorganisms play a key role. Yeasts have been used for fermenting foods since ancient times. *Saccharomyces cerevisiae* is a type of yeast used for industrial and pharmaceutical purposes in the genetic and medical fields because it is unicellular with a simple biological structure. Yeast also helps improve the intestinal environment. The present study aimed to investigate the effect of foods containing *Saccharomyces cerevisiae* on bowel movement and to validate the safety of its long-term usage. Stool frequency and consistency were also assessed.

Methods: This was a randomized, double-blind, parallel-group study. The test food contained *S. cerevisiae* NK-1 powder (1×10^{10} cells), whereas the placebo did not contain it. The food was made into sticks and provided to healthy individuals with infrequent bowel movements (3–5 movements a week), three times a day for 12 weeks. Then we investigated the changes in stool frequency, volume, and other adverse events.

Results: The number of days with bowel movement significantly increased in the test group compared with the placebo group after 8–12 weeks of consuming the test food ($p < 0.05$). Based on the blood test results, there were no adverse events associated with the consumption of the test food observed.

Conclusions: Consumption of the test food regulated intestinal function by promoting defecation in healthy individuals prone to constipation. Thus, *S. cerevisiae* NK-1 helps facilitate smoother defecation.

Clinical Trial: UMIN #000020476

Keywords: *Saccharomyces cerevisiae* NK-1, bowel movement, stool frequency volume, gastrointestinal discomfort

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Impact of packaging material and storage condition on retention of provitamin A carotenoids and xanthophylls in yellow-seeded maize flour

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ABSTRACT

Background: Pro-vitamin A carotenoid (pVAC) rich foods are those foods that contain substance which can be converted within the human body into retinol, and which contribute to the reduction of vitamin A deficiency diseases. Yellow-seeded maize flour is an example of such pVAC rich food. Identifying the right packaging materials and storage conditions that retain pVAC in this food is essential for their health benefits. Traditionally, maize flour is stored in different packaging materials to increase its shelf life. For instance, previous studies have shown that during storage in different food matrices, including maize grains, carotenoids are highly susceptible to degradation by temperature, light, and oxygen. The aim of this study is to investigate the effect of storage packaging materials (polypropylene woven sacks-PWS, high-density polyethylene bags-HDPE, and polyvinyl plastic containers-PPC) and storage condition (temperature and relative humidity) on retaining pVAC in yellow-seed maize flour.

Methods: The yellow-seeded maize grains were collected and ground into flour. The maize flour was divided into portions (200 g) and each portions was packed and sealed in PWS, HDPE, and PPC. The control samples (12 pieces) were stored on top of the storage box. The packed samples were stored in both the upper (12 samples) and lower (12 samples) compartment of a storage wooden box. The interior of the upper part was lightened with aluminum foil and fitted with fluorescent tube to increase the light intensity, while the lower compartment was darkened with gloss black painting. The flour samples were stored for 28 days, with samples collected for pVAC and xanthophylls analyses at 7 days interval using standard methods.

Results: The results showed that packaging in PPC and storing in dark compartment gave the highest total pVAC (92.39%) and total xanthophylls (89.44%) retention, and retinol equivalent (RE) (0.40 µg/g); whereas packaging in HDPE and storing in lighted compartment resulted in the lowest pVAC (44.92%) and total xanthophylls (46.76%) retention, and RE (0.19 µg/g).

Conclusions: Packaging yellow-seeded maize flour in PPC and storing in the dark may be recommended for maximum retention of carotenoids in yellow-seeded maize flour since this packaging material and storage condition gave the highest pVAC retention and retinol equivalent.

Keywords: Yellow-seeded maize, Carotenoids, Packaging materials, Storage conditions, Retinol equivalent

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Effects of *Undaria pinnatifida* (wakame) on the human intestinal environment

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ABSTRACT

Background: *Undaria pinnatifida* (wakame) is an edible seaweed that is a common constituent in the Japanese diet and exhibits various biological effects. Wakame is rich in dietary fiber. Despite the long history of its intake, changes in the intestinal environment following the ingestion of wakame are unclear. The aim of this study is to investigate the daily consumption of wakame and test the possibility of wakame use as a probiotic.

Methods: We examined the effect of a 2-week intake of wakame on defecation frequency and the intestinal microbiota of 22 healthy individuals suffering from low defecation frequency. The clinical trial was designed as an open-label study.

Results: Defecation frequency, defined in terms of times per week, days per week, and volume per week, significantly increased during the wakame intake period. Furthermore, based on terminal restriction fragment length polymorphism (T-RFLP), the fraction of bifidobacteria as a percentage of all fecal bacteria increased significantly during the wakame intake period. At the phylum, next-generation sequencing (NGS) revealed that the relative abundance of Actinobacteria after wakame intake significantly increased while the abundance of Bacteroidetes decreased. Moreover, species-level analyses revealed that the abundance of *Bifidobacterium longum* increased significantly after wakame intake. *B. longum* colony counts on wakame-containing medium were significantly higher than those on medium lacking wakame.

Conclusion: These observations suggest that wakame intake improves intestinal environment and increases the fecal population of bifidobacteria, indicating that it may have prebiotic properties.

Keywords: *Undaria pinnatifida*; wakame; bowel movement; intestinal microbiota; fiber; Bifidobacterium

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Awareness and use of probiotics among the millennials in the United States: Drivers and implications

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ABSTRACT

Background: Despite the substantial increase in the number of probiotic products available in the U.S. during the last decade and the potential for millennials to be a large market for probiotics, there is a lack of understanding about millennials' awareness, use, and preference for probiotics. This study aims to examine the relationship between the millennials' health and diet perceptions and health outcomes, estimate awareness and use levels of probiotics among the millennials, and identify the drivers of use of probiotics.

Methods: An online opt-in internet panel is used to collect national level survey data on awareness and use of probiotics from the U.S. population in the age group of 21 to 37 years old.

Results: The study finds that there is divergence in millennials' perceptions about their health and diet and health outcomes; awareness about probiotics is high and probiotics use is common among the millennials; demographic, socio-economic, and life style related attributes are influential in millennials' decision on the use of probiotics, and shakes and yogurt are the most preferred carrier forms of probiotics among the millennials. The study also finds that income constraints and perception of good health status are the major factors hindering the use of probiotics among the millennials.

Conclusion: The study shows that millennials are already an important market for probiotics and there is substantial scope for expanding that market. The ability of probiotics to address public health concerns will depend greatly on how health care providers and probiotic industry will leverage these high levels of awareness and use by the millennials. Findings from our study provide insights that are helpful for probiotics product and market development and outreach efforts that will result in increased use of probiotics among the millennials with positive implications for public health and overall economy.

Keywords: consumer preference, probiotic industry, functional foods, health outcome

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Furosap, a novel Fenugreek seed extract improves lean body mass and serum testosterone in a randomized, placebo-controlled, double-blind clinical investigation

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ABSTRACT

Background: The Indian spice *fenugreek* (*Trigonella foenum-graecum*) has been credited with numerous health benefits in cardiovascular disorders, metabolic syndrome, inflammatory conditions, glucose-insulin regulation, and sports performance. Previous studies from our laboratories demonstrated that fenugreek seed extract improved glucose tolerance and insulin sensitivity, augmented serum testosterone level, and improved cardiovascular functions. The aim of this study is to examine the efficacy of Furosap, a novel fenugreek seed extract enriched in 20% protodioscin, on exercise performance.

Methods: This randomized, double-blind, placebo-controlled, clinical study was conducted in forty healthy male athletes (n = 40) over a period of 12 consecutive weeks. Subjects were given either placebo or Furosap capsules (250 mg/day b.d.) and serum samples were used to assess serum total testosterone level and C-reactive proteins (CRP) at baseline and at the end of 12-weeks of treatment. Body fat mass, lean mass, fat mass, fat-free mass, grip strength, upper and lower body strength, maximal graded exercise stress using a digital hand dynamometer, dual-energy X-ray absorptiometry (DEXA), force plate, and treadmill with open-circuit spirometry were assessed at the baseline and at the end of 12-weeks of treatment.

Results: Furosap supplementation significantly increased mean lean body mass and fat-free mass compared to subjects receiving placebo. Additionally, Furosap-treated subjects elevated serum testosterone levels. Furosap supplemented subjects also exhibited a tendency towards lowering blood pressure during exhaustion. No adverse reports were reported.

Conclusions: Given improvement of lean body mass and serum total testosterone following intervention with Furosap, Furosap likely has benefits for exercise endurance and sports medicine.

Keywords: Fenugreek seed extract, safety, body mass, fat-free mass, blood pressure, muscle strength

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/565/1161

Cytotoxic and antioxidant properties *in vitro* of Functional beverages based on blackberry (*Rubus glaucus* B.) and soursop (*Annona muricata* L.) pulps

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ABSTRACT

Background: There are many kinds of tropical fruit available in Venezuela. Two of these fruits are the focus of our study: blackberry ("mora") and soursop ("guanábana"). These fruits have extraordinary bioactive components. For example, blackberry has antioxidant compounds such as anthocyanins, which are characteristic of the Rosaceae family. Acetogenins present in the Annonaceae family have been shown to possess cytotoxic properties that act against different types of tumor cells. In previous research, we have discovered how lyophilized soursop pulp has an elevated cytotoxic effect with an IC50 of 7.1940±1.06 in human cervix carcinoma cells (HeLa) and 0.8460±1.29 in human prostate carcinoma cells (PC3).

Objective: This study focused on the health benefits and properties of the soursop and blackberry. Our focus was to determine the antioxidant and cytotoxic properties in a formulated beverage containing blackberry, soursop, and yogurt containing probiotics and prebiotics.

Methods: The research includes the study of soursop pulp (SP), blackberry pulp (BP), and two formulations of the functional beverage selected through a sensorial analysis, F2 (BP + SP + Yogurt + Truvía® + Sacarose) and F3 (BP + SP + Yogurt + Truvía® + Sacarose + Sodium tripolyphosphate). Cell viability of prostate carcinoma cells (PC3), breast carcinoma without over- expression of the HER2/c-erb-2 gene (MCF-7), breast carcinoma in which the HER2/c-erb-2 gene is over-expressed (SKBr3) and healthy cells of human connective tissue used as control(Fibroblasts). The previous indicated samples were assessed using MTT (3- (4,5-dimethylthiazol- 2-yl)-2,5-diphenyl-2H-tetrazolium bromide). The antioxidant activity of the functional beverage was also done using a fresh preparation of 1,1-diphenyl-2-picrylhydrazyl (DPPH).

Results: The BP demonstrated the highest cytotoxicity for both lines of breast cancer cell lines, MCF-7 and SKBR3. The values of the minimum concentration required to inhibit 50 % of the cell population (IC50) was 0.12 ± 1.10 and 1.81 ± 1.68% v / v respectively, followed by SP in MCF-7 and PC3 with values of 1.40 ± 1.03 and 1.34 ± 1.06 respectively. At the same time, the effectiveness of the formulations used found that 3.60 ± 1.04% v / v of F2 beverage was necessary to achieve 50 % inhibition of cell viability of MCF-7 line. For the formulation F3, it was necessary to use a concentration of 5.21 ± 1.04% v / v for that tumor cell line. However, the F2 and F3 formulations demonstrated IC50 values of 3.69 ± 1.08% v / v and 2.50 ± 1.08% v / v respectively for the PC3 cell line. On the other hand, the antioxidant capacity of BP and SP reached elevated values at 30 minutes of exposure to DPPH, obtaining

a rate of 85.28 ± 0.11 and 80.94 ± 0.07 % respectively by using a concentration of 12.5 %, F2 and F3 formulations also reached values of 83.97 ± 0.46 and 85.62 ± 0.11 % at 100 % concentration of both drinks respectively.

Conclusion: We discovered that the cytotoxic activity of both formulations prepared, as well as the pulps were fairly good, revealing highly effective consequences for the inactivation of breast tumor cells MCF-7 and prostate tumor cells PC3. Moreover, BP and SP demonstrated a high antioxidant activity, with a synergistic effect accomplished by the mixture on F2 and F3.

Keywords: Functional beverage, cytotoxic, antioxidant, soursop, blackberry, yogurt.

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Mare's milk as a prospective functional product

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BACKGROUND

Food has a significant effect on health. The relationship between diet and health develops the importance of expanding functional food product research. Kazakhstan has a huge potential for functional products, such as saumal or mare's milk [1]. Throughout the ages, saumal has been used as an antidote because of its ability to excrete toxins. Today, saumal is used for pulmonary tuberculosis, anemia, rickets, diabetes mellitus, obesity, nerve diseases, inflammatory diseases of the stomach, and intestines. Saumal is called a longevity drink.

Mare's milk ("saumal") is a physiological, delicate, and easily assimilated biologically active product [1]. The composition of the mare's milk is similar to that of human milk and has a set of beneficial properties on our body, improving the functioning of the systems. Usually, mare's milk is used both fresh and fermented. Fermented milk is called in some countries koumiss, in Mongolia–ayrak [6].

Mare's milk contains about 40 biological components necessary for the human body: amino acids, fats, enzymes (lysozyme, amylase), microelements (calcium, sodium, potassium, phosphorus, iron, magnesium, copper, iodine, sulfur, cobalt, zinc, bromine) and vitamins (A, C, B1, B2, B6, B12, E, H, PP, beta-carotene, folic acid...) in optimally balanced proportions [1].

The mare's milk is characterized by a large amount of lactose (72.80 g / l, 0.03 s) and a reduced fat content (6.40 g / l; 04 sd) and proteins (caseins) (15.52 g / l, 0.11 s), especially caseins (13.4 g / l, 0.04 s) [1]. The milk in its composition belongs to the albumin group. While the milk of other domestic animals (with the exception of the donkeys) refers to the casein group. Albumin and casein are types of protein, giving the milk a distinctive white color [1]. Their difference lies in the fact that casein has a coarser (coarsely dispersed) structure and due to this fact is poorly absorbed. Albumin, like the underlying globulin of mother's milk, is a finely dispersed (whey) protein and is digested easier. Mare's milk also contains about 50% of casein and about 39% of whey protein, while cow's milk contains about 80% of casein [2].

Milk is a unique source of vitamins A, B1, B6, B12, C, D, E, K and minerals (Fe, Cu, Mg, Mn, Zn and Ca) [2]. According to the mineral composition of the mare, milk is very close to the maternal [3]. The mare's milk contains important amino acids for our body, such as tryptophan, tyrosine and casein [4]. As for fat, the fat contained in mare's milk is almost the best animal fat in nature. Due to the specific finely dispersed structure, it is emulsified as quickly as possible (cleaved) and absorbed. A large percentage of all fats are composed of polyunsaturated fatty acids omega 3 and 6 [2, 3, 5].

There are a number of proteins found in mare's milk. When digested, these proteins release bioactive peptides with many different properties. These include blood pressure regulators, antimicrobial, and anti-inflammatory peptides [6, 7]. Lactation of mares begins with colostrum within the first seven days after the birth. The composition of milk varies in the number and content of certain nutrients and lasts until foals are weaned at the age of 5 to 8

months. The limiting factor in the production of mare's milk is a small volume of the breast (<2 L), which requires several daily milking (5-7 times / day) distributed in intervals of 2 to 3 hours [8].

The therapeutic significance of mare's milk was has been known throughout the territory of Russia and Western Asia [9]. Mongolian medicine used mare's milk for the treatment of chronic hepatitis and peptic ulcer disease [9]. Milk also has anti-acid properties due to the high content of phospholipids and vitamin A. The use of mare's milk for the treatment of patients with tuberculosis has been practiced for a long time in the territory of Russia and Mongolia. The therapeutic effect is associated with an increase in the number of erythrocytes and lymphocytes to the normal level (sedimentation rate) of erythrocytes [9].

Chen Y. and his colleagues report that koumiss is rich in protein ACE inhibitors (angiotensin- converting enzyme) that is involved in the regulation of the blood pressure. From koumiss, 4 proteins were isolated and purified: PI, PK, PM, and PP. The PI protein is a part of the β-casein in mare's milk, the PK protein corresponds to f144-150 of the cytochrome C-type protein NrfB, and the PM and PP proteins do not correspond to more than one milk protein from the NCBI database. All 4 proteins are ACE inhibitors that make koumiss a product that can be used as a component in anti-hypertensive functional products [10].

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Glutathione inhibits expression of the proinflammatory biomarker inducible nitric oxide synthase in hepatocytes

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ABSTRACT

Background: Intracellular glutathione (GSH) plays an important regulatory role in the host response to liver injury. However, there have been few scientific reports on the anti-inflammatory effects of GSH. In the inflamed liver, proinflammatory cytokines stimulate liver cells, followed by expression of inducible nitric oxide synthase (iNOS). Excessive nitric oxide (NO) levels produced by iNOS are one of the factors involved in liver injury. Therefore, inhibiting iNOS induction is important for preventing liver injury. This study aimed to investigate the protective effects of GSH on the liver by examining interleukin (IL)-1β-stimulated hepatocytes.

Methods: Primary cultured rat hepatocytes were treated with IL-1β in the presence or absence of GSH. Induction of iNOS and its signaling pathway were analyzed.

Results: Addition of GSH decreased IL-1*β*-induced iNOS protein and mRNA expression levels, which resulted in inhibition of NO production. GSH also decreased tumor necrosis factor (TNF)-α and IL-6 mRNA expression. GSH blocked "type I IL-1 receptor upregulation", one of the essential signaling pathways for iNOS induction, through inactivation of an upstream kinase, phosphatidylinositol 3-kinase/Akt. In contrast, GSH had no effects on degradation of IκB and activation of NF-κB (nuclear translocation and its DNA binding). Transfection experiments revealed that GSH reduced iNOS mRNA levels at the promoter transactivation and mRNA stabilization steps. Delayed administration of GSH after IL-1β addition also inhibited iNOS induction.

Conclusions: Our study suggests that GSH affects induction of inflammatory mediators, including iNOS and TNF-α, indicating its therapeutic potential for organ injuries, especially for the liver.

Keywords: glutathione, inducible nitric oxide synthase, liver injury, primary cultured hepatocytes, type I interleukin-1 receptor, tumor necrosis factor-α

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Nutritional compositions, polyphenolic profiles and antioxidant properties of pigmented rice varieties and adlay seeds enhanced by soaking and germination conditions

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ABSTRACT

Background: Pigmented rice varieties are gaining interest due to their superior nutritional and phenolic properties compared to white rice varieties. With the rising risk of diabetes, cereals with higher protein contents should be consumed with rice. Adlay is one of the underutilized crops with higher protein contents and other functional properties. The germination process is one of the easy and innovative techniques for improving functional properties in seeds.

Objective: In this study, two pigmented rice varieties and adlay seeds were soaked (24 h) and germinated for 12, 24, 36, and 48 h. The physicochemical properties, polyphenolic profiles, and the antioxidant activities of these samples were evaluated.

Results: Purple rice (PR) demonstrated the highest values for polyphenolic contents, with 9 compounds detected for antioxidant activities. There were 6 compounds detected for red rice (RR). The adlay seeds had the least concentrations of phenolic compounds, with 6 compounds and higher nutritional properties identified. New compounds were synthesized. Among the rice samples, 24 h soaking (S24) gave the best results for phenolic and antioxidant properties, with 24 h germination in adlay seeds. 48 h germination yielded better results for the nutritional values in all the samples.

Conclusion: The present study demonstrates how the process of soaking is a cheap and less time-consuming process of improving bioactive compounds and antioxidant activities in pigmented rice varieties and adlay seeds.

Keywords: polyphenols, antioxidant, pigmented rice, adlay, germination.

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Effects of lactic acid bacteria-containing foods on the quality of sleep: a placebo-controlled, double-blinded, randomized crossover study

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ABSTRACT

Background: There are various types of sleep disorders, such as insomnia, hypersomnia, and rhythm disorder, which are attributed to diverse and complex background factors. Recently, many studies have reported that lactic acid bacteria, bifidobacteria, and lactoferrin, are related to fatigue and sleep.

Objective: To prepare test food samples containing lactic acid bacteria ingredients (fermentation products, living bacteria, and ground bacteria) derived from the lactic acid bacterium strain *Lactobacillus helveticus* MIKI-020 (LBH MIKI-020) and theanine, which is known to have a relaxing effect. Then testing and observing the effects of lactic acid bacteria on the quality of sleep.

Methods: In this placebo-controlled, double-blinded, randomized crossover study, we randomly selected 40 male and female subjects (aged 20-64 years) to consume four-weeks test food (lactic acid bacteria ingredients – containing) tablets and placebo control food. The physical examination and laboratory test, sleep electroencephalography, Oguri-Shirakawa-Azumi sleep questionnaire (OSA sleep questionnaire), Pittsburgh Sleep Quality Index (PSQI), and Visual Analogue Scale (VAS) questionnaire were measured.

Results: Sleep electroencephalography: the intergroup comparison in changes of the sleep efficiency (SE) until the 4th week showed a significant increase (improvements) compared with the placebo control food group. Furthermore, SE was compared within the group. In the test food group, the SE increased (improved) significantly in 4 weeks. OSA sleep questionnaire: in intragroup analyses between 0 and 4 weeks, significant increases (improvements) were found in the test food group. PSQI: in intragroup comparisons between week 0 and week 4, significant decreases (improvements) were found in the test food group. VAS questionnaire: the intergroup comparison in changes of Feeling of physical fatigue, Motivation (liveliness), and Calmness until the 4th week showed significant decreases (improvements) compared with placebo control food group.

Conclusion: The sleep efficiency (SE) and Feeling of physical fatigue, Motivation (liveliness), and Calmness were

improved by continuous consumption of test food (lactic acid bacteria- containing food). Among various sleep disorders, a large population in Japan has trouble with sleeping quality. Accordingly, consumption of lactic acid bacteria-containing foods can be a safe and effective method to improve sleep quality.

Keywords: *Lactobacillus helveticus*, lactic acid bacteria, clinical trial, quality of sleep, sleep EEG, OSA sleep questionnaire, PSQI

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Determination of bioactive properties of food grade extracts from Icelandic edible brown seaweed sugar kelp (*Saccharina latissima*) with in vitro human cell cultures (THP-1)

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ABSTRACT

Background: Sugar kelp (*Saccharina latissima,* formerly known as *Laminaria saccharina*) is a brown seaweed which naturally occurs in the North Atlantic. Seaweeds may be one of the last natural food resources abundantly available. They are known to contain many compounds which may have additional functional benefits. This edible seaweed is characterized by high content of nutrients including carbohydrates and polyphenols, which are recognized antioxidants. Because their natural environment is a 3% saline solution, they are very resistant to mild extraction methods. However, extracts from solvent extractions usually contain residual solvents, making them unacceptable for high quality functional foods and high end cosmetics. The objective of this study was to test the biological properties of three extracts from sugar kelp (*Saccharina latissima*).

Methods: Cold water, hot water, and ethanol: water (70:30 v/v) extracts were prepared. Total Carbohydrate Content (TCC) was determined by the phenol – sulphuric acid method and values were expressed as mg of fucose/g of dry extract. Total Polyphenol Content (TPC) was determined and expressed as mg of Gallic Acid Equivalent (GAE)/100g of dry extract. Oxygen Radical Absorbance Capacity (ORAC) assay was performed for all extracts and values were expressed as µM of Trolox® Equivalent/g of dry extract. Human leukemia monocytic cell line (THP-1) was used to investigate the bioactivity of *Saccharina* extracts. Extracts were applied to PMA differentiated THP-1 cells. Cytotoxicity of derived extracts was assessed by light microscopy followed by XTT proliferation assay. Enzyme-linked Immunosorbent assays (ELISA) were performed to determine secretion of interleukin – 10 (IL-10), tumor necrosis factor – α (TNF-α) and interleukin – 6 (IL-6).

Results: The cold water extract exhibited very toxic properties toward macrophages and was thereby excluded from the experimental proceedings with use of the macrophages. Among all the tested extracts, the hot water extract was richest in sugars (682±243 mg fucose/g dry extract) and polyphenols (96.5±5.6 mg GAE/g dry extract), which

was correlated to the determined ORAC values (1686±99 µM TE/g dry extract). The addition of hot water and ethanol extracts at concentrations 100 µg/ml triggered secretion of pro-inflammatory cytokine TNF-α suggesting immunomodulatory properties of Saccharina extracts toward macrophages.

Conclusions: The present study suggests that carbohydrate enriched extracts from Icelandic edible seaweed Saccharina latissima have antioxidant and immunomodulatory properties towards human THP–1 derived macrophages. The carbohydrate and polyphenol correlated with ORAC values confirming antioxidant properties of the derived extracts. The hot water extract affected the pro–inflammatory (TNF–α) and anti–inflammatory (IL–10) cytokine secretion in macrophages, suggesting their bioactivity through immunomodulatory actions and can be considered for practical applications in functional foods and cosmetics.

Keywords: Seaweeds**,** *Saccharina latissimi*, bioactivity antioxidants, immunomodulation

Link to full article: https://www.ffhdj.com/index.php/ffhd/article/view/546/1041

The anti-inflammatory effects of Indonesian and Japanese bitter melon (*Momordica charantia* L.) fruit extracts on interleukin-1β-treated hepatocytes

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ABSTRACT

Background: Bitter melon, *Momordica charantia* L. (Cucurbitaceae), grows in tropical to temperate regions in Asia, including Indonesia and Japan. Bitter melon contains triterpenoids, steroidal glycosides, flavonoids, and alkaloids. The green immature fruit of bitter melon is a popular vegetable in Indonesia and Japan and has been used as a traditional Indonesian medicine (*Jamu*) to treat microbial infections and diabetes mellitus. However, there are currently few reports about the pharmacological effects of the constituents of bitter melon.

Objective: To compare the effects of Indonesian and Japanese bitter melon, the production of pro-inflammatory mediators, such as nitric oxide (NO) and pro-inflammatory cytokines, was monitored.

Methods: Immature fruits of bitter melons collected from Indonesia and Japan were lyophilized and extracted with methanol. The resultant extracts were fractionated by hydrophobicity into ethyl acetate-soluble (A), *n*-butanol-soluble (B), and water-soluble (C) fractions. Primary cultured hepatocytes prepared from rat liver were treated with interleukin- 1β (IL-1β) and each extract or fraction. Nitrite in the medium was measured, and the half- maximal inhibitory concentration (IC50) value was determined. Lactate dehydrogenase activity in the medium was measured to monitor cytotoxicity. The expression of inducible nitric oxide synthase (iNOS) was detected by western blot analysis. The mRNA levels were measured by reverse transcription-polymerase chain reaction.

Results: Indonesian and Japanese bitter melon extracts (BMEs) suppressed NO production by IL-1β-treated hepatocytes without showing cytotoxicity. The IC50 values of the BMEs were 86 µg/mL (Indonesian) and 171 µg/mL (Japanese). Both BMEs suppressed iNOS protein expression. Fractions A and B of both BMEs suppressed NO production. The IC50 values of the Indonesian BME fractions A and B were comparable to those of Japanese BME. Fraction A of both BMEs decreased the levels of iNOS protein and mRNA, as well as those of pro- inflammatory cytokine mRNAs. Fraction C of both BMEs did not affect NO production.

Conclusion: The ethyl acetate-soluble fraction (A) of Indonesian and Japanese BMEs exhibited a comparable ability

to suppress the induction of the *iNOS* and pro-inflammatory cytokine genes. These data suggest that hydrophobic constituents in fraction A, such as cucurbitane-type triterpenoids, may be responsible for the observed anti-inflammatory effects of bitter melon from Indonesia and Japan.

Keywords: *Momordica charantia*, nitric oxide, inflammation, Jamu, Goya.

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Effects of curcumin on testis microvascular complication in streptozotocin-induced diabetes rats

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ABSTRACT

Background: Diabetes has a significant impact on the impaired function of the reproductive system in the testis.

Objective: The aim of this study was to investigate the effects of curcumin from turmeric on structural changes of testicular tissues and microvasculature in STZ-induced diabetic rats.

Methods: Rats were injected with a single dose of streptozotocin (60 mg/kg BW) to induce a diabetic condition. Three days after the injection, rats with a blood sugar level > 250 mg/dl were considered diabetic. Rats were allocated to one of three groups, diabetic (DM), diabetic rats receiving curcumin (DMC) (200 mg/kg BW), and control (C). Testicular tissues were studied eight weeks after the treatment using the histological technique. Testicular microvasculature was examined using the vascular corrosion cast technique under a scanning electron microscope (SEM).

Results: The testicular tissue of DM group showed damaged seminiferous tubules, spermatocytes, and spermatids with necrosis and germ cells degeneration. Destruction of testicular arteries and veins in pampiniform plexus were demonstrated. The destroyed capillaries, arterioles, and venules demonstrated stenosis and shrinkage. The vessel diameter in all DM groups decreased. In the DMC group which received curcumin, the appearance of all seminiferous tubules, spermatogenic, and sertoli cell was normal. The reconstruction and restoration of testicular artery, pampiniform plexus, capillary network, arterioles, and venules were clear. As a result of curcumin supplementation, the standard and healthy testis microvasculature was restored. The DMC vessels diameter increased back to a quasi normal condition, particularly at the artery, arteriole, and capillary levels.

Conclusions: The results provided evident for effects of curcumin could be associated with recovering and improvement of the testicular tissues and microvasculatures in diabetic condition.

Keywords: Diabetes mellitus, Streptozotocin, Curcumin, Testis, Microvasculature, Vascular corrosion cast, Scanning electron microscope

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Intake safety of *Lactobacillus helveticus* SBT2171 and its effects on nasal and ocular symptoms associated with mites and house dust: An open-label study and a randomized, double-blind, placebo-controlled, parallel group study

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ABSTRACT

Background: We previously reported that *Lactobacillus helveticus* SBT2171 (LH2171) inhibited the proliferation and secretion of lipopolysaccharide-stimulated inflammatory cytokines in primary immune cells. Furthermore, *in vivo* administration of LH2171 has been demonstrated to suppress the incidence and development of murine rheumatoid arthritis. This study aimed to evaluate whether the intake of drinkable yogurt (DY) containing LH2171 alleviated nasal and ocular symptoms of allergy to mites and house dust allergens. The safety of LH2171 was also confirmed in an independent, open-label study in 20 healthy subjects who consumed an excessive amount of LH2171.

Methods: In study 1, the effect of daily intake of DY containing LH2171 for 12 weeks on nasal and ocular symptoms was evaluated in healthy men and women who tested positive for house dust or mite-specific IgE in a randomized, double-blind, placebo-controlled, parallel group study. One hundred subjects were divided into two groups: subjects taking placebo DY (P group, n = 50) and subjects taking DY containing approximately 1×10^9 cells of LH2171 (LH2171 group, n = 50) daily for the 12 weeks. After excluding subjects that met exclusion criteria, data obtained from 94 subjects (LH2171 group: n = 48; P group: n = 46) were analyzed to establish LH2171 efficacy. LH2171 safety was assessed in an independent, open-label trial in 20 subjects (study 2) who consumed an excessive amount of DY containing approximately 3×10^9 LH2171 cells.

Results: In study 1, the decreases in the total scores of the nasal and ocular discomfort between week 0 and week 8 in LH2171 group were significantly larger than those in P group. Additionally, the number of sneezes decreased significantly in LH2171 group compared with P group on weeks 9–12 compared to the number of sneezes at baseline. In study 2, no adverse effects of LH2171 on systolic bold pressure, diastolic blood pressure, pulse rate, body weight, blood and urinalysis parameters were reported.

Conclusion: Daily intake of LH2171 for 12 weeks may regulate immune function and improve nasal and ocular symptoms in the subjects with mite or house dust allergy.

Keywords: *Lactobacillus helveticus* SBT2171, nasal and ocular symptoms, IgE antibodies

Clinical trial registration: UMIN000027791 (study 1), UMIN000029058 (study 2).

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Ameliorative effects of curcumin on microvascular complication streptozotocin-induced diabetic rat penis

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ABSTRACT

Background: Vascular diseases from diabetes typically result in conditions that interfere with the microvascular functions, such as erectile dysfunction (ED) of the penis. It is unrevealed which morphological changes the microvasculature of the penis may result from the treatment and supplementation of curcumin.

Objective: This study aims to determine the effects of curcumin, the active compound of turmeric, on penile microvasculature in experimentally induced diabetic rats.

Methods: Rat were divided into three groups, control (C) and diabetic (DM). Diabetic rats supplemented with curcumin (DMC) (200 mg/kg BW). For induction of a diabetic condition, rats were injected with a single intraperitoneal injection of streptozotocin (60 mg/kg BW). A histological study and vascular corrosion casting along with scanning electron microscopy (SEM) were used to determine a morphological change of microvessels in the penis of rats after 8 weeks of experiments.

Results: The histological investigations of penile tissue of DM group revealed thickly lined venous sinuses with smooth but sparse muscle layers. Dorsal arteries (DA) and deep dorsal veins (DV) of the penis were present of narrow lumen and showed thickening of collagen fibers at their wall of tunica media. An increasing thickness of collagen fibers was observed. Vascular corrosion casting revealed critically decreased diameters of DM venous sinus in the penis' glans, which were observed as shrunken and partially lacking in the distal area of the glans. The diameter of venous sinuses in corpus cavernosum (CC) of DM rats were dilated and the density of venous sinuses was decreased. Interestingly, the signs of vessel restoration and improvement were presented by increasing diameters and recovering with healthy and nourished DA, DV, venous sinus at the area of the glans, and CC of the penis in DMC groups.

Conclusion: The results have shown that the effects of curcumin could improve the destruction of the penile microvasculature in induced diabetic rats by STZ.

Keywords: Diabetes mellitus, streptozotocin, curcumin, penis, Microvasculature, vascular corrosion cast

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Phytonutrient intake and body composition: Considering colors

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ABSTRACT

Background: Being overweight or obese is one of the most harmful risk factors to the health of a population. The cause of obesity is complex and multifactorial, but a primary cause is a nutrient- poor diet. Despite excess intake of calories, diets of obese individuals commonly lack phytonutrients**.** Phytonutrients such as chlorophyll, carotenoids, and anthocyanins have all been shown to have anti-obesity effects. National data show that populations with the lowest intakes of fruit and vegetable intake also have higher obesity rates. Available data suggests that a low fruit and vegetable intake, corresponding to a low phytonutrient intake, is correlated with excess adiposity.

Objective: To determine if phytonutrient intake is correlated with body composition and to examine correlations between certain colors of fruits and vegetables.

Methods: Fifty individuals from Thibodaux, Louisiana were randomly selected to participate in this study. Three 24-hour food recalls were used to calculate phytonutrient content of the diets using the phytonutrient index (PI). A food frequency questionnaire was used to determine intake of specific phytonutrients (carotenoids, anthocyanins, and carotenoids). Body adiposity was measured using body mass index (BMI), waist circumference, and fat percentage. Pearson correlation was used to assess correlations between phytonutrient index and body adiposity measures. Analysis of variance (ANOVA) with post-hoc tests was used to determine differences in PI and phytonutrient intakes among the BMI, waist circumference, and percent body fat groups.

Results: Participants who met healthy standards for BMI, waist circumference, and fat percentage all averaged significantly higher PI scores compared to those classified as obese/overweight. A strong inverse relationship was found between PI and BMI ($r = -0.753$, $p = 0.00$), waist circumference ($r = -0.730$, $p = 0.00$), and body fat percentage ($r = -0.701$, $p = 0.00$). Individuals with higher weekly intakes of chlorophyll, carotenoid, and anthocyanin-rich foods had better body composition compared to those who consumed less ($p<0.05$).

Conclusion: Results suggest a strong correlation between higher phytonutrient intake and improved body composition. Overall diet quality seems to make the most difference, but phytonutrients are likely a key reason for those benefits.

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Effect of Welsh onion (*Allium fistulosum* L.) green leaf extract on immune response in healthy subjects: a randomized, double-blind, placebo-controlled study

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ABSTRACT

Background: Welsh onion belongs to genus *Allium*. Although its medicinal benefits, such as cold prevention, are well known by tradition, the underlying mechanism and active components have never been elucidated. The recent study revealed that Welsh onion mucus enhances tumor necrosis factor-α and monocyte chemotactic protein-1 production from RAW 264 cells and natural killer (NK) cell activity in murine spleen cells. This mucilage was abundant in the leaf blade of Welsh onion. The aim of this study is to investigate the effect of Welsh onion green leaf extract (GLE) on immune competence in human clinical trials.

Methods: A randomized, double-blind, placebo-controlled trial was conducted. Fifty-five healthy subjects were enrolled after the screening based on NK cell activity, and each sample (placebo, low-dose GLE or high-dose GLE) was supplemented for four weeks. The immune competence activity was evaluated through the primary endpoints that were NK cell activity, and the score of immunological vigor (SIV). The SIV was calculated from lymphocyte subset analysis by flow cytometry method.

Results: NK cell activity was enhanced in all supplemented groups including placebo; especially, NK cell activity was significant in both GLE groups. The immune score result showed that the immunity of the high-dose GLE group did not change although it was significantly lowered in the placebo group ($p<0.01$), suggesting that GLE ameliorated the immunity suppression. In addition, when SIV was compared between pre- and post-intake, the ratios of the improved subjects in two GLE groups were higher than that of the placebo group while those of the aggravated subjects showed the opposite result. In particular, they were remarkable in high-dose GLE group.

Conclusion: These results suggest that the intake of low- or high-dose GLE might positively regulate immune competence.

Keywords: Welsh onion, immunity, natural killer cell, clinical trial

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/569/1156

A comparative pharmacokinetic evaluation of bioavailable curcumin formulation Curene® with curcumin formulation containing turmeric volatile oil and standard curcuminoids 95% in healthy human subjects

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ABSTRACT

Background: Curcumin, a major active component of turmeric, is one of the most studied botanicals for its numerous health benefits and high safety profile. In spite of its potential clinical health benefits, its applications are limited due to its poor bioavailability. The current study was carried out to compare the oral bioavailability of the newly developed bioavailable curcumin formulation Curene® with a curcumin formulation containing turmeric volatile oil (CP-01) and standard curcuminoids 95% in healthy human volunteers.

Methods: In this current open-label, randomized, three-treatment, single oral dose, single-period, parallel, comparative pharmacokinetics study, 12 healthy male volunteers participated. The test product Curene® (test treatment - T), reference products CP-01 (reference treatment - R1) and standard curcuminoids 95% (reference treatment - R2) were orally administered as a single dose of 3 grams per subject. Plasma samples were withdrawn from each subject at predetermined time points, and samples were analyzed by LC-MS/MS.

Results: Based on the pharmacokinetics data, Curene® (Free curcumin; AUC0-t) was found to be ~112.7 times more relatively bioavailable when compared to the standard curcuminoids (R2).

Conclusion: The oral bioavailability of Curene® was found to be significantly higher compared to CP-01 and standard curcuminoids (95%). Furthermore, Curene® was also found to be safe in healthy human subjects under the study conditions.

Keywords: Absorption, bioavailability, Curene®, pharmacokinetic

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Assessment of anti-inflammatory effects of Japanese Kampo medicine and functional foods

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ABSTRACT

Traditional Japanese drugs called Kampo medicine are widely used in Japan. Each Kampo medicine consists of several crude drugs, most of which are derived from medicinal plants. Clinical administration has empirically evaluated the effects of Kampo medicine. In contrast, functional foods are prepared from foods and edible plants (e.g., herbs, vegetables, and fruits). Due to the relatively low content of pharmacologically active constituents in functional foods, their effectiveness has not been well evaluated and thus should be better investigated. Kampo medicine and functional foods have beneficial effects for humans, and many of them exhibit anti-inflammatory effects. Here, we discuss the principles and methods to assess the anti- inflammatory effects of functional foods and Kampo medicine.

To investigate pharmacological effects of functional foods and Kampo medicines, their constituents should be isolated to identify their chemical structures. Cell-based studies are commonly performed to evaluate anti-inflammatory effects of the constituents in Kampo medicine and functional foods. Primary cultured rat hepatocytes are used and produce pro- inflammatory mediators, including nitric oxide. When an extract from a Kampo medicine, functional food, or a respective constituent is added to the medium, pro-inflammatory mediator production decreases, and the anti-inflammatory activity is estimated. Animal experiments have been performed using disease models, such as the endotoxemia model for animals, to which bacterial endotoxin is administered. Administering an effective functional food or Kampo medicine improves the survival of the model animals. The action of the anti-inflammatory effects of functional foods and Kampo medicines can be investigated by the above-mentioned methods. The studies using cells and animals will provide a basis for the safe and effective use of functional foods and Kampo medicine in humans to treat diseases or improve health conditions.

Keywords: herbal drug, Kampo medicine, nitric oxide, inflammation, hepatocytes.

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An open label trial of a standardized extract of cultured *Lentinula edodes* mycelia (ECLM) in children with refractory epilepsy

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ABSTRACT

Objectives: This open-label trial was performed to assess the immune markers in a cohort of children with refractory epilepsy in order to identify diagnostic and therapeutic markers and to also investigate the effect of an immunologically active supplement derived from mushroom, a standardized extract of cultured *Lentinula edodes* mycelia (ECLM), on the clinical status and on the immunological markers in the subjects.

Methods: Eighteen pediatric patients diagnosed with refractory epilepsy in which antiepileptic therapy was not effective were enrolled. All subjects were also treated with anticonvulsant medications for their seizures. Patients were administered 0.6 g/day (< 3 years old) or 1.2 g/day (≧3 years old) of ECLM (fine-granule equivalent) orally for one month. Immunological markers were assessed at baseline and after one month. Video electroencephalogram (EEG) was taken twice, once before the trials and once at the end of ECLM treatment. Seizure frequency and behavioral symptoms were measured by a questionnaire survey of the parents. A two-month follow-up was also performed for surveillance of secondary infections.

Results: The subjects treated with ECLM showed significant elevation of several immune parameters including immunoglobulin G (IgG), CD3, CD4, and CD20 lymphocytes, and phagocytic index. Six of the 18 children on stable anticonvulsant drugs had fewer seizures reported during the ECLM treatment. The ECLM-treated patients also had less sharp and spike activity in the EEG measurement. At the two-month follow-up, the ECLM-treated subjects had developed fewer infections and viral syndromes compared to their condition before the trial. The children's family reported other subjective behavioral improvements, leading to improved quality of life (QOL).

Conclusion: ECLM administration to the pediatric patients with refractory epilepsy contributed to improvement of epileptic manifestation and decrease of epileptic seizure, possibly by suppressing the reactivation of herpes virus, as well as improvement of QOL. In addition, it was demonstrated that ECLM is a safe supplement for infants and

children.

Keywords: ECLM, epilepsy, children, pediatric, mushroom

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Effect of probiotics on stool characteristic of bottle-fed infants

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ABSTRACT

Background: Approximately 70% of all newborns in South Korea are fed a commercial formula as their sole source of nutrition or as a supplement to breast milk. It is common for many formula-fed infants to be switched from one formula to another because of perceived abnormalities in stooling patterns (too much/too little, too hard/too loose). Also, probiotics may have been recommended by a clinician or practitioner when there is thought to be a problem with the babies stool based on many reports.

Aims: The primary objective of this study was to determine whether probiotic (nLp-nF1) exposure during the first 6 months of life is safe. The secondary objective was to assess if nF1 exposure correlated with changes in formula-fed infants' stool characteristics.

Result: We recruited 49 healthy formula-fed infants aged 0-6 months from Bundang Cha Medical Center. Infants were given a 14-day supply of probiotics (nf1: Lactobacillus plantarum 2.5 X 1010/g/pack, 2 pack/day). The overall rate of stool change after probiotics is 83% (41/49). Among them, 75.6% (31/41) participants answered fairly about the change of stool characteristics. The significant change of stool frequency, stool color and flatulence after probiotics intervention was reported. The number of infants who defecated once daily was increased from 53% (26 of 49) to 77.5% (38 of 49) (P=0.075). Mustard yellow colored feces increased from 22 to 40 (p=0.018). Only 9 out of 20 infants with flatulence (>3 times) showed persistence of symptoms after probiotics (p<0.001). After taking probiotics, Bristol Stool Scale 4-5 stool was reported from 23 to 37(p=0.018).

Conclusion: By taking probiotics, the color of the stool changed, and the incidence of flatulence production decreased. Although the results are not statistically significant, the quality and quantity of stool improved according to the Bristol Stool Scale.

Keywords: Probiotics, Bristol Stool Scale, stool

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Continuous intravenous vitamin C in the cancer treatment: re-evaluation of a Phase I clinical study

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ABSTRACT

Background: Intravenous high-dose vitamin C (IVC) therapy is widely used in naturopathic and integrative oncology. A number of Phase I and Phase II clinical trials were launched to prove the benefits of the IVC therapy. Many case studies demonstrated the effectiveness of IVC, with various degrees of success. Clinical trials using IVC to treat cancer have, to date, demonstrated its safety without conclusively proven its efficacy. One difficulty in administering IVC is determining the optimal treatment schedule. To this end, data from a previous Phase 1 clinical trial conducted in 1998 using continuous vitamin C infusions was analyzed to examine the effects of this regimen on key prognostic parameters. This study aims to investigate if continuous infusions of IVC has any benefit to cancer patients.

Method: Twenty-four subjects were given continuous IVC at doses between 150 and 710 mg/kg/day. Most of the patients had colon cancer with liver and lung metastasis and three patients had pancreatic or liver cancer. All patients had several chemotherapy/radiation treatments before entering the study. Patients were treated by pharmaceutical grade sodium ascorbate diluted in Lactated Ringers solution with the rate of infusion of 20 ml/hr or 10 ml/hr for lower doses. This diluted solution was administered by continuous infusion.

Results: Prior to treatment, serum lymphocyte counts and ascorbate concentrations tended to be low while serum levels of lactate dehydrogenase (LDH), neutrophils, and glucose tended to be high. Improvements were seen during IVC therapy. In patients with initially elevated neutrophil levels, numbers tended to decrease. In contrast, increased absolute neutrophil and lymphocyte numbers were seen in patients with initially low counts. Neutrophil to lymphocyte ratios (NLR) proved to be a good indicator of cancer patients' survival times (high NLR, low survival). This was also true of LDH, creatinine, and glucose concentrations. In patients with the highest pre- treatment NLR, rate of growth of this ratio decreased significantly during therapy. IVC treatments were also associated with decreases in glucose concentrations, restoration of vitamin C levels, and, in about 40% of cases, reductions in LDH levels.

Conclusions: As the result of the study we found that continuous IVC infusions improved several parameters associated with poor cancer prognosis. The data suggests a strategic benefit to using lower IVC doses in continuous infusions: raising the dose above 300 mg/kg/day (20 grams in 70 kg human) increased the frequency of side effects without noticeably increasing plasma ascorbate levels. Moreover, improvements in lymphocyte counts at low IVC doses tended to decrease at the higher doses. In conclusion, continuous infusions had benefits to cancer patients and further research in this area is warranted.

Keywords: ascorbic acid; continuous infusion; cancer patients; clinical trial; lymphopenia; neutrophil to lymphocyte ratio; hyperglycemia; safety.

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/590/1155

Effects of daily intake of Harudori-kombu: A randomized, double-blind, placebo-controlled, parallel-group study

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ABSTRACT

Background: Kombu (*Laminariaceae*) is traditionally consumed in Japan. "Harudori-kombu" is young kombu harvested in spring. Harudori-kombu contains functional components, such as fucoxanthin—a carotenoid—which confer various biological effects. This study aimed to test the intake of Harudori-kombu and the effects on adiponectin levels and body fat.

Methods: In this study, we investigated effects of the continuous intake of dried Harudori-kombu (2.0 g/day) for 6 weeks. We conducted a randomized, double-blind, placebo-controlled, parallel- group study including 70 healthy Japanese subjects with body mass index between 22 and 30 kg/m^2 and low-density lipoprotein cholesterol levels between 120 and 160 mg/dL. Subjects were randomly assigned to either Harudori-kombu group or placebo group. Subjects ingested 9 capsules per day for 6 weeks. We conducted medical interviews, vital sign examinations, and blood sampling at weeks 0 (baseline), 2, and 6. Moreover, we assessed body composition at weeks 0 and 6.

Results: Harudori-kombu intake did not improve the lipid profile but did reduce body fat. In addition, adiponectin levels were significantly improved.

Conclusions: Harudori-kombu intake showed beneficial health effects, such as reduction in body fat and improvement of adiponectin levels and was deemed safe at the dose administered in this study.

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Lipids derived from Camel milk regulate NLRP3 inflammasome subunit-dependent inflammatory responses in human macrophages

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ABSTRACT

Background: Camel milk is widely used for its reported anti-diabetic and health promoting effects. Lipids derived from the milk have also been shown to exhibit potent anti-inflammatory effects. The mechanism through which these lipids and constituent fatty acids exert these effects remains elusive. The aim of this study was to investigate the effect of camel milk on glycated protein-mediated macrophage inflammation.

Methods: To determine the effect of Total Lipids (TL) and Total Fatty Acids (TFA) derived from camel milk on an *in vitro* model of diabetic inflammation, differentiated THP-1 (dTHP-1) cells stimulated with glycated serum albumin (gBSA) was employed. Cells were pre-treated with TL or TFA before challenging cells with gBSA.

Results: Gas Chromatography-Mass Spectrometry **(**GC-MS) analysis found that TL was 96% triacylglycerol (TAG) while the TFA comprised 65% saturated and 35% unsaturated fatty acids. Both TL and TFA significantly ($p<0.05$) decreased gBSA-induced secretion of pro-inflammatory cytokines (Tumour necrosis factor-(TNF)-α, Interleukin-(IL)-1β/18). TL also demonstrated the ability to regulate the expression of p50/p65 sub-units of Nuclear Factor-kappa B (NF-κB), while concomitantly increasing the expression of regulatory cytokines IL-10, IL-1 Receptor Antagonist (IL-1Ra) and Cluster of Differentiation 163 (CD163)-shifting cells towards an M2 macrophage phenotype. Additionally, we found that TL significantly regulated the expression of Nucleotide- binding oligomerization domain-like receptor family pyrin domain containing-3 (NLRP3) inflammasome subunit and its regulator; Ten-Eleven Translocation-2 (TET-2).

Conclusion: This paper demonstrates the ability of camel milk lipids to regulate gBSA-induced macrophage inflammation *in vitro,* by modulating the expression of key inflammatory regulators such NF-B and NLRP3 inflammasome subunit.

Keywords*:* Camel milk lipids, Macrophages, NF-B, NLRP3-inflammasome, TET-2

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/567/1053

Effect of coordinated probiotic/prebiotic/phytobiotic supplementation on microbiome balance and psychological mood state in healthy stressed adults

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ABSTRACT

Background: Interest in and knowledge of the gut microbiome has increased exponentially in the past decade. This once overlooked component of the gastrointestinal tract is now implicated in multiple aspects of human health, including mental (e.g. depression, anxiety, stress), metabolic (e.g. diabetes/obesity), neurological (e.g. Alzheimer's, Parkinson's, Autism Spectrum Disorder), gastrointestinal (e.g. irritable bowel syndrome, Crohn's), and immunological (e.g. inflammation, cancer) wellness, among others. Previous research has demonstrated the "strain specificity" of probiotic therapy (e.g. Lactobacillus helveticus R0052 for serotonin/depression; Bifidobacterium longum R0175 for GABA/anxiety; Lactobacillus rhamnosus R0011 for cortisol/stress). Similarly, probiotic bacteria demonstrate different growth trajectories based on availability of preferred fiber substrates (e.g. prebiotics) and phytonutrients such as flavonoids/polyphenols (e.g. phytobiotics). Thus, our objective was two-fold: to determine the change in microbiome ecology/balance and to evaluate the psychological mood state following a coordinated pro-/pre-/phyto-biotic supplementation regimen.

Methods: Thirty-two healthy subjects screened for "moderate" levels of psychological stress were randomly assigned to 1-month of Supplement (*Amare Fundamentals*, N=21) or matching Placebo (N=11). Microbiome balance was assessed in fecal samples using a PCR-based analysis (*BiomeTracker*) that has previously compared favorably to 16S sequencing for abundance quantification for major phyla/families of bacteria. Psychological mood state parameters were assessed using the validated Profile of Mood States survey (POMS) to generate scores for Global Mood State, and six sub-scales (Depression, Tension, Fatigue, Anger, Confusion, and Vigor).

Results: Following supplementation, there was a significant increase in populations of "good" bacteria in the Supplement group (+28% Lactobacillus; +30% Bifidobacterium) and overall composite score (+17%) versus Placebo ($p<0.05$). Psychological indices were significantly improved in the Supplement group for both positive (+25% Global Mood; +44% Vigor) and negative (-64% Fatigue; -55% Depression; -54% Anger; -45% Tension; -43% Confusion) mood state parameters versus Placebo ($p<0.05$).

Conclusion: The World Health Organization has identified mental wellness issues as the leading contributor to global health burden – highlighting the urgency to develop lifestyle interventions to effectively manage depression, anxiety, and stress. These results demonstrate the close relationship between microbiome balance and psychological parameters – and the utility of targeted supplementation to positively influence the gut-brain-axis for improved mental wellness.

Keywords: Lactobacillus helveticus, Bifidobacterium longum, Lactobacillus rhamnosus, depression, anxiety, stress, vigor, mood state, mental wellness

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/599/1050

Supplementation of concentrated Kurozu, a Japanese black vinegar, reduces the onset of hepatic steatosis in mice fed with a high-fat diet

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ABSTRACT

Background: Hepatic steatosis is among the most common causes of chronic liver diseases, although established effective treatments are not evident. Previous studies reported that Kurozu improved hypercholesterolemia and carbohydrate metabolism. However, the effect of Kurozu on the incidence of hepatic steatosis is not clear.

Objective: The effect of Kurozu on the onset of hepatic steatosis by administering a high-fat diet (HFD) for 110 weeks was evaluated in C57BL/6J mice.

Methods: HFD treatment for 110 weeks accelerated the onset of hepatic steatosis more than a standard diet, whereas concentrated Kurozu (CK) supplementation ameliorated the effect of an HFD feeding. The effect of supplementation with resveratrol in an HFD on the onset of hepatic steatosis was also evaluated. To elucidate the mechanism of the effect of Kurozu on the expression of lipid metabolism genes, acute treatment for 10 days with Kurozu was also examined.

Results: Supplementation with resveratrol in HFD-fed mice did not ameliorate hepatic steatosis. Body weights were significantly lower in the CK + HFD and Resveratrol + HFD groups than in the control HFD group in middle age. No significant differences in all-cause mortality were observed following supplementation with CK or resveratrol. CK and resveratrol supplements significantly inhibited decreases in dehydroepiandrosterone sulphate serum levels at postnatal week 120. CK and resveratrol supplements did not affect the survival of mice. The ingestion of Kurozu for 10 days significantly elevated the expression levels of *Sirt1*, *Pgc-1α*, *Lpin1*, and *Igfbp1* in the liver.

Conclusion: These results suggest that ingesting CK may delay the onset of hepatic steatosis HFD feeding causes.

Keywords: Kurozu, steatosis, Sirt1, Igfbp1, Lpin1, Pgc-1α, resveratrol

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Traditional Indonesian rempah-rempah as a modern functional food and herbal medicine

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ABSTRACT

Rempah-rempah are endemic spices from Nusantara (Southeast Asia archipelago) that have been used traditionally as food flavoring for centuries. Traditionally, rempah-rempah has been processed in a variety of ways including boiled, fried, distilled, fermented, extracted, and crushed and mixed fresh with other foods. Foods flavored with rempah-rempah are served daily as beverages, hot drinks, snacks, and crackers. Nowadays, the consumption of synthetic ingredients was increased globally, but rempah-rempah was rarely used in food. In traditional medicine, various parts of rempah-rempah have been used in many countries for the treatment of a number of diseases. Unfortunately, information concerning the human health benefits of rempah-rempah is still limited. Therefore, a detailed ethnomedical, phytochemical review of the correlated chemical compounds of rempah-rempah was performed.

This review summarizes the most recent research regarding the phytopharmaceutical actions of rempah-rempah like immunomodulatory, antioxidant, analgesic, digestive, carminative, and antibacterial effects, as well as other physiological effects. Modern pharmacological studies and clinical studies performed note that rempah-rempah ameliorates potential disease threats. Such rempah-rempah include ginger (*Zingiber officinale*), Katuk (*Sauropus androgynus* (L.) Merr), andaliman (*Zanthoxylum acanthopodicum*), antarasa (*Litsea cubeba*), kecombang (*Nicolai speciosa* Horan), tapak liman (*Elephantropus scaber* L.), kedondong laut (*Polyscias obtusa*), mengkudu (*Morinda citrifolia*), kapulaga (*Amomum cardamomum*), lemongrass (*Cymbopogon fleuopsus*), sirsak (*Anona muricata*), and kunyit (*Curcuma* sp.). Due to its nutritional and medicinal values, rempah-rempah can be categorized as a functional food with natural ingredient that provide health benefit for some diseases. The resolution of various issues, such as packaging, canning, preserving, and marketing, is needed for future improvement of rempah-rempah as a traditional Indonesian flavor and functional food.

Keywords: Functional food, herbal medicine, rempah-rempah, spices, *Zingiber officinale*, *Sauropus androgynus*, *Zanthoxylum acanthopodicum*, *Litsea cubeba*, *Nicolai speciosa*, *Elephantropus scaber*, *Polyscias obtusa*, *Morinda citrifolia*, *Amomum cardamomum*, *Cymbopogon fleuopsus*, *Anona muricata*, *Curcuma* sp.

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/571/1051

Passionflower extract improves diurnal quality of life in Japanese subjects with anxiety: A randomized, placebo-controlled, double-blind trial

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ABSTRACT

Background and objective: *Passiflora incarnata* (passionflower) has traditionally been used to treat insomnia and anxiety. We recently reported that an aqueous ethanol extract of passionflower (PFE) and its flavonoid glycosides, enhanced the expression of *Period* (*Per*) 2, a clock gene, in mouse liver and fibroblasts. However, the influence of PFE on daily activities or emotions has not been examined in humans.

Aim: This study conducted a clinical trial of PFE supplementation in healthy Japanese participants and investigate if PFE influences sleep and emotions.

Methods: This randomized, double-blind, placebo-controlled study examined the effects of PFE (200 mg daily) containing 3% flavonoid glycosides (6 mg daily). We enrolled 44 Japanese men and women who were reluctant to work, do house chores or engage in irregular shift work. All subjects were randomly allocated into either the PFE group (n=22) or the placebo group(n=22) using a computerized random-number generator. Capsules containing either PFE or placebo were administered for 12 weeks between August 2017 and January 2018. Both emotional status and sleep quality were evaluated by using the Japanese version of Medical Outcomes Study Short-Form 36-Item Health (SF-36) questionnaire and the Oguri-Shirakawa- Azumi (OSA) sleep inventory score at 6- and 12-week of ingestion.

Results: The per protocol set comprised 20 subjects in the PFE group and 18 subjects (20 subjects for OSA and safety evaluation) in the placebo group. After intake of PFE (200 mg/day) for 6 weeks, some of the SF-36 domain scores were significantly improved compared with those of the placebo group, including the scores for role/social component summary, social functioning, and role-emotional. After 12 weeks, the scores for mental component summary and vitality showed significant improvement in the subjects taking PFE (200 mg/day) compared to those taking placebo. In contrast, none of the OSA sleep score parameters were significantly improved by PFE compared with placebo. Laboratory tests did not reveal any abnormalities suggesting adverse effects of PFE.

Conclusions: Intake of PFE (200 mg/day for 12 weeks) improved several emotional parameters related to daytime

social and mental activities. PFE was suggested to be useful for improving anxiety.

Trial Registration: UMIN-CTR: UMIN000028622

Foundation: Oryza Oil & Fat Chemical Co., Ltd.

Keywords: SF-36 questionnaire; passionflower; *Passiflora incarnata*; flavonoid; emotion; Oguri-Shirakawa-Azumi sleep inventory

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/593/1153

Relaxant mechanism of *Eulophia macrobulbon* ethanolic extract and 1-(4′-hydroxybenzyl)-4,8-dimethoxyphenanthrene-2,7-diol on human corpus cavernosum

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ABSTRACT

Background: *Eulophia macrobulbon* (E.C.Parish and Rchb.f.) Hook.F. has been shown to be a promising phosphodiesterase-5 (PDE5) inhibitor that relaxes rat isolated pulmonary artery.

Objective: To test this plant's possible application in human erectile dysfunction (ED) using an ethanolic extract of *E. macrobulbon* tubers (EM extract), and an isolated constituent, 1-(4′- hydroxybenzyl)-4,8-dimethoxyphenanthrene-2,7-diol (HDP).

Methods: Dried tubers of *E. macrobulbon* (EM) were extracted with 95% ethanol and the HDP was isolated by open column chromatography and high-performance liquid chromatography (HPLC) methods. The relaxant mechanism of the EM extract and the HDP was studied on isolated human cavernosal (HC) strips.

Results: EM extract relaxed HC strips, and this effect was not modified by N^G-nitro-L-arginine (L-NNA), ODQ, tetraethylammonium, nor glybenclamide. HDP relaxed HC strips to the same extent as that of sildenafil. EM extract and HDP potentiated relaxation of the HC strips to glyceryl trinitrate in a similar manner to that of sildenafil. EM extract and sildenafil, but not HDP, increased cGMP content of the HC strips in a concentration-dependent manner. In the thapsigargin-pretreated HC strips, nifedipine or EM extract, but not HDP, suppressed the contractile response of the HC strips to phenylephrine. When nifedipine and/or SKF 96365 were added, followed by EM extract or HDP, further suppression was found in the case of HDP but not with EM extract. Ca^{2+} free Krebs solution, suppressed the phenylephrine contraction on HC strips and further suppression was found when adding EM extract or HDP.

Conclusion: These results indicate that EM extract causes a relaxation of HC strips by serving as an inhibitor of PDE5, of voltage- and stored-operated Ca^{2+} channels, and of intracellular Ca^{2+} mobilization. Thus, EM extract might be a good choice for development as a functional food for erectile dysfunction in men. However, further studies are needed to identify other PDE5 and the Ca^{2+} channel inhibiting components of the extract.

Keywords: *Eulophia macrobulbon*; human cavernosum; phosphodiesterase-5 inhibitor; sildenafil; Ca^{2+}channel inhibitor

Human Ethic Number: EC.57/B 06-004

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/591/1064

Amelioration of bowel movement by daily ingestion of Kumaizasa (*Sasa. senanensis*) powder: A placebo-controlled, randomized, double- blind, parallel-group comparison study

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ABSTRACT

Background: Kumaizasa (*Sasa. senanensis* (Franchet et Savatier) Rehder) is a bush-type bamboo grown in Hokkaido, Japan and has traditionally been used as a material for herbal medicine and health food. The purpose of this study was to investigate the effect of daily ingestion of Kumaizasa powder (4.2g/day) for 2 weeks for improvement of constipation.

Methods: We conducted a placebo-controlled, randomized, double-blind, parallel-group comparison study on 80 healthy Japanese men and women between the ages of 20 and 65 who complained of chronic constipation.

Results: The stool frequency per week as the primary outcome showed a significant increase after 2- week ingestion of the active food (Kumaizasa powder) compared with the placebo (starch). The stool odor was also significantly improved after 2-week ingestion of Kumaizasa powder compared with the placebo. Abdominal condition was also significantly improved by visual analogue scale (VAS) evaluation.

Conclusions: We concluded that daily ingestion of Kumaizasa powder is useful for improvement of constipation.

Clinical trial registration: UMIN000029430

Keywords: clinical trial, Kumaizasa, constipation

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/603/964

Redox-dependent and independent mechanisms of selective pro- and anti-apoptotic activity of Georgian legumes crops extracts on Jurkat and MDCK cells

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ABSTRACT

Background: Possibilities of pharmacological regulation of apoptosis play an important role in the treatment of different diseases. Polyphenol-rich plant extracts as well as isolated polyphenols can regulate cell apoptosis primarily through intrinsic and extrinsic mechanisms of action and are the most intriguing and studied class of compounds that can be therapeutics for a wide range of common diseases, including cancer. Polyphenols are well known as powerful antioxidants, and their action is also associated with pro-apoptotic function in various types of tumor cells. The purpose of this study was to establish the anti-and pro-apoptotic activity of Georgian legume crops in model cellular systems.

Methods: Legume crop extracts (LCEs) were prepared in water-alcohol solute. Polyphenol content in the extracts was determined using the Folin–Ciocalteu method; antiradical activity (AA) - according the comparative time of the 50% neutralization of 2,2-diphenyl-1-picrylhydrazyl (DPPH) cleavage.

Studies were carried out on human leukemic mature T cells (Jurkat) and normal epithelial MDCK cell lines. For modelling of oxidative stress, 30% hydrogen peroxide was used. LCEs were added to intact or incubated Jurkat and MDCK cells under oxidative stress conditions. Cell viability was determined by 3-(4,5-dimethyltiazol-2)-2,5-diphenyl-tetrazolium-bromide (MTT) test. Catalase and Superoxidedismutase (SOD) activity in cellular supernatant was measured by spectrophotometry.

Results: LCEs revealed selective pro- and antiapoptotic activity on the intact and incubated cells under oxidative stress conditions Jurkat and MDCK cells. The cytotoxic effect of LCEs on intact Jurkat and MDCK cells was independent of their AA and activity of enzymatic cellular antioxidant defense system.

The cytoprotective effect of LCEs on MDCK cells was realized through redox-dependent mechanisms and is associated both with the own AA of the extracts and with the stimulating effect of the extracts on enzymatic cellular antioxidant defense system activity, where catalase played a leading role. LCEs didn't protect Jurkat cells from oxidative stress-induced apoptosis.

Conclusion: The obtained results allow us to conclude that in cancer chemotherapy, the legume extracts might be combined with prooxidant drugs in order to protect normal cells, but not malignant ones, from their apoptosis-inducing effect. On the other hand, these extracts may protect non- malignant tissues/organs from various

apoptosis-related disorders.

Keywords: Georgian legume crop polyphenol extracts, antiradical activity, antioxidant enzymatic system, oxidative stress, pro-/antiapoptotic activity

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Leveraging budding yeast *Saccharomyces cerevisiae* for discovering aging modulation substances for functional food

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ABSTRACT

Functional food has been a practical mean to be used for health promotion and morbidity compression in the aging population. The discovery and development of bioactive substances with aging modulation actions are critical steps for more potent and safer functional food for aging modulation. Budding yeast (*Saccharomyces cerevisiae*), as a single-cell eukaryotic organism, displays genes, molecular and cellular mechanisms conserved with mammalians. It is a well-developed model for replicative and chronological aging in mammalians. This model organism, with its amenability by genetic and molecular tools, have thus served well for discovering bioactive compounds for aging modulation and health promotion of a variety of age-related health conditions in humans.

In this paper, we have, by synthesizing existing literature, summarized the characteristics of the budding yeast as a practical model for aging for mammalians including humans, then conceptualized a framework for discovering bioactive compounds using yeast cellular system for aging modulations for functional food research and industry. This framework consists of four components: uncovering targets for aging modulation, discovering and validating diet restriction mimetics, acting as cellular systems for screening natural products or synthetic compounds for aging modulation and being a biological factory for producing bioactive compounds according to the roles the yeast systems play. While these four components are continuously being harnessed in both research and industry, the last component of being a biological factory for producing bioactive compounds has largely unexplored, thus presenting a novel opportunity for the functional food industry.

Keywords: Aging modulation, budding yeast, functional food, bioactive substances, cell factory

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Isomalto-oligosaccharides from rice and their potential use as pharma-nutraceuticals in prevention of colon cancer

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ABSTRACT

Background: Isomalto-oligosaccharides (IMO) were enzymatically produced from rice (rIMO) alone or in combination with product (instant rice porridge mixed rIMO) demonstrated bifidogenic and butyrogenic effects in *in vitro* studies. The potential use of IMO from rice for pharma-nutraceuticals to prevent or risk reduction of colon cancer was further investigated in rats in this study.

Objective: To investigate potential use of IMO from rice on prevention or risk reduction of colon cancer and gut microbiota modulation in rats, colonic polyp formation, histological changes, gut microbiota modulation, and butyrogenic properties were evaluated.

Methods: An acute toxicity test was performed in ICR mice with a single dose of 2,000 mg/kg of tested IMO. The effects of rIMO were performed in AOM/DSS-induced Wistar rats. The animals were divided in 8 groups and treated three times a week with vehicle, three doses of rIMO, cIMO, and product (instant rice porridge mixed rIMO) before and after carcinogen administration. Animals were sacrificed at the end of 19th week.

Results: Oral administration at up to 2,000 mg/kg of rIMO and product containing rIMO could be considered safe. Additionally, the animals chemically induced with AOM/DSS and treated with rIMO (1,500 mg/kg) and product containing rIMO significantly lower the occurrence of colonic polyps about 60%. There were no changes in other blood hematologic and biochemistry values but an improved gut barrier function when compared with animals in control and vehicle groups. AOM/DSS-induced rats supplemented with product containing rIMO could retard the reduction of beneficial bacteria and butyric acid production and thereby suppres the increase of harmful bacteria through the AOM/DSS post-induction phase.

Conclusion: The results of this *in vivo* study suggest that consumption of rIMO alone or in combination with brown rice porridge could potentially help protect histological changes and risk reduction of developing for colon cancer. IMO from rice has potential use for pharma- nutraceuticals for risk reduction of colon cancer.

Keywords: colon cancer, isomalto-oligosaccharides, prebiotic, rice, gut modulation

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Effect of acute bitter melon intake on postprandial glucose and insulin in sedentary, abdominally obese persons

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ABSTRACT

Background: Lifestyle modifications have been considered to be the primary prevention strategies for diabetes. However, there is a lack of evidence guiding the use of functional food that potentially possess anti-hyperglycemic effects. The objective of this study was to investigate the acute effect of bitter melon intake on postprandial glucose and insulin levels in sedentary, abdominally obese persons.

Methods: In this study, 16 sedentary, abdominally obese participants were randomly assigned to receive either 100 ml of bitter melon juice or placebo juice 30 minutes prior to an oral glucose tolerance test. Plasma glucose and serum insulin were measured every 30 minutes during the 2- hour postprandial period. Two-way repeated measure ANOVA was used to test the effects of bitter melon on postprandial glucose and insulin levels after adjustment for covariates.

Results: The 2-h postprandial glucose was significantly lower in bitter melon group as compared with control group (99.5 ± 22.3 vs 133.9 ± 36.9 mg/dL, P=0.04), resulting in an absolute glucose reduction of 34.4 mg/dL (95% confidence interval, 1.7 to 67.1 mg/dL) and a relative glucose reduction of 26%. There was a fairly significant reduction in 2-h postprandial glucose incremental area under the curve (iAUC) (52.9 ± 29.5 vs 94.7 ± 47.3 mg/dL·h, P=0.052), resulting in a relative glucose reduction of 44%.

Conclusion: Our acute study demonstrated that the single-dose intake of bitter melon juice decreased postprandial glucose levels among sedentary, abdominally obese persons. Bitter melon juice appears to be a promising functional food to manage hyperglycemia for people who are at elevated risk of developing diabetes.

Key Words: Functional Food; Momordica Charantia; Hyperglycemia; Sedentary; Obese

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/605/1099

Chemoprevention against colon cancer by dietary intake of sulforaphane

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ABSTRACT

Background: Sulforaphane (SFN) is a phytochemical compound which belongs to isothiocyanates family found in abundance in broccoli sprouts. SFN induces a variety of antioxidant enzymes via NF-E2-related factor 2-Kelch-like ECH-associated protein 1- mediated pathway, thereby protecting cells from injury induced by various kinds of oxidative stresses. We have previously shown that SFN protects gastric mucosa from oxidative injury induced by *H. pylori* infection. SFN also down-regulates histone deacetylase (HDAC) activity, thereby inducing apoptosis and inhibiting proliferation of tumor cells in variety of tissues. On the other hand, the incidence of colon cancer has increased in Japan.

Aim: Since numerous epidemiological studies have shown that colon cancer is inversely associated with intake of anti-oxidant vegetables, this study examines whether daily intake of SFN prevents colon tumorigenesis in mice and human subjects.

Methods

1. **Effects of SFN on Colonic tumorigenesis in Mice Treated with Chemical Carcinogen:** Effects of SFN on colonic tumorigenesis were examined in the ICR male mice, pretreated with a chemical carcinogen, azoxymethane (AOM) (15 mg/kg). The mice treated with AOM for 3 or 6 times were fed for 8 or 24 weeks with or without sulforaphane glucosinolates (SGS: 2,200 ppm/kg/day), which is a precursor of SFN. Effects of SGS treatment on formation of the microscopic aberrant crypt foci (ACF) and the macroscopic tumors in colonic mucosa were evaluated.

2. **Effects of SFN on formation of Colonic ACF in patients with colonic adenoma:** Effects of intake of raw broccoli sprouts (BS), 50 g/day containing 220 mg SGS every other day, for 6 months on changes in the number of ACF in rectal mucosa was examined by colonoscopy in patients with colonic adenoma.

3. **Effects of SFN on intestinal microbiota in human subjects:** Effects of dietary intake of raw BS, 20 g/day, which

contains 88 mg SGS every other day, for 2 weeks on intestinal microbiota in healthy volunteers was assessed by measuring composition of stool bacteria, using a method of terminal restriction fragment length polymorphism flora analysis. In human studies, alfalfa sprouts, which contains no SFN, was used as a placebo control.

Results: 1. Daily administration of SGS suppressed formation of microscopic ACF and macroscopic colonic tumors in the AOM-pretreated mice in vivo. 2. Intake of BS for 6 months tended to decrease the number of colonic ACF in patients with colonic adenoma. 3. Intake of BS for 2 weeks increased percentages of *Bifidobacterium* and *Clostridium XVIa*, which has been shown to enhance protection of colonic mucosa by increasing butyrate production in colonic lumen.

Conclusions: 1. Daily intake of SFN affords chemoprotection against colonic tumors in the mice treated with a chemical carcinogen. 2. The present study further suggests that, in addition to previously reported mechanisms, changes in the intestinal microbiota by SFN intake may also play a role in chemoprevention against colon cancer. Further studies are required to prove this possibility.

Keywords: sulforaphane, colon cancer, chemoprevention, aberrant crypt foci, intestinal microbiota

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Mechanism of action of functional lipids and metabolites for patients with chronic kidney disease

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ABSTRACT

Chronic kidney disease (CKD) is a general term for a diverse variety of causes affecting kidney structure and function. The term "chronic" is because the damage to the kidneys happens slowly over a long period. Damaged kidneys cannot filter extra water and wastes out of blood as compared to the healthy kidneys. The disease prognosis and control are categorized based on disease severity, which is evaluated by glomerular filtration rate (GFR) and albuminuria, and clinical diagnosis. Progression of CKD thus causes wastes to build up in the body and is associated with many severe complications, including increased incidence of cardiovascular disease, hyperlipidemia, anemia, and metabolic bone disease.

Forty percent of CKD is a result of complications associated with diabetes. Patients with diabetes are suggested to intake components that have reduced amount of carbohydrates and increased amount of proteins. Patients with CKD are suggested to intake a low protein diet. Thus, there is a fine need for CKD patients to understand the food constituents and functional components. Given the intricacies of the renal diet and the difficulties faced by patients due to conflicting recommendations and complexities faced in understanding processed food labels, there is a lot of emphasis in the present world to change the focus in CKD away from what not to eat to the concept of good nutrition as positive medicine or therapy for kidney patients.

Specifically, there has been a surge in consumer interest on the beneficial role of specific foods with physiologically-active food components, so-called functional foods benefitting CKD. In the past century, increased attention to lifestyle and healthy diets has led to an increase in demand for functional foods.

Thus, this review will discuss the key components that have been investigated *in vivo* using rodent models, some clinical trials and studies for being identified as a 'nutraceuticals' for patients with CKD.

Keywords: Chronic kidney disease, Functional food, Conjugated Linoleic acid, LDL, HDL, Protein diet, Omega fatty acids, L-Carnitine.

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Astaxanthin sources: Suitability for human health and nutrition

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ABSTRACT

Background: Astaxanthin (AX) has been consumed as a nutritional supplement for approximately twenty years. The primary source has been a natural plant-based supplement from the single-cell alga *Haematococcus pluvialis* (NAT-AX). Recently, Astaxanthin from other sources has entered the marketplace. The primary alternative source in the human nutritional supplement market has been a synthetic form of Astaxanthin produced from petrochemicals (SYN-AX). Additionally, a very small amount of Astaxanthin from a genetically-manipulated yeast *Xanthophyllomyces dendrorhous* (former nomenclature *Phaffia rhodozyma,* still commonly referred to as "*Phaffia*") (PH-AX) is also available in some supplement products. The three forms have substantial chemical differences. In addition to the chemical differences between sources of AX, *in-vitro* research has demonstrated profound differences in antioxidant strength and animal research has revealed fundamental differences in health benefits. In all cases, NAT-AX has proven more biologically active than the other sources. This review is designed to assist readers in understanding which form(s) of AX are suitable for consumers desiring preventive or therapeutic health benefits.

Results: In head-to-head antioxidant experiments, NAT-AX demonstrated 14X to 90X greater antioxidant activity than SYN-AX. In numerous animal trials in diverse species, NAT-AX in esterified form has demonstrated superior efficacy in increasing lifespan; treating skin cancer; preventing the formation of gastric ulcers; improving resistance to stress; decreasing reactive oxygen species (ROS); increasing retinol conversion in the liver; augmenting enzyme levels; increasing growth rates; and improving exercise endurance.

From a safety perspective, NAT-AX has been the subject of human clinical trials demonstrating safety and a wide variety of health benefits. In addition, no documented adverse events have surfaced during its twenty years of distribution as a food supplement for humans. SYN-AX and PH-AX have not been proven safe for direct human consumption and have not demonstrated any health benefits in clinical trials. Due to these facts, SYN-AX and PH-AX have not been allowed for human consumption by government regulators in many countries while NAT- AX is widely accepted in most countries around the world.

Conclusion: Based on our review of the literature below, we recommend NAT-AX as the sole form of AX for human consumption until SYN-AX and PH-AX have been proven safe and efficacious through human clinical research.

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Anti-inflammatory and anti-allergic activities of Skipjack tuna (*Katsuwonus pelamis*) dark muscle hydrolysates evaluated in cell culture model

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ABSTRACT

Background: Oxidative stress and inflammation are inextricably linked and play major roles in the onset and development of Non-communicable diseases (NCD) which are the most common cause of death and disability in modern world. Hydrolyzed proteins have also been suggested to be used to manage adverse food allergic reaction. Therefore, this study aimed to investigate anti- inflammatory and anti-allergy activities of dark muscle tuna hydrolysates using biological cell line systems as a function of enzyme, the extent of hydrolysis and molecular weight range.

Methods: Dark muscle tuna hydrolysates were prepared with two different enzyme types; Alcalase and Flavourzyme. Anti-inflammation activity was measured by inhibitory effect of nitric oxide (NO) production on lipopolysaccharide (LPS)-stimulated RAW 264.7 macrophage cells. Anti-allergy was determined from ability of hydrolysates to inhibit -hexsosaminidase (- HEX) release from RBL-2H3 mast cells. Cytotoxicity was also investigated in both RAW 264.7 macrophage cells and RBL-2H3 mast cells.

Results: No cytotoxic effect on RAW 264.7 macrophage cells and RBL-2H3 mast cells was observed. The NO inhibition and -HEX release were found significant in dose dependent manner ($p<0.05$). Alcalase hydrolysates demonstrated greater anti-inflammatory and anti-allergic activities than Flavourzyme hydrolysates ($p<0.05$). IC50 of both effects were lower than theunhydrolyzed control, > 45.44 g/ml for NO inhibition and > 65.23 g/ml for -HEX release inhibition. These effects increased with the extent of hydrolysis and enzyme concentration. The peptide of lowest molecular weight range (< 3 KDa) was highest in anti-inflammatory and anti- allergic actions. Reducing secretion of TNF-, IL-6 and IL-1 was found greater in Alcalase hydrolysate than Flavourzyme one.

Conclusions: Skipjack tuna dark muscle hydrolysates from Alcalase resulted in peptides with anti-inflammation activity, as determined by NO production in LPS-stimulated RAW 264.7 macrophage cells and anti-allergic properties as measured by a suppression of degranulation of sensitized RBL-2H3 cells. Anti-inflammatory effect may be due to their anti-oxidative capacity and relevant inflammatory factors attenuated with hydrolysate by reducing secretion

of pro- inflammatory cytokine (TNF-, IL-6 and IL-1). Inhibition of -HEX release by peptides may be due to membrane-stabilizing action or/and blockade of IgE antibody at fragment region.

Keywords: *Skipjack tuna, anti-inflammation, enzymatic hydrolysate, dark muscle, anti-allergy*

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/618/1071

Immuno-regulatory and anti-inflammatory actions of phycocyanin on Caco-2/U937 cells co-culture as a model of the intestinal barrier

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ABSTRACT

Background: Phycocyanin, a photosynthetic pigment protein of cyanobacteria *Spirulina platensis*, has been used as a health or functional food because of its health promoting and medicinal effects such as its antioxidant, anti-inflammatory, immunomodulatory, and anticancer effects. This aim of this study is to investigate the immuno-regulatory and anti- inflammatory actions of phycocyanin using a developed *in vitro* co-culture model.

Methods: Under the co-culture system using a human colorectal cancer cell line, Caco-2 cells, and differentiated U937 macrophages in the presence of sodium butyrate (SB) and/or lipopolysaccharide (LPS), immune-regulatory and anti-inflammatory activities of phycocyanin were examined.

Results: Phycocyanin attenuated a certain damage in the tight junction of co-cultured Caco-2 cells induced by LPS in the presence of SB, and suppressed IL-6 and IL-8 and conversely enhanced TGF-β1 productions. Phagocytic and bactericidal abilities of the differentiated U937 cells were also regulated under the co-cultivation.

Conclusions: Phycocyanin contributes to protecting against inflammation and to regulating macrophages in the mucosal immune responses partly through release of cytokines in the presence of butyrate.

Keywords: *Spirulina*, phycocyanin, Caco-2 cells, U937 cells, IL-6, IL-8, TGF-β1

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Gender difference in plasminogen activator inhibitor-1 activity in patients with type 2 diabetes with and without albuminuria, a matched case-control study

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ABSTRACT

Background: Women with type 2 diabetes are more susceptible to coagulopathy disorders and endothelial dysfunction. One possible explanation is the effects of different sex hormones in inflammatory conditions. Increased plasminogen activator inhibitor-1 (PAI-1) activity has been observed as a possible predisposing factor for coagulopathy disorders and endothelial dysfunction. However, the effect of gender on PAI-1 in patients with type 2 diabetes (T2D) and albuminuria has not been studied sufficiently.

Objectives: In this study, we examined whether changes of PAI-1 activity according to the albuminuria state in patients with type 2 diabetes are different in males and females.

Materials and Methods: A matched case-control study was performed among participants with T2D, as 38 microalbuminuric patients were matched with 38 normoalbuminuric patients who were similar in age and body mass index (BMI). PAI-1 activity was compared between the two groups with and without gender stratification.

Results: PAI-1 activity in microalbuminuric women was higher in comparison to that of the normoalbuminuric controls (P-value < 0.05). There was no significant difference in PAI-1 activity between macroalbuminuric and normoalbuminuric men. In women with type 2 diabetes and albuminuria, PAI-1 activity was independently and significantly associated with urinary albumin excretion.

Conclusions: Gender differences in PAI-1 activity, seen in the early stages of diabetic nephropathy, are a possible explanation for the higher incidence of vasculopathy in women with type 2 diabetes

Keywords: plasminogen activator inhibitor-1; coagulopathy; microalbuminuria; type 2 diabetes; gender

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/595/1072

Effects of probiotics and synbiotic on lipid profiles in adults at risk of type 2 diabetes: A double-blind randomized controlled clinical trial

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ABSTRACT

Background: The use of probiotics and/or prebiotics as an effective means of regulating gut microbiota may have a beneficial effect on metabolic disorders.

Aims: This study was designed to assess the ability of probiotics and synbiotic to modify lipid profiles in subjects with prediabetes who are at risk of diabetes and cardiovascular diseases.

Methods: In a randomized double-blind placebo-controlled clinical trial, 120 pre-diabetic adults aged 35-70 years from the first-degree family of type 2 diabetic patients were recruited and randomly equally assigned to consume 6 g/d either probiotic or synbiotic or placebo supplements for 6 months. The probiotics used were *Lactobacillus acidophilus, Bifidobacterium bifidum, Bifidobacterium lactis, and Bifidobacterium longum*. Food record, physical activity, anthropometric measures and lipid profiles were assessed repeatedly at baseline, and 3- and 6- month supplementation.

Results: Probiotics and synbiotic were effective in reduction of serum triglycerides after 6 months of intervention (SMD=- 10.6 and -9.4 respectively). Compared with the placebo, synbiotic resulted in a significant reduction in serum triglyceride levels (MD±SE: -9.4 ± 6.6 mg/dl vs. +13.2±6.8 mg/dl, p=0.02). Serum total-, LDL-, and HDL-cholesterol were statistically unaffected by probiotic or synbiotic.

Conclusion: The results of this study showed that supplementation with probiotic and especially synbiotic could decrease the concentration of triglyceride in prediabetic adults. This finding could warrant future studies to determine the therapeutic and preventive effects of these supplements in individuals at risk of diabetes and cardiovascular diseases.

Trial registration: Iranian Registry of Clinical Trials: IRCT201511032321N2. Date registered: February 27, 2016.

Keywords: probiotic; synbiotic; prediabetes; lipid; lipoprotein

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Effect of Astaxanthin supplementation on psychophysiological heart-brain axis dynamics in healthy subjects

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ABSTRACT

Objective: Marine microalgae is the predominant source of natural astaxanthin (NAX), a red- orange carotenoid with powerful antioxidant and anti-inflammatory properties. Previous studies suggest that NAX supplementation improves antioxidant capacity and reduces oxidative stress, while also enhancing fat utilization, exercise endurance, cardiovascular function, and neurological parameters. The purpose of this study was to assess the effects of NAX on the psychophysiological "heart-brain-axis" while nutrition (astaxanthin) may impact physiology (cardiovascular function) and psychology (mood state) in a coordinated manner.

Methods: Using a double-blind parallel design, 28 healthy subjects (male=14, female=14, age=42) were supplemented for 8 weeks with NAX (12mg/day *Haematococcus pluvialis* algal extract) or a matching placebo. Before and after supplementation, subjects performed a cardiovascular stress test (VO2max) and completed a validated Profile of Mood States (POMS) survey to assess global mood state (GM) and related subscales: Vigor (V), Tension (T), Depression (D), Anger (A), Fatigue (F), and Confusion (C).

Results: Subjects in the NAX group showed a significant ~10% lower average heart rate at submaximal exercise intensities compared to those in the placebo group (aerobic threshold, AeT; NAX 130+17 v. PL 145+14; and anaerobic threshold, AT; NAX 139+20 v. PL 154+11, $p<0.05$). Significant improvements were found in the NAX group for both positive mood state parameters: GM (+11%, $p<0.05$) & V (+5%, NS); and negative mood state parameters: T (- 20%, NS), D (-57%, $p<0.05$), A (-12%, NS), F (-36%, $p<0.05$), and C (-28%, NS).

Conclusions: NAX supplementation lowered average heart rate at submaximal endurance intensities (suggesting a "physical" heart benefit) and improved mood state parameters (suggesting a "mental" brain benefit). While previous studies have shown NAX supplementation to improve parameters associated with heart health (antioxidant, fat oxidation, endurance) and brain health (neuro-inflammation, cognition, antidepressant/anxiolytic), these results suggest that natural astaxanthin supplementation supports the psychophysiological "heart-brain-axis" with simultaneous improvements in both physical and mental wellness.

Keywords: Antioxidant; Carotenoid; Cardiovascular; Mood State; Mental Wellness

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Effect of powdered beverages containing Pu-erh tea extract on postprandial blood glucose levels

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ABSTRACT

Objective: The current study aimed to examine the effect of a single ingestion of a beverage containing Pu-erh tea extract (Pu-erh tea polyphenol 18.00mg, eq. gallic acid) on postprandial blood glucose levels through a comparison using a crossover test.

Method: A total of 20 participants, of which 10 were men and 10 were women, aged between 29 and 64 years were instructed to ingest beverages containing Pu-erh tea extract or placebo beverages at the same time as load food (in addition to cooked rice). Their blood glucose levels were measured before and 30, 60, 90, and 120 min after ingestion.

Results: In phases I and II of the trial, three participants who had large differences in the quantity of the ingested food on the day before the trial were removed from the study. Finally, the analysis was conducted on 17 participants. Result showed that the group who ingested the beverage containing Pu-erh tea extract had significantly lower blood glucose levels than the group who consumed the placebo beverage 60, 90, and 120 min after ingestion. In terms of the amount of variation before ingestion, the group who ingested beverages with Pu-erh tea extracts had significantly lower blood glucose levels than the group who consumed the placebo beverage 60, 90, and 120 min after ingestion. In terms of area under the curve (AUC) and increase in the area under the curve (IAUC) for blood glucose levels with some variations, the time it took for the participants to consume the trial beverage compared with the placebo beverage was significantly lower.

Conclusion: Beverages containing Pu-erh tea extract were found to be effective in suppressing the increase in postprandial blood glucose levels after being loaded with cooked rice.

Keywords: Pu-erh tea, postprandial blood glucose, cooked rice, type 2 diabetes

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/635/1143

Fatty acid profile, phenolic compounds and potential antioxidant activity of fresh and cooked Massaman curry paste

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ABSTRACT

Background: The fresh herbs and spices used in Thai food are what make Thai cuisine unique. Some of these herbs and spices have been scientifically studied for health benefits. However, there is limited evidence for cooked food.

Objective: To determine proximate composition, fatty acid profile, phenolic and flavonoid contents and antioxidant activity of fresh Massaman curry paste (MCP) and cooked Massaman curry including beef and chicken Massaman curry (BMC and CMC, respectively).

Methods: The chemical composition and fatty acid profile of freeze-dried samples were analyzed. Food samples were extracted by three solvents: water, absolute methanol or ethanol. The total phenolic and flavonoid contents (TPC, TFC, respectively) of the extracts were measured spectrophotometrically and identified through high performance liquid chromatography (HPLC). The antioxidant activities of extracts were evaluated by 2,2- dyphenyl-1-picrylhydrazyl (DPPH) scavenging and ferric reducing antioxidant power (FRAP) assays.

Results: Carbohydrate, protein, and fat were the main components of all sample studies. Chicken Massaman curry (CMC) contained highest fat and energy contents. Fatty acid profile of CMC showed high content of lauric acid (9460 mg/100 g), oleic acid (6050 mg/100 g) and palmitic acid (4220 mg/100 g). MCP showed high content of linoleic acid (213.70 mg/100 g) and palmitic acid (195.71 mg/100g). Methanol extract of MCP showed the highest content of TPC (1.076±0.013 mg gallic acid equivalent (GAE)/100g crude extract), TFC (27.10±0.31 mg CE/ 100g crude extract) and antioxidant activity by FRAP assay (0.311 ± 0.002 mg Trolox/100g crude extract). While ethanol extract of MCP showed the highest activity of DPPH at value as 11.81±0.06 mg GAE/100 g crude extract, following by methanol extract of MCP (11.02 ± 0.05 mg GAE/100 g crude extract). Cooked Massaman curry including BMC and CMC showed low content of TPC and TFC and antioxidant than fresh MCP. Ferulic acid was the main phenolic acid in these samples which was the highest in methanol extract, followed by ethanol and then water extraction. After cooking process, some activities of food were altered.

Conclusion: The results of this study suggest that fresh Massamun curry paste and cooked Massuman curry in ready-to-eat foods could potentially show antioxidant activity. It provided that the health benefits from plants source still remained in the products after cooking process.

Keywords: Thai food, Massaman curry, Antioxidant activity, Fatty acid profile, Phenolic compounds

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/644/1056

Medicinal mushroom *Taiwanofungus camphoratus*: A potential cure for cancer

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ABSTRACT

Based on traditional and folk medicine , mushrooms have been developed into anti-cancer therapeutics. In this article, a brief overview is given of the most important medical mushroom species and their specific anti-cancer functions and mechanisms. *Taiwanofungus camphoratus* (*Antrodia cinnamomea*), is a medical fungus chosen to examine the process from ethnomedicine to developing new products for the market based on scientific, analytic, and experimental evidence. The bioactive compounds have indirect effects in cancer treatment by benefiting the immune system as well as having direct cytotoxic effects on cancer cells.

Taiwanofungus camphoratus is a fungus endemic to Taiwan and one of the most popular known alternative remedies for liver cancer in Taiwan. To date, more than 150 liver cancer patients have survived using *T. camphoratus*. The treatment has caused tumor shrinking, as well as the disappearance of a tumor altogether in some cases. The ratio between male and female patients has been nearly equal, with ages ranging between 20-79 years. The most effective candidates are those between the ages of 40-60 years.

The complex mixture of bioactive compounds in natural fruit bodies is a challenge for artificial production *in vitro*. Particular problems in developing *T. camphoratus* into therapeutics for the global market are its rarity in nature and its close dependence on an endemic tree in Taiwan. These challenges can help promote new solutions which could be utilized in the future with other medical fungi

Keywords: Medicinal mushrooms, anti-cancer therapeutics, *Taiwanofungus camphoratus*, liver cancer.

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/576/1135

Changes in plasma concentration of flavonoids after ingestion of a flavonoid-rich meal prepared with basic foodstuffs

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ABSTRACT

Background: As flavonoids have a variety of functions, such as antioxidant activity, there is a growing interest in the development of flavonoid supplements. However, there have been reports of DNA damage due to exposure to flavonoids at high concentrations in rats, which could suggest that a habitual intake of flavonoid supplements may cause toxicity. Therefore, we considered that ingesting flavonoids from a typical meal combined with basic foodstuffs is safe because it is unlikely to result in high concentrations like supplements and focused on the intake of flavonoids from a typical meal. Thus, this study investigated the absorption of flavonoids in humans after the consumption of a typical meal.

Methods: On the first 2 days of the study, seven healthy volunteers were provided with meals low in flavonoids (flavonoid content below the detection limit by HPLC: less than 0.24 mg/meal) three times a day as a washout. A flavonoid-rich meal (40.44 ± 1.49 mg/meal) was then provided for breakfast on the third day. Blood was collected from all volunteers 0, 2, 3, 7, 8, and 9 h after the flavonoid-rich meal was consumed. After enzyme hydrolysis of the plasma, the plasma concentrations of flavonoids aglycone of quercetin, daidzein and genistein were measured using LC-MS. Urine was also collected and pooled 24 h after the flavonoid-rich meal was consumed. Thereafter, the urine was treated with enzyme hydrolysis, and the measurement of urinary flavonoids was performed.

Results: Plasma flavonoid peaks were observed 8 h after consumption of the flavonoid-rich meal (quercetin: 4.29 ± 1.46 μM, daidzein: 0.51 ± 0.41 μM, genistein: 0.91 ± 0.73 μM). Furthermore, flavonoids were confirmed to be present in plasma even at 9 h after the intake meal. The urinary recovery of flavonoids was 3.43 ± 1.50% for quercetin, 13.87 ± 6.68% for daidzein, and 16.89 ± 11.40% for genistein.

Conclusion: These results suggest that consuming a typical meal that combines a variety of basic foodstuffs delays attainment of the plasma flavonoid peak compared with consuming a single type of food or supplements as previously reported. In addition, the flavonoid urinary recovery was also reduced compared with those previously reported.

Trial Registration: UMIN000037001

Key words: Flavonoids, plasma concentration, flavonoid-rich meal, human study

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/643/1062

Glycemic index and load responses of indigenous vegetable sauces among healthy young female adults

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ABSTRACT

Background: Low glycemic index, load, and response food has been implicated in reducing the incidence of Type 2 Diabetes Mellitus (T2DM). Also, the use of locally made foods has been advocated for in the management of diabetes mellitus in recent times. The aim of this study is to investigate glycemic and load response of non-diabetic females with a diet consistent of various indigenous vegetables.

Methods: The recipe for the test food was developed and standardized. Proximate and dietary fiber analysis was carried out on the test food (okra, African spinach, and lettuce sauces) and reference food (white bread). Thirty-six non-diabetic undergraduate students of Imo State University, Nigeria were selected after diabetes screening using oral glucose tolerance test (OGTT), glycated hemoglobin, anthropometric indices, blood pressure, and other exclusion criteria. Subjects consumed a serving portion of vegetable sauce containing 25g of digestible carbohydrate. Postprandial plasma glucose was measured at 0, 15, 30, 45, 60, 90, and 120 minutes. The glycemic index and load were calculated per serving. Means and standard deviations were used to compute the average. Analysis of variance (ANOVA) was used to compare the means while Tukey's test was used to separate the means. Significant difference and decision criterion were set at $p<0.05$ using Statistical Package for the Social Sciences (SPSS) version 22.0.

Results: Moisture content ranged from 64.10±0.57% (okra sauce) to 64.62±0.66% (lettuce sauce) did not differ significantly ($p<0.05$). Fat, fiber, and ash content higher in lettuce sauce 3.40± 0.24%, 1.69±0.1%2, and 4.40±0.24% respectively, carbohydrate was higher in African spinach (15.07±0.77%) while dietary fiber (3.26±0.01%), protein (15.15±0.09%) and energy (136.62±2.24 kcal) was higher in okra sauce. Sauces were not significantly different. White bread shows that moisture content was 17.62, fat 1.53%, protein 14.86%, ash 6.90%, carbohydrate 58.88%, energy 308.66kcal, and dietary fiber 0.33.The anthropometric indices show that body mass index (BMI) of the subjects ranged from 23.12kg/m^2 in African spinach sauce subjects to 23.53kg/m^2 (okra sauce subjects). Waist hip ratio (WHR) was highest in lettuce sauce subjects (0.84). All the subjects that participated were all females. HbA1C was higher in okra sauce (5.23%) group subjects. Systolic blood pressure was 119.08mmHg (African Spinach sauce subjects) while diastolic blood pressure was highest in lettuce sauce subjects (85.68mmHg). Pulse rate (85.17) was highest in okra sauce subjects. The incremental area under curve (IAUC) for the white bread was significantly ($p<0.05$) higher in all the subjects compared to the vegetable sauces with a high glycemic index and load of 93.25 and 54.91 respectively.

African spinach sauce had a lower postprandial plasma glucose peak of 88.00mg/dl at 60 minutes compared to okra and lettuce sauces. All the vegetable sauces had a low glycemic index of 17.02 (okra sauce), 14.05 (African spinach) and 36.76 (lettuce), and low glycemic load was 0.75, 0.38 and 3.80 for okra, African spinach, and lettuce sauces, respectively.

Conclusion: All the vegetable sauces studied should be recommended while planning meals for diabetic patients.

Keywords: vegetable sauces, glycemic response, healthy female adults

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Evaluation of the changes in physicochemical and antioxidant properties of honey during storage

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ABSTRACT

Background: Despite having a lot of information about the physicochemical and antioxidant properties of honey from different geographical regions, there is only limited information about the changes in these characteristics during long-term storage of honey. Hence, this study was conducted to evaluate these changes in five different types of honey, including alfalfa, milkvetch, lotus, thyme, and multifloral honey, during one year of storage at room temperature.

Methods: Samples were analyzed for pH, free acidity, Ash, moisture, electrical conductivity, hydroxymethylfurfural, color, total phenolic content, DPPH radical-scavenging activity and ferric reducing antioxidant power.

Results: Changes were observed in all the physicochemical characteristics of honey during the storage period. However, these changes did not exceed the maximum acceptable limits and after one-year of storage, the physicochemical properties of all types of honey were within the standard limits except for HMF content in multifloral honey (43.89 mg/kg). Regarding the antioxidant capacity of honey, our results showed 38.92-73.3 % decrease in DPPH radical scavenging activities and 43.29-67.0 % decrease in FRAP values of different types of honey during the storage period.

Conclusion: From a nutritional point of view, a decrease in the antioxidant capacity of honey is of particular importance. Therefore, these levels of reduction in antioxidant capacity could certainly affect the nutritional and health benefits of honey.

Keywords: Honey; Physicochemical; Antioxidant capacity; Changes; Storage

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/616/1061

Beneficial effects of maltobionic acid on bone density in healthy Japanese adult women: A randomized double-blind placebo-controlled study

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ABSTRACT

Background: Osteoporosis is characterized by reduced bone mineral density (BMD) and increased fracture risk, with a higher incidence in post-menopausal women. This study aimed to evaluate the safety and efficacy of long-term ingestion of maltobionic acid on BMD in healthy Japanese women.

Methods: A randomized, double-blind, placebo-controlled, parallel-group study was conducted from February to December 2018. Thirty-eight healthy Japanese women aged 50–69 years who were at least 1 year past the onset of natural menopause were allocated to two groups (19 in each group) using a computerized random-number generator: one in which participants ingested 7 g of corn syrup containing maltobionic acid and another in which participants ingested 7 g of placebo (maltose syrup) per day for 24 weeks. BMD and bone metabolism parameters were measured dual- energy X-ray absorptiometry (DEXA) method and a peripheral blood test, respectively, whereas safety was evaluated via a physical examination, peripheral blood test, urinalysis, assessment of subjective symptoms, and a medical questionnaire.

Results: Of the 38 subjects, one subject discontinued the study halfway and 14 were excluded before the efficacy analysis because of conflicts with control criteria. Thus, the final study population was 23 subjects (10 in the Test food group and 13 in the Placebo group). There were no adverse events related to consumption of the test food. Consumption of corn syrup solids containing maltobionic acid was maintained during the intervention period, and BMD, bone mineral content, and young adult mean values were found to be improved ($P < 0.05$). No safety concerns were observed during the intervention period.

Conclusion: These results indicate that the consumption of maltobionic acid may contribute to the prevention of osteoporosis.

Trial registration: UMIN-CTR ID: UMIN000031489; Foundation: San-ei Sucrochemical Co., Ltd.

Keywords: Maltobionic acid; bone mineral density; safety; long-term intake; osteoporosis; menopause

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The impact of persistent milk consumption in the pathogenesis of type 2 diabetes mellitus

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ABSTRACT

Background: Milk and sugar are excessively consumed in a Western diet. There is increasing epidemiological evidence that the intake of unfermented pasteurized cow´s milk is associated with an increased risk of type 2 diabetes mellitus (T2D). It is the intention of this review to provide translational biochemical evidence for milk´s diabetogenic mode of action. Milk proteins provide the highest amounts of branched-chain amino acids (BCAAs) and thus contribute to total BCAA intake, which enhances BCAA plasma levels associated with increased risk of T2D. The consumption of pasteurized milk raises plasma levels of miRNA-29b, which is a diabetogenic miRNA promoting insulin resistance (IR). miRNA29b inhibits the activity of branched-chain α- keta acid dehydrogenase, the rate limiting enzyme of BCAA catabolism, which is impaired in patients with IR and T2D. Milk consumption stimulates mTORC1 activity and increases insulin synthesis. β-cell mTORC1 is overactivated in T2D patients resulting in impaired autophagy which enhances endoplasmic reticulum (ER) stress associated with a greater risk of early β-cell apoptosis, the pathogenic hallmark of T2D. Chronic insulinotropic action of milk-derived BCAAs, IR- promoting mTORC1 overactivity, and miRNA-29b signaling combined with excessive glucose- mediated insulin secretion overburden β-cell insulin homeostasis. Epidemiological and translational evidence identifies continued milk intake as a promoter of T2D, the most common metabolic disease of Western civilization.

Keywords: Branched-chain amino acids, branched-chain α-keto acid dehydrogenase, diabetes mellitus type 2, insulin resistance, milk, miRNA-29b, mechanistic target of rapamycin complex 1.

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/654/1033

Effects of medicinal plant ipe on expression of inducible nitric oxide synthase in inerleukin-1β-stimulated Hepatocytes

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ABSTRACT

Background*:* The traditional medicine ipe is thought to have various pharmacological actions including anticancer and anti-inflammatory activities. However, there is little scientific evidence to demonstrate the organ-protective effects of ipe. The prevention of nitric oxide (NO) production in inflamed livers by inducible NO synthase (iNOS) is an indicator of liver protection. We examined proinflammatory cytokine-stimulated hepatocytes as a simple "*in vitro* liver injury model" to determine ipe's liver-protective effects of ipe and clarify its mechanisms. This study aims to examine whether ipe influences iNOS induction and NO production, and if so, the mechanisms involved in its action.

Methods: Primary cultured hepatocytes were treated with interleukin (IL)-1β in the presence or absence of ipe. The induction of iNOS and its signal pathway were analyzed.

Results: Ipe inhibited the production of NO stimulated by IL-1β and showed the greatest effect (more than 90% inhibition) at 2 mg/ml. Ipe decreased iNOS protein and mRNA expression. Ipe decreased NF-κB activation (its translocation to the nucleus and DNA binding), although there was no effect on IκBα degradation. Ipe inhibited Akt activation, followed by decreased the type I IL-1 receptor mRNA and protein levels. Transfection experiments revealed that ipe decreased both activities of iNOS promoter transactivation and mRNA stability. In support of the latter observation, ipe inhibited the expression of the antisense transcript of the iNOS gene.

Conclusion: Ipe blocked IκB kinase and phosphatidylinositol 3-kinase/Akt signal pathways, which caused the reduction of iNOS mRNA synthesis and its stability. This resulted in the inhibition of iNOS induction and NO production. Ipe may have a potent beneficial effect against NO-mediated injury in organs including the liver.

Key words*:* ipe, inducible nitric oxide synthase, liver injury, primary cultured hepatocytes, nuclear factor-κB, the type I interleukin-1 receptor, iNOS antisense transcript

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Effect of Vitamin D3 and Virgin Coconut Oil on Cartilage Degeneration, Inflammation and Functional Abilities in Early Knee Osteoarthritis

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ABSTRACT

Background*:* Knee osteoarthritis (KOA) is a chronic, degenerative knee joint disorder associated with inflammation, pain, stiffness, and reduced functional abilities, thereby impacting the patient's quality of life. The prevalence of KOA is growing rapidly in India and around the globe, even in younger populations. Vitamin D plays a crucial role in musculoskeletal health and deficiency of this vitamin is highly prevalent across the age groups impacted by KOA. Consumption of vitamin D rich foods along with functional foods possessing antioxidant and analgesic properties needs to be explored as a potentially novel, low cost dietary strategy for the prevention and management of chronic musculoskeletal disorders such as KOA.

Objective*:* To assess the effect of vitamin D3 and Virgin Coconut Oil (VCNO) supplementation on vitamin D3 status, cartilage degeneration, inflammatory status, and functional abilities in early KOA.

Methods*:* One hundred vitamin D deficient, age and gender-matched adults afflicted by early KOA (30-65yrs) were selected purposively from K. J. Somaiya Hospital and Research Centre, Mumbai, India after obtaining ethical clearance from the institute. Informed consent was obtained from the participants. They were then counselled on making required dietary modifications, with due emphasis on vitamin D3 rich foods, and were given an at-home KOA exercise program. The participants were divided equally into two experimental groups: E1 (n=50) and E2 (n=50), with equal number of males and females in each group. The groups were either supplemented with Vitamin D3 alone (group E1) or Vitamin D3 + VCNO (group E2). All the participants were assessed for vitamin D status (serum 25 (OH) D levels (CLIA), Vitamin D3 intake (3-day diet recall and FFQ), pain (VAS), stiffness, functional abilities (WOMAC and 6 MWT), and inflammation (ESR and serum CRP). The cartilage marker (s-COMP (ELISA)) was assessed only in a subset of participants (n =40) from each group, both pre and post intervention. Data were analyzed using SPSS 16.0.

Results*:* A significant rise in Vitamin D3 intake and serum vitamin D3 levels ($p<.001$) was observed post-supplementation in both groups. sCOMP (<.001), ESR, and serum CRP (<.001) were significantly reduced in both the groups, indicating a decline in cartilage degeneration and inflammatory status. VAS score (<.001) was significantly reduced in both groups, indicating reduced pain intensity. Total WOMAC score ($p<.001$) was significantly reduced, with a highly significant improvement in the distance covered during the 6 MWT (<.001), indicating improved functional abilities. The mean difference of effect in all the above parameters was higher in the vitamin D3 and VCNO

supplementation group (E2) than the group which received vitamin D3 alone (E1).

Conclusion: Supplementation of vitamin D3 along with VCNO could be an effective strategy for delaying the progression of KOA by reducing cartilage degeneration, inflammation and pain, as well as improving functional abilities. Thus, simultaneous improvement of vitamin D3 status and oxidative stress should be considered in early KOA management. Non- conventional antioxidant and anti-inflammatory functional foods such as VCNO could be further explored.

Key words: Knee osteoarthritis, vitamin D, virgin coconut oil, anti-inflammatory, functional food, functional abilities, cartilage degeneration, inflammation, WOMAC, sCOMP.

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Tilapia Protein Hydrolysate Enhances Transepithelial Calcium Transport in Caco-2 cells

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ABSTRACT

Background: Adequate calcium intake is essential for calcium balance and normal health. Prolonged deficiency of calcium is associated with osteoporosis, dental changes, cataracts, and alterations in the brain. However, calcium is difficult to be directly absorbed from food due to the insoluble calcium salt precipitation that occurs in the intestinal environment. The aim is to investigate TPH produced by Nile tilapia and the stimulation of TPH-calcium-binding activity.

Methods: Tilapia protein hydrolysate (TPH) was prepared by alcalase digestion. Calcium-binding activity was measured using calcium colorimetric assay; absorption was at 612 nm. The interaction between TPH and calcium was examined by spectroscopic analysis, ultraviolet absorption, and fluorescence measurement. TPH-calcium-binding stability in the human digestion system was evaluated by in vitro pepsin-pancreatin hydrolysis simulating human gastric and intestinal digestion. The effects of food components on TPH-calcium-binding activity was also analyzed. The enhancement of transepithelial calcium transport by TPH was determined by in vitro Caco2 epithelial cell-like monolayer.

Results: TPH produced from Nile tilapia (*Oreochromis niloticus*) exhibited calcium-binding activity. Peptides in the hydrolysate that contributed to calcium binding since the spectroscopic changes induced by calcium were characteristic of peptide bonds and tryptophan residues. The calcium binding of TPH was compatible with food matrices. Most food components including saccharides, amino acids, and vitamins showed either positive or no effects on calcium binding. The calcium binding of TPH was also stable in the simulated gastrointestinal digestion system. Pepsin and pancreatin did not considerably change the calcium-binding activity of TPH. Of note, TPH reduced precipitation of calcium by oxalate and phytate, the two most anti-nutritional factors present in green leafy vegetables. Finally, we showed that TPH significantly promoted transepithelial calcium transport in the Caco-2 cell permeability model.

Conclusions: Tilapia protein hydrolysate produced by alcalase digestion possessed calcium- binding activity and

prevents precipitation of calcium by a mineral-chelating agent as well as enhanced transepithelial calcium transport in the Caco-2 cell. The result implicated the potential of TPH as a functional food ingredient for promoting calcium absorption.

Keywords: *Tilapia protein hydrolysate; Calcium binding peptides; Calcium absorption*

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Leptin, hs-CRP and HOMA-IR in patients with type 2 diabetes: The role of different levels of vitamin D deficiency

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ABSTRACT

Background: To evaluate the effects of different levels of vitamin D deficiency on blood glucose, leptin, high sensitivity C-reactive protein (hs-CRP), and insulin resistance and their associations.

Methods: We quantified serum vitamin D level, hs-CRP, leptin, and fasting blood sugar (FBS) levels in 25 type-2 diabetic patients with deficient serum levels of 25-hydroxy vitamin D (≤15 ng/ml) and 25 type-2 diabetic patients with insufficient serum levels of 25-hydroxy vitamin D (16 to 30 ng/ml). The two groups were matched according to age, sex, and body mass index (BMI). Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated by a formula based upon values of FBS and insulin concentrations.

Results: The mean value of vitamin D levels was 7.67±3.10 in the vitamin D deficient group and 23.20±9.97 in the vitamin D insufficient group. Patients with vitamin D deficiency had significantly higher FBS, postprandial glucose (PPG) and hemoglobin A1C (HbA1C) as compared to vitamin D insufficient group ($p<0.01$). We studied correlations of hs-CRP, HOMA- IR, and leptin in both vitamin D insufficient and deficient groups. There were significant positive correlations between leptin with hs-CRP ($r = 0.58$, $p<0.01$) and with HOMA-IR ($r = 0.49$, $p<0.05$) in vitamin D deficient group. These correlations remained significant after multiple adjustment for age, sex, BMI, systolic and diastolic blood pressure.

Conclusion*:* In conclusion, vitamin D deficient diabetic patients had elevated FBS, PPG and HbA1C compared with insufficient ones. The results also could possibly point the effect of vitamin D deficiency level on leptin associations with hs-CRP and insulin resistance.

Keywords: Vitamin D deficiency, type 2 diabetes, leptin, C reactive protein, homeostasis model assessment of insulin resistance

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The impact of dietary supplement NT-020 with *Rhodiola rosea* on energy, fatigue, and perceived exertion

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ABSTRACT

Purpose: Evaluate the effectiveness of a commercially available nutraceutical product on levels of exercise-related energy, fatigue, and exertion before and after 4 weeks of supplementation. Primary ingredients within the product include a proprietary blend of blueberry extract, green tea extract, L-carnosine, Vitamin D3 (NT-020; 920mg), and *Rhodiola rosea*, a plant that purports to boost energy and hold antioxidant and anti-inflammatory properties.

Methods*:* Twenty-seven participants (13 females, 14 males, mean BMI = 23, mean age ± SD = 24 ± 6 years) completed a baseline assessment of aerobic fitness (mean VO2 peak = 40 mL x kg^{-1} x min^{-1}) before being randomized into a placebo or supplement group for four weeks. All participants were involved in regular physical activity three or more days per week. Assessment of energy, fatigue, and perceived exertion responses during and immediately following moderately intense cycle ergometry exercise was conducted before and after the 4-week ingestion period during which participants were instructed to maintain existing exercise activities.

Results: Data were analyzed by way of repeated measures ANOVA and dependent t-tests to determine the presence of significant differences across time and between the supplement and placebo conditions. Participants receiving the supplement reported: greater levels of energy and lower levels of fatigue during the initial moments after completing the exercise trial ($p < 0.05$), greater levels of energy at the midpoint of the exercise trial ($p < 0.05$) but not at the end of the exercise session ($p > 0.05$), and lower perceived exertion at four of the six measurement points during exercise ($p < 0.05$). No differences were observed from pre to post intervention within the placebo condition ($p > 0.05$).

Conclusions: Findings indicate that a commercially available supplement marketed to boost energy and reduce fatigue can deliver the purported benefits at least in part. Related findings that supplementation for a 4-week period can allow for equal work at a lower rating of perceived exertion provides further, though limited support that this product may have efficacy.

Keywords: fatigue; perceived exertion; energy; *Rhodiola rosea*; NT-020

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/656/1132

Effects of six weeks consumption of coconut milk oil on vascular functions and fasting blood glucose and lipid profile in middle-aged male rats

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ABSTRACT

Background: Coconut milk consumption in middle- aged male rats can cause increased blood vessel endothelial nitric oxide synthase (eNOS) and cystathionine- γ- lyase (CSE) protein expression, and decreased fasting blood glucose.

Objective: The present study aimed to investigate whether coconut milk oil (CO), the major constituents of the coconut milk, was responsible for those effects.

Methods: CO was isolated from dried fresh coconut milk and gavaged (1 and 3 ml/kg) to middle- aged male rats for 6 weeks. Animal body weight and food intake, internal organ weight, blood biochemistry, lipid profile, basal blood pressure and heart rate and vascular functions were investigated.

Results: In comparison to a distilled water control group, no differences were observed in any of the parameters studied in the group fed 1 ml/kg of CO except for an increase in retroperitoneal fat accumulation. Feeding 3 ml/kg of CO caused decreased fasting blood glucose, plasma alkaline phosphatase and blood urea nitrogen and liver cell lipid accumulation, but increased retroperitoneal fat tissue. It also caused decreased maximal contractile response of endothelium- intact thoracic aortic rings to phenylephrine although the effect disappeared in the presence of N-nitro-L-arginine (L-NA) or removal of the endothelium. DL-propargylglycine together with L-NA caused a higher contraction to phenylephrine in the CO-treated groups than in the control group. It also caused an increase in vasodilatation to acetylcholine, but not to glyceryl trinitrate, of the phenylephrine pre-contracted aortic rings. CO treatment caused increased vascular wall eNOS and CSE protein expression.

Conclusion: CO at a dose of 3 ml/kg causes some decrease in cardiovascular risk factors in middle- aged male rats, although the amount of CO consumption should be limited as it caused an increase in retroperitoneal fat.

Keywords: Coconut oil; blood vessel; liver lipid; NO; H2S

Animal Ethic No: Ref. 06/57

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Improvement of bioavailability of bioactive compounds of medicinal herbs by drying and fermentation with *Lactobacillus plantarum*

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ABSTRACT:

Background: Medicinal and aromatic plants, which are rich sources of bioactive conpounds, have been used in traditional medicine for ancient times. Epidemiological studies have shown that bioactive compounds of medicinal plants possess antioxidant, anti-inflammatory, antiatherosclerotic, antitumor, antimutagenic, anticarcinogenic, antibacterial and antiviral activities. Intake of natural antioxidants derived from medicinal plants into body has been associated with reduced risks of cancer, cardiovascular disease, diabetes, and other diseases. It has also been demonstrated that the fermentation of plants is a versatile way for improvement of their functionality and bioavailability. The aim of this study was to determine the effect of probiotic fermentation and vacuum drying on the bioavailability of peppermint (*Mentha piperita*) and basil (*Ocimum basilicum*) exposed to *in vitro* digestion.

Methods: Fresh basil and peppermint were divided to 3 lots, one lot of each plant was vacuum dried at 40 °C for 8 hours to obtain the dried samples while one lot was fermented with probiotic *Lactobacillus plantarum* for 21 days at room temperature after incorporation with sterile brine (1:20 w:v) containing 5 % of NaCl. Thereby, 3 samples were obtained: Fresh peppermint/basil, vacuum dried peppermint/basil and fermented peppermint/basil. During the *in vitro* digestion comprised from gastric and pancreatic digestion, bioavailability of the samples were investigated by measurement of their total phenolic contents (TPCs), total flavonoid contents (TFCs) and antiradical activity. TPC was determined using Folin-Ciocalteu method while TFC was measured aluminum chloride colorimetric assay. The antiradical activity of the samples was analyzed by determination of the DPPH radical scavenging activity.

Results: The initial (undigested) TPC levels of fresh, vacuum dried and fermented mint and basils ranged from 166.24 to 295.08 mg gallic acid equivalent (GAE)/g. Drying and fermentation increased TPCs of the plants. Similarly, TFCs and antiradical activities were also increased by these treatments. When considering bioavailability of the bioactive compounds, fermentation process enabled higher recovery levels after *in vitro* digestion while basil exhibited higher percent recovery than mint.

Conclusion: This study demonstrated that vacuum drying and fermentation of basil and mint with probiotic *Lactobacillus plantarum* provided much stronger antioxidant activity and bioavailability than fresh ones and increased their *in vitro* bioavailability.

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Combinations of vitamins A, D2 and D3 have synergistic effects in gastric and colon cancer cells

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ABSTRACT

Background: Vitamin D was first hypothesized to play a role in cancer chemoprevention in 1980 when it was observed that there was a higher rate of colon cancer in the Northern USA as compared with populations living in the South. While cholecalciferol (vitamin D3) has been tested in many cancer-cell lines, published results for ergocalciferol (vitamin D2) are lacking for most epithelial cell cancers, and combination studies of both D2 and D3 and vitamin A (retinoic acid) are lacking in general. The goal of the study was to investigate the effects of vitamins D2, D3, and A, alone and in combination on the growth of all gastric and colon cancer cell lines in vitro.

Methods: Colon (SW480 and HCT-116) and gastric (AGS and NCI-N87) cell lines were treated with varying concentrations of D2, D3 and all-trans retinoic acid (ATRA) and combinations thereof. Cell viability and cytotoxicity were measured using the CellTiter-Glo® 2.0 assay, while caspase activities and cytotoxicity were determined using the Caspase-Glo® 3/7, Caspase 8, ApoTox-Glo™ Triplex assays. Autophagy was determined using the CYTO-ID® Autophagy Detection Kit 2.0. Gene expression studies were performed using qPCR.

Results: Both vitamin D2 and D3 inhibited the growth of all cell lines tested, with IC50 ranging from 19-56 µM. However, when combined (1:1), the IC50 for the combination of D2 and D3 was significantly reduced to a range of 5-6.0 µM indicating synergism. ATRA also inhibited the growth of all cell lines tested with an IC50 range of 2.6 to 5.6 µM. When ATRA was combined with D2 and D3, the IC50s were significantly reduced to 0.65 to 1.4 µM, further indicating synergistic effects. In the gastric and colon cancer cell lines, the combination induced apoptosis via caspase 3/7 and 8, increased the Bax/Bcl-2 ratio, while in the SW480 colon cancer line, the combination also induced autophagy.

Conclusion: Our data demonstrated that vitamins D2, D3 and ATRA inhibit the proliferation of colon and gastric cancer cells. The combinations of D2+D3 or ATRA+D2+D3 had synergistic effects or additive effects on all cell lines tested, increased Bax expression and the Bax/Bcl-2 ratio, and increased caspase 3/7 and 8 activities to favor apoptosis. In SW480 colon cancer cells the combination also induced autophagy. This data suggest that combinations of vitamins A and D have synergistic effects in colon and gastric cancers, and considering the potential clinical implications, further research is justified.

Key words: apoptosis, autophagy cholcalciferol, ergocalciferol, gastric cancer, colon cancer, caspase, synergism

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Forest West African indigenous diet and modernization diseases

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ABSTRACT

This review paper notes that the nutritional essence of an indigenous people's diet can, broadly, be outlined in terms of their food-inherent bioactive chemical functions. Two food crops; Yam (*Dioscorea* spp.) and the Oil-palm (*Elaeis guineensis*), define Forest West Africa, agriculturally, as *Yam* or *Palm* belt. They can also be said to, broadly, define the diet of the region, which staple base they constitute, as the *Yampalm Diet* type. Some unique, bioactive, chemical functions of yam identified include; dioscorin, lipoic acid, potassium, biotin and, thiocyanate, while those of oil-palm include; tocotrienols, carotenoids, retinoids and lauric acid. These alkalizing food functions are, in theory, complementary to the acidic tropical physiology of Forest West Africans. Fed on other than the *Yampalm* diet, Forest West Africans have been demonstrated to be highly susceptible to metabolic syndrome, and some other diseases, due to adopted alien diets. Examples are lactose intolerance from milk and inflammation reaction to wheat gluten. Some food functions of *Yampalm* diet; dioscorin in yam and tocotrienol from oil-palm, as examples, are efficacious in metabolic syndrome management. They are potential '*Gene-adapted food-function supplements*' for emigrants from this area who adopt alien diets. Experiments have shown that restoration of the Forest West African diet ameliorates metabolic syndrome among the people, including their Diaspora in America. Restoration of, genetically or epigenetically, adapted indigenous diet among peoples recommends itself as part of management strategy for modernization diseases.

Key terms: Yampalm diet, food function, dioscorin, tocotrienol, alien diet, lactose intolerance, metabolic syndrome, epigenetic adaptation

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Effect of concentrated Kurozu, a traditional Japanese vinegar, on expression of hepatic miR-34a, -149-3p, and -181a-5p in high-fat diet-fed mice

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ABSTRACT

Background: Long-term high-fat diet (HFD) feeding, which can induce obesity, can also induce nonalcoholic steatohepatitis (NASH) and liver tumorigenesis. A previous study reported that concentrated Kurozu (CK) supplementation reduced the incidence of HFD-induced hepatic steatosis in mice. It was showed that CK supplementation improved dyslipidemia in animal and clinical study. Small noncoding RNAs, micro RNAs (miRs), play crucial roles in the biology of cell functions, lipid metabolism and neoplasms. However, the effect of CK treatment on the relationship between HFD and expression of miRs is unclear.

Objective: To evaluate changes in the expression of hepatic miRs and lipid metabolism- associated genes on administering a HFD for 60 weeks in C57BL6J mice. The onset of hepatic steatosis induced by HFD treatment was also observed.

Methods: The mice received a HFD, HFD with CK, or standard diet (SD) for 60 consecutive weeks. The effect of CK treatment on the expression levels of lipid metabolism-associated genes in the liver was evaluated.

Results: HFD feeding significantly increased expression of *Tnf*, and significantly decreased *Adipoq* and *Mlxipl* in the liver. The ingestion of CK elevated the expression levels of *Pgc-1α* and *Igfbp1* in the liver compared with the SD group. HFD feeding significantly increased the expression of *miR-488-5p*, and significantly decreased *miR-29b* and -*122a-5p* in the liver. The ingestion of CK elevated the expression levels of *miR-34a*, *-149-3p*, and *-181a-5p* in the liver compared with the SD group. Expression levels of *miR-488-3p* in the serum HFD group were significantly higher than in the SD group. The ingestion of CK elevated the expression levels of *miR-181a-5p* in the serum compared with the SD group.

Conclusion: These results suggest that CK supplementation reduced the onset of hepatic hyperplasia, and increased hepatic *miR-34a*, *-149-3p*, and *-181a-5p*. These miRs may function as suppressors of tumors caused by HFD feeding.

Key Words: High-fat diet, carcinogenesis, Kurozu, microRNA, miR-34a, miR-122a-5p, miR-149, miR-181a, miR-488

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/668/1219

Bitter melon fruit extract affects hepatic expression of the genes involved in inflammation and fatty acid metabolism in *ob*/*ob* mice

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ABSTRACT

Background: The fruit of bitter melon (*Momordica charantia* L.) has traditionally been used as a crude drug to treat obesity and diabetes mellitus. Previously, we reported that an ethyl acetate (EtOAc)-soluble fraction of bitter melon fruit extract showed anti-inflammatory effects on interleukin-1β-treated rat hepatocytes. The liver plays a pivotal role to maintain homeostasis of glucose and lipid. It is speculated that the administration of an EtOAc-soluble fraction of a bitter melon fruit extract (BMFA) may change the expression profile of hepatic genes involved in inflammation, glucose metabolism, and lipid metabolism.

Objective: We aimed to evaluate the effects of BMFA on the gene expression in the liver of *ob*/*ob* mice, which are deficient in leptin and are used as a diabetes mellitus model. The changes may be related to hepatic steatosis and obesity.

Methods: Male 8-week-old *ob*/*ob* mice (average body weight, 40.9 g) were fed a standard diet with and without BMFA (*ob*/*ob*+BMFA and *ob*/*ob*–BMFA groups, respectively; 4 mice/group) for seven days. The livers were excised to prepare total RNA for microarray expression analyses. Signal ratios (*i.e.*, *ob*/*ob*+BMFA *versus ob*/*ob*–BMFA group) were calculated to compare gene expression.

Results: The mRNA levels of 2,632 genes were significantly changed in the livers of *ob*/*ob*+BMFA mice when compared with those of *ob*/*ob*–BMFA mice. As expected, proinflammatory cytokine and chemokine genes were significantly downregulated by BMFA. The acyl-Coenzyme A thioesterase 3 gene in fatty acid oxidation was upregulated in *ob*/*ob*+BMFA liver, whereas free fatty acid receptor 2 and solute carrier family 27 member 3 genes were downregulated. Most genes involved in glycolysis and gluconeogenesis were not affected by BMFA. In contrast, the level of peroxisome proliferator-activated receptor γ coactivator 1α mRNA significantly increased in *ob*/*ob*+BMFA mice, suggesting that BMFA administration may reduce insulin resistance in *ob*/*ob* mice.

Conclusion: Our study suggested that BMFA may possess anti-inflammatory effects and enhance fatty acid metabolism in *ob*/*ob* mouse liver. These data imply the possibility that EtOAc-soluble constituents in bitter melon fruit may improve lipid accumulation in the liver during obesity and diabetes mellitus, as well as non-alcoholic fatty liver disease.

Keywords: *Momordica charantia*, gene expression, inflammation, diabetes mellitus, non- alcoholic fatty liver disease.

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Modulation of Gut-Brain Axis Improves Microbiome, Metabolism, and Mood

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ABSTRACT

Objective: There is a close bidirectional relationship between overweight/obesity and depression, which may be largely modified through the microbiome and the gut-brain axis. Previous research has shown targeted weight loss effects and anti-depressive benefits of diets high in fiber and phy- tonutrients and low in sugar and processed foods. Thus, our objective was to determine changes in parameters common to both obesity and depression (e.g., microbiome balance, metabolic bi- omarkers, and psychological mood state) following a coordinated supplementation regimen com- bining probiotics, prebiotics, and phytonutrients ("phytobiotics").

Methods: Thirty-three (33) healthy subjects participated in a 6-week supplementation trial (Amare "Project b3") containing a targeted blend of probiotics, prebiotics, and phytobiotics. Microbiome balance was assessed in fecal samples using a novel PCR-based analysis (BiomeTracker) that has previously compared favorably to 16S sequencing. Biomarkers, including blood lipids, glucose, cortisol, and butyrate kinase, were assessed as indicators of effects on cardiovascular, inflamma- tory, and energy metabolism. Psychological mood state was assessed using the validated Profile of Mood States survey (POMS) to generate scores for Global Mood State and six sub-scales (De- pression, Tension, Fatigue, Anger, Confusion, and Vigor).

Results: Following supplementation, there was a significant increase in populations of "good" bacteria (+8% Bifidobacterium, +33% Lactobacillus, +62% S. Thermophilus, +90% Akkerman- sia) as well as bacterial ratios associated with a healthier "obesity-resistant" metabolism (+6% composite score, -11% Firmicutes, +6% Bacteroidetes, -14% F/B ratio). Metabolites associated with stress and glycemic control improved post-supplementation (-11% cortisol; +89% butyrate kinase, -6% glucose), as did body fat (-2%) and blood lipids (-8% total cholesterol, -5% LDL, +3% HDL, -23% triglycerides, -7% TC/HDL). Psychological indices were significantly improved post- supplementation for both positive (+17% Global Mood; +23% Vigor) and negative mood states (- 38% Depression; -41% Tension; -42% Fatigue; -31% Confusion; -39% Anger).

Conclusions: These results demonstrate the close relationship between microbiome balance, sys- temic metabolism, and psychological parameters – and the utility of targeted supplementation to optimize gut-brain-axis balance for both improved metabolism and enhanced mental wellness.

Keywords: Obesity; Depression; Anxiety; Stress; Probiotics; Prebiotics; Diet; Supplement

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Georgian legume crop extract as an effective remedy during oral cavity soft tissue inflammation

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ABSTRACT

Background: Recovery of dental arch defects, related to insertion of a foreign bodies into the oral cavity, and the impact of mechanical pressure, allergic-toxic effects, and the related inflammatory and degenerative processes is one of the most urgent problems in dentistry. The purpose of the study was to evaluate the efficacy of Georgian bean extract tincture as mouthwash for patients using a lever system to correct deformities of the jaw and teeth.

Methods: Twenty-eight patients (aged 12-25 years) with deformities of the jaw and teeth were studied. Patients were examined 6-8 months after the bracket system was installed, and before and after the use of tincture mouthwash for 10 days. Patients were randomly divided into 2 groups: the control group for the mouthwash used standard tincture ("Octenidol" Schulke and Mayr - Germany); the patients of the experimental group used tincture made from the Georgian legume crop extracts (GLCE). Before and after the use of both types of tincture, the data were taken for calculation of Schiller Pisarev's test (SPT), Papillary-Marginal Alveolar (PMA) index, and the oral hygiene index (OHI). Saliva was collected in a glass tube without stimulation, on an empty stomach. The content of cytokines IL-1β, IL-10 in saliva was determined by the ELISA kit.

Results: The study demonstrated significant positive clinical efficacy of the mouthwash tincture prepared from the GLCE which increases the resistance of dental tissue. This was revealed by significantly lower values of OHI, PMA index, SPT and increased content of IL-10 in saliva.

This data indicates that tincture prepared from the Georgian legume crop extracts, which is designed to increase the stability of oral tissue, does promote an increase in resistance to the aggressive mechanical pressing.

Conclusion: Tincture from the GLCE is characterized by a much stronger anti-inflammatory effect than standard tincture "Octenidol" (Schulke and Mayr -Germany) used against inflammation of the oral cavity soft tissue. This allows us to recommend the tincture from the GLCE for the treatment and prevention of inflammatory processes in the oral cavity soft tissue.

Keywords: Georgian legumes crop extracts (GLCE), oral cavity soft tissue inflammation, Hygiene Index, PMA index, Schiller Pisarev's test.

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Diversification of health-promoting phytochemicals in radish (*Raphanus raphanistrum*) and kale (*Brassica oleracea*) micro-greens using high light bio-fortification

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ABSTRACT

Background: Fruits and vegetables contain significant amounts of biologically active phytochemicals (such as polyphenols, glucosinolates, phytoestrogens, and carotenoids, amongst others), which have associated with human health and nutrition. Numerous bio-fortification strategies are employed to enhance the nutritional profile of plant-based foods to address and minimize the severe outcomes of malnutrition.

Methods: Using an established high light-induced bio-fortification strategy, we aimed to augment the accumulation of health-promoting phytochemicals in a selection of Brassica micro-greens (kale and radish). High throughput tandem mass spectrometry was used to identify the differential accumulation of phytochemicals and subsequently determined their antioxidant capacity. Using a classical DNA protection assay, we demonstrated that human genomic DNA could be protected from oxidative stress.

Results: We report here on the potential link between the increased phytochemicals, total antioxidant, capacity and potential consequent role in human DNA protection.

Conclusion: Bio-fortification implemented as a future strategy could enhance the phytochemical profile and consequent antioxidant potential for the development of functional foods and food supplements.

Keywords: antioxidant, bio-fortification, Brassica, DNA protection, high light, micro- greens, phytochemicals

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Physicochemical and antibacterial assessment of Iranian Propolis

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ABSTRACT

Background: Propolis is one of the useful bee colony products that have been used in traditional medicine for centuries. In this study, the physicochemical characters and their antibacterial effect of Iranian Propolis collected from Qazvin province was assessed.

Methods: In this study, Thin Layer Chromatography and Vacuum Liquid Chromatography to detect different compounds of the extract have been used. In the initial evaluation of Propolis extract, it was found that the extract includes variable compounds with different polarity. Therefore, the initial classification of extract with different polarity solvents was essential. Finally, 0.1 gr hydro alcoholic Propolis was injected to the HPLC by ultrasound. The antibacterial effect of Iranian ethanol extract Propolis was measured using a microdilution method against *Pseudomonas aeruginosa: P. aeruginosa* and *Staphylococcus aureus: S.aureus* standard strains and the minimum bactericidal and inhibitory concentration were defined.

Results: Primary analysis of the ethanol extract by analytical Thin Layer Chromatography, demonstrated the presence of flavonoid and phenol in it. minimum inhibitory concentration and minimum bactericidal concentration for *Staphylococcus aureus: S.aureus* standard strain was 2.5mg/ml. The same procedure was done for *Pseudomonas aeruginosa: P. aeruginosa* standard strain and the minimum inhibitory concentration and minimum bactericidal concentration were 50mg/ml of Propolis extracts.

Conclusion: According to the results, the alcoholic extract of propolis from Qazvin province of Iran provides significant antimicrobial activity. Its powerful activity may be due to high total phenolic and flavonoid contents.

Keywords: Iranian propolis, Antibacterial activity, Phenolic compounds, Flavonoid compound

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Antioxidant activity of a new multiflorane-type triterpene from *Cucurbita argyrosperma* seeds and their protective role in hydrogen peroxide induced oxidative stress

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ABSTRACT

Background: *Cucurbita argyrosperma* seeds have acquired a reputation as an herbal remedy to treat various diseases because this plant is a predominant source of natural compounds with powerful anti-inflammatory and antioxidant properties, and supplementation with seeds improves oxidative stress. Previous studies indicated that an imbalance between H2O2 production and elimination capacity is responsible for β-cell vulnerability thereby making β-cells a susceptible target for pathogens. The aim of this investigation was to evaluate the protective effects of one new multiflorane-type triterpene 3β-trans-caffeoyloxymultiflor-8-ene- 7α,12β, 18 β-triol (**1**) from MeOH extract from*C. argyrosperma,* on rat pancreatic β cells (INS-1 cells) exposed to hydrogen peroxide (H2O2) induced oxidative stress conditions.

Methods: The chemical structure of the novel triterpene, which was identified as 3β-trans- caffeoyloxymultiflor-8-ene- 7α,12β, 18 β-triol (**1**), was established based on the interpretation of spectroscopic analyses. The antioxidant activities of **1** were led by the detected radical scavenging potential of 2,2-dyphenyl-1-picrylhydrazyl (DPPH) and 3.1 2,2'-Azino-bis(3- Ethylbenzothiazoline-6-Sulfonic Acid) ABTS. The assays were conducted on INS-1 cell lines exposed to increasing concentrations of **1** at 5, 10 and 20 µg/mL and H2O2 at 250 µM. Then the experiments, cell viability, cell integrity (LDH; lactate dehydrogenase release), mitochondrial function (ATP analysis), ROS formation, lipid peroxidation (MDA), and caspase-3, 9 activities were measured in the cells. We also determined the effect of **1** on antioxidant enzyme levels and cytotoxicity in pancreatic β cells under oxidant conditions.

Results: The results showed that triterpene displayed high free-radical-scavenging activity, which is similar to that of standard antioxidants used. Concentrations of 5, 10, and 20 μg/mL protected INS-1 cells against H2O2 induced cytotoxicity with a decrease in cell death and a marked increase in cell viability as well as sustained cellular functionality (ATP). Antioxidant enzymes such as glutathione peroxidase (GPx), glutathione reduced (GSH), catalase (CAT), superoxide dismutase (SOD), and the non-antioxidant enzyme (GSH) increased in INS-1 cells with **1** pre-treatment. MDA in pancreatic cells was ameliorated by **1** pre-treatment reducing intracellular reactive oxygen species level. Findings also demonstrated that H2O2 induced apoptosis in INS-1 cells and produced modulation of the caspase-3, 9 expressions in INS-1 cells exposed to **1**. Exposure to **1** significantly inhibited ROS and apoptosis, reducing β cell dysfunction under oxidant conditions.

Conclusions: Triterpene consequently could be a promising natural antioxidant for use in maintaining the integrity of pancreatic β-cells exposed to oxidative stress conditions and being able to participate in the control type 2 diabetes.

Keywords: *Cucurbita argyrosperma;* antioxidants; multiflorane; free radical scavenging: oxidative stress

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Metabolomic analysis of SMP30/GNL knockout mice treated with fermented vegetable and fruit extract (OM-X®)

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ABSTRACT

Background: A dietary supplement developed in Japan, OM-X®, is the result of extended fermentation of dozens of edible vegetables, fruits, seaweeds, mushrooms, and includes 12 strains of Lactic acid bacteria (LAB) and *Bifidobacterium*. The supplements powerful antioxidant, anti- inflammatory properties, and regulatory effect on metabolizing liver enzymes have been reported. Senescence marker protein-30 (SMP30)/Gluconolactonase (GNL) Knockout (KO) mice, which lack the ability to biosynthesize Vitamin C (VC) in the body, were used in this study. The mice exhibited decreased antioxidant capacity in the blood, decreased liver function, and had poor hair growth due to the VC deficiency. The aim of the study was to examine the effects of oral administration of OM-X® on VC deficiency from the viewpoint of comprehensive analysis of liver metabolism.

Methods: SMP30/GNL KO and C57BL/6 (WT) mice were used in this study. The KO mice were divided into the following three groups: VC non-administration (VC minus), VC (0.15 W/V %) administration (VC plus), and no VC plus 0.6% OM-X® administration (OM-X®) groups (n = 6 per group). Mice were kept under experimental conditions until they were euthanized at week 8 (age: 16 weeks old). Body weight and plasma biochemistry levels were measured. Metabolomic analyses of harvested livers were performed.

Results: In the VC minus group, a significant decrease in body weight and significant changes in plasma biochemistry parameters compared with the WT control or VC plus groups was observed. In the OM-X® group, significant suppression or a suppressive trend was observed compared with the VC minus group. Liver metabolomic analysis showed that total adenylate levels decreased in the VC minus group, whereas OM-X® administration significantly elevated total adenylate levels. In addition, the ratios of Glutathione (GSH)/ Glutathione disulfide (GSSG) and S-adenosylmethionine (SAM)/ S-adenosyl-L-homocysteine (SAH) and total glutathione levels were all significantly higher in the OM-X® group than in the VC minus group. The glycerol 3- phosphate/ Dihydroxyacetone phosphate (DHAP) and putrescine/spermidine ratios were elevated in the VC minus group, whereas it was significantly lower in the OM-X® group.

Conclusion: The results showed that in SMP30/GNL KO mice, some organ damage may have occurred during VC deficiency, as indicated by weight loss, hepatic injury, and changes in triglyceride-related markers. OM-X® had an effect on energy charge maintenance by elevating total adenylate levels, inducing antioxidant capacity via enhancing

glutathione levels, and promoting protein synthesis, including polyamine synthesis. Altogether, the results revealed that OM-X® prevents the adverse biological changes caused by VC deficiency in SMP30/GNL KO mice.

Keywords: OM-X®, SMP30/GNL KO mice, Vitamin C, metabolomic analysis.

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Evaluation on antioxidative capacity, nephroprotective effect, and DNA damage protection of mixed low potassium vegetables and fruits juice powder in HEK-293 cells

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ABSTRACT

Background: An imbalance between free radical production and antioxidant defenses is one of the multifactorial natures contributing to many disorders. One of them is chronic kidney disease (CKD). The development of novel diets to slow progression or reduces complication of CKD are highly needed. Therefore, the objective of this study was to evaluate the *in vitro* antioxidative capacity and nephroprotective effect of a product, mixed low potassium vegetables and fruits juice powder (MJP) in HEK-293 cells.

Methods: The produced MJP was determined for phenolics and flavonoids content. The antioxidative capacity was examined by DPPH, FRAP and ABTS assay. The cell viability to MJP and hydrogen peroxide (H2O2)-treated were determined by MTT assay. The intracellular antioxidative capacity was determined by co-treatment of MJP and H2O2-induced HEK-293 cell damage including reactive oxygen species (ROS) production, intracellular enzymes activities, and DNA damage protection.

Results: The MJP at the concentration of 5 and 10 mg/ml showed positive effects on H2O2- induced HEK-293 cells protection and significantly increased cell viability. The ROS production measured by 2',7'-dichlorodihydrofluorescein diacetate (DCF) were increased in the H2O2 treatment approximately 2 times but significantly decreased in the MJP treatment. The result of intracellular enzymatic antioxidant markers, including superoxide dismutase (SOD) and catalase (CAT) activities were increased while the Malonaldehyde (MDA) level was attenuated in the co-treatment of MJP and H2O2-induced HEK293 cells compared with only H2O2-inducing. In the examination of the morphological change due to oxidative stress exhibited less nuclei fragment in the cell of MJP treatment. In addition, the isolated DNA was protected by MJP application.

Conclusion: The produced MJP contains bioactive phenolic and flavonoid compounds. MJP possesses potential antioxidative capacity through the reducing H2O2-induced HEK-293 cells damage and increasing the intracellular antioxidant enzymes. In addition, the nephroprotective effects of MJP related to the antioxidant enzymes was involved in the free radical scavenging. Therefore, MJP could be a functional drink for individual limiting potassium and liquid uptake.

Keywords: Antioxidative capacity, DNA damage protection, low potassium vegetables and fruits, nephroprotective, chronic kidney disease

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/698/1244

Hydrolase-treated royal jelly attenuates LPS-induced inflammation and IgE-antigen-mediated allergic reaction

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ABSTRACT

Background: Royal jelly (RJ) is one of the most effectual and beneficial remedies for human beings and currently utilized in many sectors, ranging from the pharmaceutical and food industries to cosmetic and manufacturing sectors due to RJ possessing many bio-therapeutical activities including anti-tumor, antimicrobial and antioxidant activities, vasodilative and hypotensive activities, as well as growth-stimulating, infection-preventing, anti-hypercholesterolemic and anti- inflammatory activities. However, some reports showing direct consumption of RJ can lead to severe allergic reaction and has been linked with acute asthma, dermatitis, and life-threatening anaphylaxis. Thus, this research purposes to explore the potential anti-inflammatory and anti- allergic activities of hydrolyzed RJ as a function of enzyme and the extent of hydrolysis.

Methods: RJ was enzymatically hydrolyzed with three commercial enzymes (Alcalase®, Flavourzyme® and Protamex®). Anti-inflammatory activity of the hydrolysates was measured by their inhibitory effect on nitric oxide (NO) production of lipopolysaccharide (LPS)-stimulated RAW264.7 macrophage cells. Anti-allergy was determined from the ability of the hydrolysates to inhibit *β*-hexsosaminidase (*β*-HEX) release from RBL-2H3 mast cells. Cytotoxicity was also investigated in both RAW264.7 macrophage cells and RBL-2H3 mast cells.**Results:** The electrophoretic profiles indicated that Alcalase® and Flavourzyme® hydrolysates did not show the presence of proteins causing allergic reaction after 60 mins of hydrolysis while these allergens disappeared from Protamex® hydrolysate at the hydrolysis time of 240 min. It was observed that hydrolyzed RJ showed no toxicity on RAW264.7 and RBL-2H3 cells. With the progression of hydrolysis, IC50 values of NO production inhibition significantly decreased while degree of hydrolysis (DH) was increased in all hydrolyzed samples ($p < 0.05$). Results of *β*-HEX release inhibition were found in the same fashion. Flavourzyme® hydrolysate at the 240 min time point effectively mitigated the oxidative stress and protected DNA in a dose dependent manner.

Conclusions: RJ hydrolysates from Flavourzyme® resulted in peptides with anti-inflammatory activity as determined by the inhibition of NO production in LPS-stimulated RAW264.7 macrophage cells and anti-allergic property as measured by the suppression of degranulation of sensitized RBL-2H3 cells. Anti-inflammatory effect may be due to their anti-oxidative capability. Inhibition of *β*-HEX release may be due to their membrane-stabilizing effects or/and blockade of IgE antibody binding to its receptors.

Keywords: *anti-inflammation, enzymatic hydrolysate, royal jelly, anti-allergy*

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A randomized observational analysis examining the correlation between patients' food sensitivities, micronutrient deficiencies, oxidative stress response and immune redox status

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ABSTRACT

Background: Malnutrition due to insufficient intake of micronutrients, or due to impaired delivery of micronutrients to patients' cells, is suppressing immune functions that are fundamental to host protection. Concurrently, an excessive triggering of patients' immune reactions as the result of adverse responses to certain food antigens, can also lead to various chronic health conditions.

Objective: To examine nutritional and immunological status in patients' groups varying in age, dietary regimens and gastrointestinal condition; and explore a possible correlation between an impaired patients' immune status and micronutrient deficiencies, food sensitivity and oxidative stress responses.

Methods: This is a population-based study consisting of a American residents, age 13 and older, who completed the investigator's provided questionnaires with application of cell-based individualized functional assays. Data for this paper were collected from 845 individuals between May and September 2019, as part of CSS CNA beta study. Micronutrient deficiencies, immune Redox status, antioxidative responses and food sensitivity profiles were assessed for each patient participating in this study.

Results: The group of patients with low Redox status demonstrated significantly higher percent of immune reactivity (17%) to food antigens as compared to15% reactivity detected in the groups with the average and strong Redox response. An average number of identified micronutrient deficiencies, as well as beneficial anti-oxidative protective compounds, was also significantly higher in the group with the weak immune function as compared to other two groups.

Conclusion: This study suggests that high food sensitivity is associated with a higher nutrient deficiency, a stronger oxidative stress response and a lower immune redox status.

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Effect of oral supplementation with enzymatically synthesized glycogen (ESG) on cognitive function: a randomized, double-blind, placebo-controlled study

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ABSTRACT

Background: There is a well-established correlation between aging and decreasing cognitive performance in healthy adults. Furthermore, with increasing levels of stress in modern societies, cognitive decline is a growing concern. With our focus on these concens, we prepared enzymatically synthesized glycogen (ESG) from starch, and aimed to examine whether ESG supplementation improved cognitive functions in humans.

Methods: In a randomized, double-blind, placebo-controlled, cross-over trial, 40 healthy participants were administered 5.0 g of ESG or maltodextrin (placebo) beverages for 4 weeks, respectively. A washout period of 4 to 5 weeks was set between treatments. The primary endpoint was the effect of orally administered ESG on cognitive function, which was assessed by using the CogHealth test battery. In addition, the fatigue VAS (visual analog scale) score and salivary levels of anti-fatigue factors (such as cortisol and secretory IgA) were determined.

Results: Two participants dropped out for personal reasons, therefore data for the remaining 38 subjects was analyzed. It was found that visual discrimination and long-term memory were significantly potentiated by the ingestion of ESG for 2-4 weeks compared with placebo treatment. On the other hand, the fatigue VAS score and salivary levels of anti-fatigue factors showed no significant differences between the ESG group and the placebo group.

Conclusions: Our study shows that oral administration of ESG significantly potentiates the cognitive performance of healthy volunteers. We speculate that glycogen is not only a vital energy source, but is also involved in enhancement of cognitive function.

Keywords: Glycogen, ESG, cognitive performance, CogHealth, long-term memory, visual discrimination

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The application and effectiveness of *Difructose Anhydride* III to increase absorption of calcium in calcium-deficient rats

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ABSTRACT

Background: Dried yogurt enriched by *Difructose Anhydride* III when used as a functional food has been observed to increase calcium absorption, making it useful in osteoporosis prevention. The objective of this study was to analyze the effectiveness of *Difructose Anhydride* III in increasing the absorption of calcium in female rat models, strain Sprague Dawley, in the pre- menopausal age during which they're calcium deficient.

Methods: The effectiveness test of *Difructose Anhydride* III to increase absorption of calcium in pre-menopausal Sprague Dawley rats was performed in calcium-deficient conditions. A completely randomized experimental design was used with 4 treatments for 6 weeks and 4 replications: normal rats fed with purified diet (C), calcium-deficient rats fed with calcium- deficient diet (CD), calcium-deficient rats fed with calcium-deficient diet and DFA III (dahlia tubers) fortified in dry yogurt (CD+DFA III dahlia), and calcium-deficient rats fed with a calcium- deficient diet and DFA III (chicory roots) fortified in dry yogurt (CD+DFA III chicory). The parameters measured were serum calcium concentration, femur bone calcium concentration, femur bone matrix condition, and femur bone strength.

Results: DFA III (dahlia tubers and chicory roots) fortified in dry yogurt contained 0.334% and 0.322% of calcium concentration. The provision of a calcium-deficient diet for 12 weeks was shown to reduce the serum calcium concentration of the deficient calcium rat to 7.72±1.08 mg dL^{-1} and the control rat to 11.60±0.85 mg dL^{-1}. CD+DFA III chicory treatments also showed a high calcium concentration in the femur bone (34.94±3.21%), a relatively higher bone strength (9.34±3.61 kg cm^{-2}), and a denser femur bone matrix condition than the control. The femur bone calcium level of rats treated with CD+DFA III dahlia and chicory tubers was 28.95±1.95% and 34.94±3.21%, respectively. These results were significantly different than the CD treatment (17.49±4.38%).

Conclusion: The evidence from this study suggests that sufficient calcium intake could provide high calcium deposits in the bones. Diets containing 3.60% w/w DFA III fortified in dry yogurt have been shown to enhance calcium absorption in calcium-deficient rats. Additionally, the effectiveness of dried yogurt enriched by DFA III from chicory tubers was higher than that of the dried yogurt enriched by DFA III from dahlia tubers.

Preclinical Trial Registration: Animal Ethics Committee at IPB University No. 12-2013

Keywords: Bone femur; calcium deficiency; effectivity of *Difructose Anhydride* III

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Effect of ellagic acid on body fat and triglyceride reduction in healthy overweight volunteers: a randomized, double-blind, placebo-controlled parallel group study

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ABSTRACT

Background: Worldwide, those categorized as overweight or obese are increasing at an alarming rate, posing a serious public health problem. Current management methods vary, ranging from surgery, dieting and exercise, to the use of synthetic and natural compounds. Previous studies reported the use of an *Irvingia gabonensis* extract containing ellagic acid in reducing weight and other related parameters in overweight participants. The present study investigated the efficacy of ellagic acid on anthropometric parameters as well as body fat ratio and blood triglyceride levels in otherwise healthy overweight Japanese adults.

Participants and Methods: Overall, 32 participants (23 males and 9 females) aged between 20 and 64 years with a BMI of 25 or more but less than 30 kg/m^2 and a visceral fat area of 80 cm^2 or more were included in this randomized double-blind clinical trial. The 20-week intervention involved two groups of participants -placebo group and ellagic acid (3.0 mg per day) group. The placebo or ellagic acid was taken daily with water 30 minutes before the main meal. At baseline (T0) and at 6 and 12 weeks, anthropometric measurements (body weight, BMI, body fat ratio, waist circumference, hip circumference), CT scans and blood triglyceride levels were measured.

Results: Compared to the placebo, ellagic acid brought about statistically significant reductions in body fat ratio, triglycerides, body weight, BMI, waist circumference, hip circumference and visceral fat over the twelve-week trial period.

Conclusion: The use of 3.0 mg ellagic acid daily for a 12-week period was effective in reducing body fat ratio and blood triglycerides as well as other anthropometric parameters, confirming the potential use of ellagic acid in the management of overweight patients.

Keywords: Ellagic acid, *Irvingia gabonensis*, overweight, obesity, body fat, triglyceride, body weight, metabolic syndrome.

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/702/1253

Bowel movement improvement by Mulukhiyah (Corchorus olitorius)-containing food (AOTSUBU) consumption: A randomized, double-blind, placebo-controlled, parallel- group comparison trial

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ABSTRACT

Background: Mulukhiya (Corchorus olitorius) richly contains dietary fiber and is suggested to improve bowel movement.

Objective: This study aimed to investigate the effects of mulukhiya-derived dietary fiber (MDF) on the intestinal environment in healthy Japanese adult subjects.

Methods: This randomized, double-blinded, placebo-controlled study enrolled 22 healthy Japanese adult subjects who typically defecate three to five times per week and do not consume enough dietary fiber. All subjects were randomly allocated into the MDF group (4 men and 7 women; 45.1 ± 11.4 years) or the placebo group (3 men and 8 women; 41.6 ± 9.5 years) by using a computerized random number generator. Each subject was administered with assigned 30 tablets (active [77-mg dietary fiber] or placebo) daily for two weeks. We asked the subjects to record their defecation condition in a bowel movement diary from 1 week before the start of test food consumption to the day before two weeks after the start of the test-food consumption (three weeks in total). Then, we evaluated the items in the bowel movement diary such as the occupancy rate of enteric, organic acids in feces, and subjective symptoms related to constipation.

Results: At one and two weeks after the start of the test-food consumption, the MDF group exhibited a significant increase in stool days, stool frequency, and stool volume compared with the placebo group ($P < 0.05$). Regarding the occupancy rate of enteric bacteria, Prevotella ($P = 0.025$) and Clostridium cluster IV ($P = 0.045$) were significantly increased in the MDF group compared with those in the placebo group at 2 weeks after the start of the test-food consumption. As for organic acids in feces, n-butyric acid was significantly higher in the MDF group

than in the placebo group at 2 weeks after the start of the test-food consumption (P = 0.037). Furthermore, no safety concerns were noted.

Conclusions: The consumption of MDF-containing food for 2 weeks resulted in the increase of stool frequency, stool volume, useful enteric bacteria, and organic acids in feces in healthy Japanese adult subjects.

Clinical trial registration number: UMIN-CTR: UMIN000035613.

Keywords: Mulukhiya, enterobacterial flora, dietary fiber, stool frequency, organic acid levels

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Mechanisms of selected functional foods against viral infections with a view on COVID-19: Mini review

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ABSTRACT

Following research obtained from the previous SARS and MERS outbreaks, we've gained knowledge about the mechanisms of bioactive plant ingredients against the attachment and replication of COVID-19 as well as overshooting immune responses. This could be used for designing COVID-19 trials utilizing bioactive compounds. The receptors for SARS, ACE-2, and CD26 show associations with mechanisms that regulate human senescence. Several functional foods interact with the epigenetic regulation of viral infection and mechanisms of senescence. This review concentrates on the link between bioactive plant ingredients and their activities against mechanisms of viral infections.

Keywords: COVID-19, Epigenetic, Quercetin, Curcumin, Epigallocatechin gallate, Phloretin, Berberine

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Different impacts of plant proteins and animal proteins on human health through altering gut microbiota

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ABSTRACT

Dietary proteins exert a wide range of nutritional and biological functions. Apart from their nutritional roles as the source of amino acids for protein synthesis, they take part mainly in the regulation of food intake, blood pressure, bone metabolism, glucose and lipid metabolism, and immune functions. The interaction of dietary proteins with the gastrointestinal (GI) tract plays a chief role in determining the physiological properties of proteins. The enzymes protease and peptidase hydrolyze dietary protein to generate dipeptides, tripeptides, and amino acids in the lumen of the gastrointestinal tract. These products digested from dietary proteins are utilized in the small intestine by microbes. Moreover, the microbes also convert the macro and micronutrients from the diet into an enormous number of compounds that may have either beneficial or adverse effects on human health. The present review discusses the various impacts caused by both dietary plant and animal protein sources on microbiota in the GI tract.

Keywords: Animal protein; Plant protein; Dietary proteins; Gut microbiota; Human health.

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Inhibitory effect of black raspberry extract on AGE accumulation and degradation, and ROS production in HUVEC cells

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ABSTRACT

Background: A critical event in age-related diseases involves the glycation of various proteins in the animal body to generate advanced glycation end products (AGEs). We have previously found that black raspberry extract (BRE) has effects on age-related diseases. From this observation, we expected that berry extracts, specifically BRE, would have positive effects on AGE-stimulated cell events that link to age-related diseases.

Objective: To discuss the potency of berry extracts against diseases attributable to the AGE-dependent changes of cellular events, in this study, we examined the effects of berry extracts on the cellular events changed upon AGE stimulation of human umbilical vein endothelial cells (HUVECs) through AGE receptors.

Methods: After HUVECs were incubated with AGE-BSA in the presence of serially diluted berry extracts, mRNA and protein levels of AGE receptors, intracellular AGE accumulation, and ROS production in the cell were determined by qRT-PCR and Western blotting, ELISA, and staining with the fluorescent probe, respectively.

Results: Although concentration-dependent effects of berry extracts tested on mRNA levels of AGE receptors in HUVECs were not clear, mRNA level of the AGE receptor RAGE that is involved in the intracellular ROS production was increased by Blabina, which contains BRE, and the well-known anti-glycation compound aminoguanidine (AGD). In contrast, the protein expression level of RAGE was decreased by BRE and Blabina, but not by AGD. It was also found that BRE and Blabina suppressed AGE-BSA-stimulated ROS production in HUVECs. The extent of inhibition in the RAGE protein expression by BRE and Blabina was correlated well with the ROS generation measured in these samples.

Conclusions: The results obtained in this study demonstrate that BRE has the most potent inhibitory effect on ROS accumulation in the cell, probably due to the suppression in the expression level of the RAGE protein. These observations suggest that black raspberry could be a potential nutraceutical to prevent various age-related diseases.

Keywords: AGEs; RAGE; ROS; black raspberry; HUVECs.

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Screening of the antimicrobial activity of some extracts of edible wild plants in Morocco

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ABSTRACT

Background: Despite the availability of cultivated food crops and processed food, a large part of the Moroccan population, more particularly the populations of rural areas, still depend on the traditional use of wild plants, which constitute an important component of their food system. However, there is a lack of information on these plants and their medicinal and pharmacological properties, this is why our study aims to detect the antimicrobial activity of certain wild edible plants.

Methods: disc diffusion method was used to evaluate the antimicrobial activities of extracts of *Mercurialis annua* L, *Papaver rhoeas* L, *Foeniculum vulgare* Mill, *Chenopodium mural* L, and *Scolymus hispanicus* L against the bacterial species Staphylococcus *aureus*, *Enterococcus faecalis*, *Escherichia coli*, *Pseudomonas*sp, and against the yeasts *Cryptococcus neoformans*, and *Candida albicans*

Results: The results showed that the crudeextracts from all the plants studied showed more or less important antimicrobial activities on one or other of the pathogenic microorganisms tested, except for the extract of *M.*

annua, which showed no activity against all microbial strains. The highest antibacterial activity was observed for *Scolymus hispanicus* L extract against *Escherichia coli* (diameter of the inhibition zone: Ø=9mm), the highest antifungal activity was marked for *Foeniculum vulgare* Mill extract against *Candida albicans* (Ø=8mm), and the extract of *Scolymus hispanicus* L against *Cryptococcus neoformans*(Ø=8mm).

Conclusion: These results reveal that, in addition to the role they play in the diet, the food plants studied have an additional biological value due to their bioactive compounds.

Keywords: In vitro antibacterial activity; Antifungal activity; Food wild plants; crude extract, Morocco

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A review of Kurozu, amber rice vinegar made in pottery jars

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ABSTRACT

Brewed rice vinegar, Kurozu, is a traditional Japanese vinegar with a dark amber color. Kurozu is produced in a regional area of Japan using traditional techniques and made inside handcrafted pottery jars. Kurozu is used as both a seasoning and a healthcare supplement. *In vitro* and *in vivo* investigations of ingredients in Kurozu have been carried out. Studies of the functional aspects of Kurozu began in the 1980s, and the health promoting and disease preventing effects of Kurozu have since been elucidated. It was reported that Kurozu improved the symptoms of hypertension, allergies, hypercholesterolemia, enhanced carbohydrate metabolism, and inhibited tumor growth. Kurozu-Moromi is an insoluble product created from the fermentation of Kurozu. Kurozu-Moromi also shows valuable properties, including improvement in dyslipidemia, prevention of hyperglycemia, antitumor effect, and antiallergic activity.

Keywords: Amber color, Brewed vinegar, Functionality, Moromi, Pottery jars

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/713/1284

Nutritionally-complete formula fortified with isomalto-oligosaccharide for hemodialysis patients

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ABSTRACT

Introduction: Recent studies have demonstrated that chronic kidney disease (CKD) is associated with dysbiotic gut microbiota. Therefore, the gut microbiota may be used as a biomarker and therapeutic agent to improve the health of CKD patients.

Objective: To study the probiotic selectivity of isomalto-oligosaccharide (IMO) produced from tapioca starch and its application in a novel nutritional formula developed for hemodialysis patients.

Methods: IMO was produced from tapioca starch in a pilot-scale reactor. The selectivity of IMO for probiotic strains was studied. Among six probiotic strains tested, two probiotic strains were selected for the development of a nutritionally-complete formula for CKD patients.The sensory attributes, probiotic survival and decapsulation, and the microbiological quality of the formula were evaluated.

Results: IMO showed prebiotic properties by promoting the growth of pure cultures of the probiotics tested. The IMO powder and the commercial probiotics, *Lactobacillus paracasei* and *Bifidobacterium animalis* were used as ingredients to develop a nutritional formula for CKD patient with an energy distribution from protein:carbohydrate:fat of 18.43:35.29:43.27 and a total energy per 80 g serving of 400 kcal. It was found that 89.47% of the encapsulated probiotics in the formula survived gastrointestinal tract conditions and 96.90% of the probiotics were released after exposure to phosphate-buffered saline (pH 7.2) for 6 h. The sensory evaluation of the nutritional product showed no significant difference ($p > 0.05$) in its viscosity, taste,

sweetness, saltiness and overall characteristics compared to a commercial product (Nepro®).The product also met relevant standards for the microbial quality of food products containing probiotics.

Conclusion: The nutritionally complete formula developed, fortified with a synbiotic combination of IMO and probiotics successfully met the requirements of the WHO and the Thai FDA regulation. This novel formula for CKD patients is the first reported with fortification by probiotics and an IMO prebiotic.

Keywords: chronic kidney disease, isomalto-oligosaccharide, hemodialysis patient, nutritional formula, probiotic

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/716/1297

Absorption pathway of dietary flavonoids: the potential roles of the lymphatic transport in the intestine

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ABSTRACT

Flavonoids are one of the major dietary polyphenols and have a variety of chemical structures. They are considered as functional food factors to have physiological effects to prevent various diseases. Dietary flavonoid aglycons are taken up are and converted to their corresponding conjugated metabolites by phase II enzymes in the enterocyte. The bioavailability of flavonoids affects their physiological function. Recently, we found dietary flavonoids are absorbed not only via the portal vein but also via the intestinal lymphatic pathways.

Most of dietary nutrients are absorbed in the small intestine, and the intestinal lymphatic system is generally used to absorb lipids and lipophilic vitamins as the form of chylomicrons. In the case of lipophilic drugs, the lymphatic transport pathway makes the medicine avoid the first-pass metabolism in the liver and deliver the drugs as a more active form to the target tissues. In this review, the several reports on the lymphatic transport of flavonoids are summarized, mainly in the cause of quercetin and its derivatives. In addition, the potential of physiological importance of lymphatic flavonoid absorption will be discussed.

Keywords: flavonoid, bioavailability, lymphatic transport, quercetin, glycoside

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/723/1295

Frequently used medicinal herbs and spices in weight management: a review

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Please cite this article as: Kaufman-Shruqui V., Sherf-Dagan S., Salem H., Navarro D.A., Boaz M. Frequently Used Medicinal Herbs and Spices in Weight Management: A Review. ***Functional Foods in Health and Disease*** **2020; 10(7): 305-323 DOI: https://doi.org/10.31989/ffhd.v10i7.719**The acceptability of '*Star*

ABSTRACT

Background: Obesity rates have increased globally during the last half, and with it there has been increased interest in herbs and dietary supplements for weight management

Objectives: The purpose of the present review is to examine evidence for the efficacy and safety of herbal preparations including cinnamon, capsaicin, black pepper and curcumin, which are popularly used for weight reduction.

Methods: A list of herbs and dietary supplements frequently used in weight management was developed by reviewing both scientific and popular literature. Included herbs/supplements were evaluated in terms of pre-clinical and clinical studies.

Results: Included in the review were cinnamon, capsaicin, black pepper and curcumin. For all of the included herbs, proof of concept could be demonstrated. Few well-designed, adequately powered clinical trials were available but those that were suggested efficacy.

Conclusions: While underlying metabolic/physiological mechanisms have been identified in pre-clinical studies, human studies of efficacy are sparse. An indication towards efficacy in humans exists for all of these products; however, treatment guidelines cannot be developed until better quality randomized clinical trials can provide clear findings.

Keywords: Cinnamon; Capsaicin; Black Pepper; Curcumin; Weight Management

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/719/1299

Yellow,' a Cameroonian functional food that could curb the spread of the COVID-19 via feces

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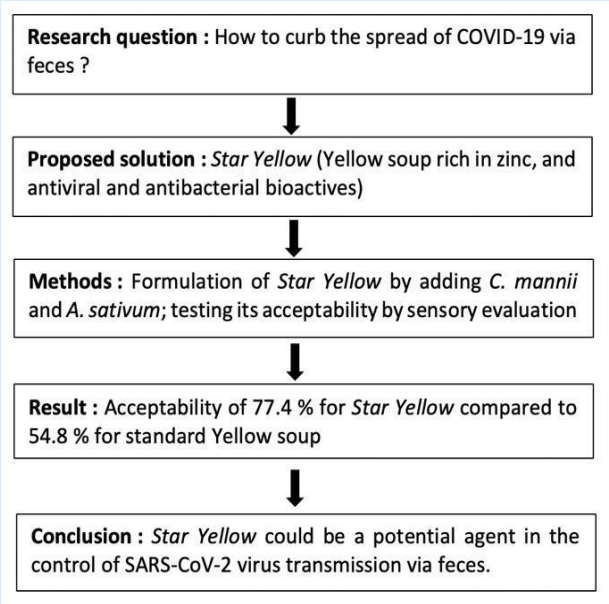
ABSTRACT

Background: COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Despite the World Health Organization's publication of different measures to curb the spread of COVID-19, new cases are reported daily. These protective control measures put in place assumed that transmission of COVID-19 was mediated essentially through droplets released from the nasal and respiratory secretions of infected persons. Recent scientific evidence however puts forward the occurrence and shedding of active COVID-19 virus in stools of infected persons. The present study tested the acceptability of an improved version of the 'Yellow soup' which contains ingredients/spices with known antibacterial/antiviral properties.



Methods: *Star Yellow* was made by using a palm oil/limestone base to which was added spices /ingredients rich in zinc and known for their antiviral/antibacterial activity. Sensory evaluation of the resulting mixture was done by a taste panel comprising habitual eaters of 'Yellow soup' using a hedonic scale of 1 to 5.

Results and Conclusion: Sensory assessment of Star Yellow showed a mean acceptability of 77.4% compared to 54.8% obtained for the commercial Yellow Soup served in restaurants. This indicates the acceptable taste of *Star Yellow* and opens up potential new avenues of research in the control of SARS-CoV-2 virus transmission via feces.

Keywords: Yellow soup, COVID-19, feces, gastrointestinal tract, zinc, RNA replication.

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/715/1303

Black soybean seed coat polyphenols promote nitric oxide production in the aorta through the Akt/eNOS pathway

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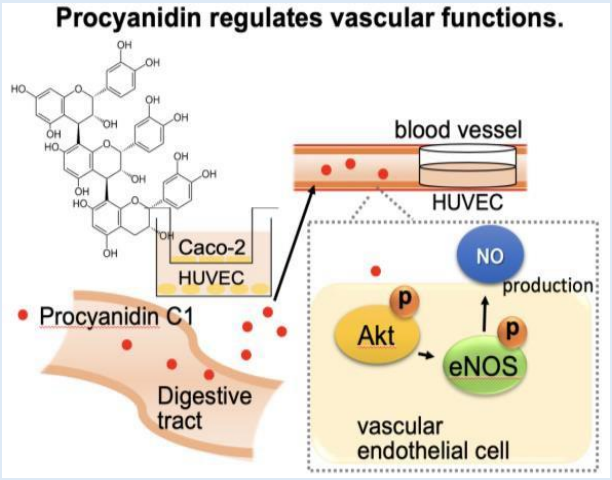
ABSTRACT

Background: Black soybean seed coat contains an abundance of flavan-3-ols and possesses various bioregulatory functions. Nitric oxide (NO) is produced by endothelial nitric oxide synthase (eNOS) in vascular endothelial cells and regulates vascular function through vasodilation and the inhibition of platelet aggregation in blood vessels. It has been reported that flavan-3-ols increase NO production, but many previous reports used a high concentration of flavan-3-ols. In the present study, we investigated the effect of flavan-3-ol-rich black production at a lower concentration that is close to the concentration after permeation through the monolayer of Caco-2 cells.



Methods: Human umbilical vein endothelial cells (HUVEC) were incubated with BE, and then NO production in the medium and eNOS phosphorylation in the cells were examined. Intestinal epithelial Caco-2 cells on the upper side of a transwell filter were co-cultured with HUVEC on the basolateral compartment of the transwell apparatus. BE was added from the upper side, and the basolateral medium was collected to measure the concentration of NO and the content of flavan-3-ols. Furthermore, HUVEC were incubated with each flavan-3-ol in order to individuate the most effective compound in BE.

Results: BE significantly increased NO production in the medium of HUVEC. When polyphenols in BE were removed from the basolateral medium by ethyl acetate extraction, increased NO production from HUVEC was not observed. Additionally, BE increased phosphorylation of eNOS and Akt in HUVEC. A portion of flavan-3-ols in BE had permeated through intestinal epithelial cells. Among the flavan-3-ols that had permeated, procyanidin C1 had the strongest effect on NO production in HUVEC at the concentration that had permeated the monolayer of Caco-2 cells. Procyanidin C1 (0.05 μM) also induced phosphorylation of eNOS and Akt in HUVEC without affecting the cAMP level.

Conclusion: A portion of flavan-3-ols in BE directly promoted NO production through the Akt/eNOS pathway in vascular endothelial cells. These findings suggest that flavan-3-ols in the black soybean seed coat may contribute to improve the vascular function.

Keywords: Black soybean seed coat polyphenols; NO; eNOS; Akt; vascular endothelial cells

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/722/1305

An *in vitro* study to explore the modulation of eosinophil effector function in human allergic peripheral blood eosinophils using enzymatically extracted salmonid oil

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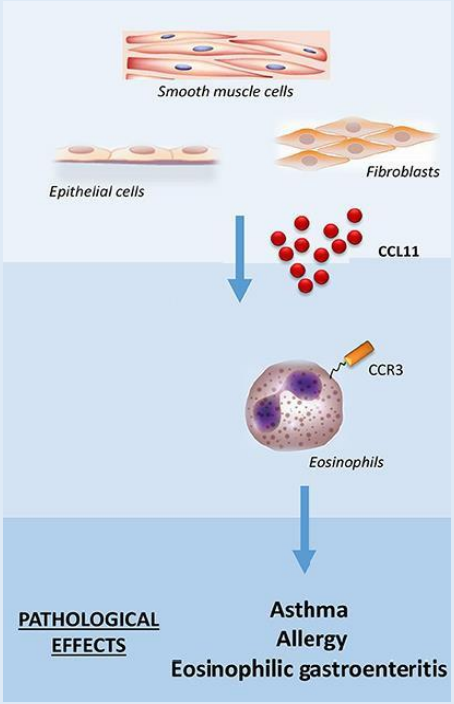
ABSTRACT

Background: The consumption of oily fish in early childhood diets has been correlated to a reduction in the progression of asthma during adolescence and young adulthood. Extending these results to studies on supplementation with omega-3 fish oils has led to equivocal results, with no clear results. One subset of asthma patients is classified as steroid-treatment resistant, which may be attributable to eosinophil dysfunction. This in-vitro study investigated the prophylactic effect of enzymatically extracted salmon oil, as a proxy for eating fresh whole oily fish, on eosinophil function using allergic human peripheral blood eosinophils.



Methods: We measured three eosinophil effector functions in allergic human peripheral blood eosinophils after prophylactic treatment with enzymatically extracted salmonid oil. We measured changes in: i) eosinophil shape change in normal PMNL ii) integrin upregulation in normal PMNL and iii) eosinophil apoptosis. We further measured changes in these functions after prophylactic treatment with omega-3 fish oil, krill oil, and fractions of the salmon oil subjected to several commercial fish oil processing conditions.

Results: Prophylactic treatment of allergic human peripheral blood eosinophil with 100 ug/ml of enzymatically extracted salmonid oil showed modulation of eosinophil effect functions and apoptosis comparable to APOA-IV at 3ug/ml. Vigorous processing conditions applied to the salmon oil degraded the observed eosinophil modulation. Krill oil and standard fish oil showed no to low eosinophil modulation.

Conclusions: Enzymatically extracted salmonid oil demonstrates potential therapeutic promise for the treatment of eosinophil effector malfunction-based allergic and inflammatory conditions, particularly certain types of asthma and COPD. Treatment of the oil with commercial marine oil processing conditions significantly reduces or eliminates this eosinophil effector function modulation.

Keywords: Eosinophils, asthma, salmon oil, APOA-IV, apoptosis

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/730/1315

FFC's Advancement of the Establishment of Functional Food Science

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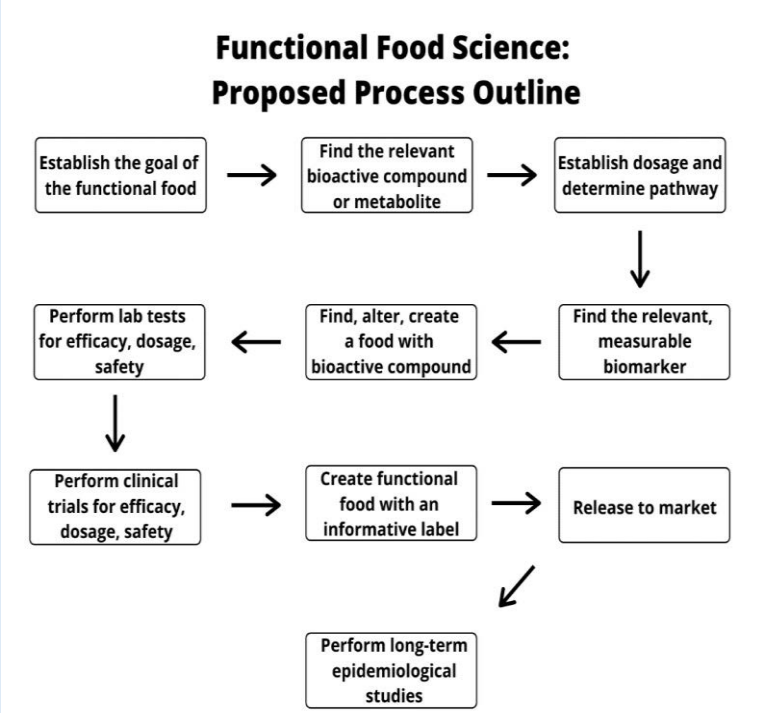
ABSTRACT

The Functional Food Center (FFC) has previously defined functional food as foods which have scientifically-proven benefits toward improving general health and ameliorating the effects of chronic diseases. Given this useful working definition of functional food, it's now imperative to delineate and establish a field of functional food science. Currently, there are no published articles on what functional food science is. Defining functional food science is necessary so that a legitimate field can be established and recognized by the government as well as a global network of researchers and scientists. In this way, appropriate funding and advancements can be made, and functional foods can make their way towards significantly improving the lives of people in the United States and also around the world, as is the goal. As a result of this need, functional food science will be defined as the process of preparing functional foods as well as a field intersecting the realms of health and medical treatment. In this sense, functional food science not only deals with preparing functional foods but also with the efficacy of their health benefits. More specifically, as sciences are often defined by their processes, functional food science can be defined as the comprehensive, aggregate, interdisciplinary, and



collaborative processes of: establishing a target and finding a bioactive compound that enables that effect, finding the correlated measurable biomarker, running testing to find proper dosage and effectiveness, performing clinical trials to ensure efficacy, creating the functional food with an informative label, releasing to market and running epidemiological studies to verify it. Although this understanding and definition is nascent, this can be a starting ground for the FDA and other governmental bodies, as well as the scientific and functional food community, to develop a robust, extrapolatable, and useful outline of functional food science. With an established field of functional food science, functional foods can be researched, produced, and made official and trustworthy, so that there can be large positive impacts on public health, both in disease prevention and in maintenance of good health.

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/729/1307

Moriche Palm (Aguaje) Extract improves indefinite complaints in Japanese females: a randomized, placebo-controlled, double-blind trial

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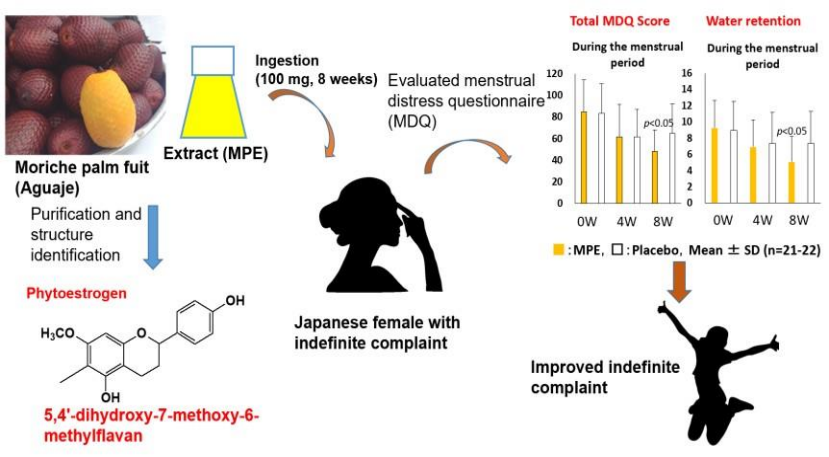
ABSTRACT

Background and objective: The fruit of *Mauritia flexuosa* (moriche palm), which is known as "Aguaje," has been used for beverages and processed foods. Recently, we found that several methoxyflavans are contained in the fruit and they exhibit estrogenic activities. Therefore, moriche palm extract (MPE) may function as a phytoestrogen and improve the symptoms induced by estrogen deficiency. However, the clinical effects of MPE on females has not yet been reported. We conducted a clinical trial of MPE on undefined complaints related to premenstrual syndrome (PMS) in healthy Japanese females.

Methods: This randomized, double-blind, placebo-controlled study examined the effects of MPE (100 mg daily) containing 2 µg of 5,4'-dihydroxy-7-methoxy-6-methylflavan. Forty-four Japanese women with indefinite complaints in premenstrual and menstrual periods were enrolled in the study. All subjects were randomly allocated into either the MPE (100 mg) group (n=22) or the placebo group (n=22) using a computerized random-number generator. Capsules containing either MPE (100 mg) or placebo were administered for 8 weeks between October and December in 2018. The severity of uncertain complaints and emotional status were evaluated using the Japanese version of the menstrual distress questionnaire (MDQ) as a primary outcome, and Medical Outcomes Study Short-Form 36-Item Health (SF-36) questionnaire at 4 and 8 weeks of ingestion. Blood, urine, and body parameters were also evaluated.



Results: Forty-three subjects completed the trial, and the per protocol set comprised 21 subjects in the MPE (100 mg) group and 22 subjects in the placebo group. After ingesting MPE for 4 weeks, arousal in the premenstrual period significantly improved in the MPE (100 mg) group. After 8 weeks, the summary score, water retention, impaired concentration and control during menstrual period significantly improved in the MPE (100 mg) group. Contrarily, among SF-36 domain scores, significant ameliorating effects of MPE were not observed compared with those of the placebo group. Laboratory tests revealed no abnormalities suggesting adverse effects of MPE.

Conclusions: MPE (100 mg/day for 8 weeks) improved several indefinite complaint parameters related to mensuration. MPE was suggested to be useful for improving anxiety related to PMS.

Keywords: Menstrual distress questionnaire; SF-36 questionnaire; moriche palm; *methoxyflavan*; indefinite Complaint

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/742/1319

Nobiletin represses change in the levels of blood coagulation markers in the LPS-induced rat DIC model

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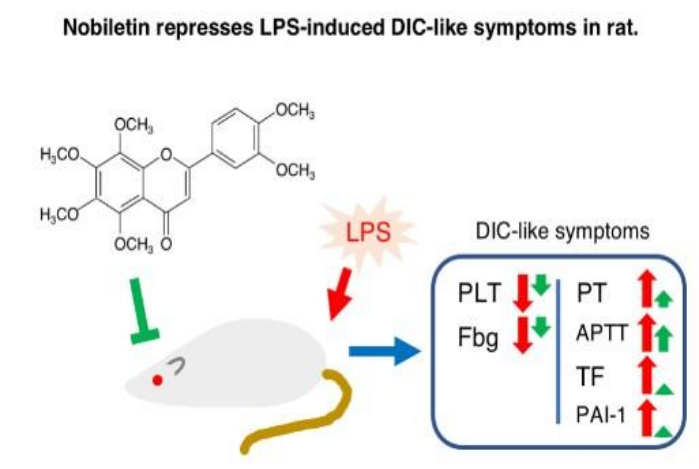
ABSTRACT

Background: Nobiletin is contained in Shiikuwasa fruit, a popular citrus fruit from Okinawa Prefecture in Japan. Nobiletin reportedly acts as a strong antioxidant, an anti-inflammatory agent, and an anti-cancer agent, and it suppresses the expression of TF which triggers blood coagulation. However, *in vivo* verification of *in vitro* reports is necessary. This study used a rat model of LPS-induced microthrombosis based on the *in vivo* studies as previously reported. Sustained intravenous injection of LPS changed all blood coagulation indicators in the direction of thrombus formation. The aim of this study was to determine if intake of nobiletin could suppress DIC-like symptoms.



Methods: Experimental SD rats were fully anesthetized and fixed to an operating table. Either LPS alone or nobiletin (50 mg/kg) plus LPS was given to rats to investigate the repressive effects of nobiletin on the expression of blood coagulation factors

Results: After 4 h of LPS infusion (12.5 mg/kg/h, i.v.), PLT counts and Fbg levels in rat plasma decreased by 80% and 74%, respectively. PT and APTT were extended by 180% and 256%, respectively. TF activity and PAI-1 antigen levels were remarkably increased (54- and 86-fold, respectively vs. control). Pretreatment on nobiletin (50 mg/kg, p.o.) reduced or suppressed fluctuations in blood coagulation indices caused by LPS. TF activity was repressed almost completely by nobiletin pretreatment. After 4 h, PAI-1 antigen levels in nobiletin-treated animals were repressed 82.6% compared to LPS-treated rats. Nobiletin repressed LPS-induced changes in TF and PAI-1 more effectively than other parameters. Further, nobiletin repressed fibrin thrombi formation in the renal glomeruli induced by LPS treatment.

Conclusions: Nobiletin was found to reduce LPS-induced DIC-like symptoms in rats. In the fluctuations of blood indices related to the coagulation cascade, nobiletin suppressed the LPS-induced expression of PAI-1 and TF more effectively than other indices. The binding sites of transcription factors that are activated by LPS-induced signals reside in the promoter areas of TF and PAI-1 gene sequences. Thus, the suppression of TF and PAI-1 expression by nobiletin appears similar to mechanisms previously evaluated during *in vitro* experiments. Importantly, nobiletin repressed fibrin deposition in the renal glomeruli induced by LPS treatment and improved overall health. Nobiletin may function as an anti-thrombogenic agent when ingested daily.

Keywords: nobiletin; LPS; DIC model; blood coagulation; anti-thrombogenic

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/732/1325

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Continuous ascorbate infusions in the management of the patients with advanced colon cancer

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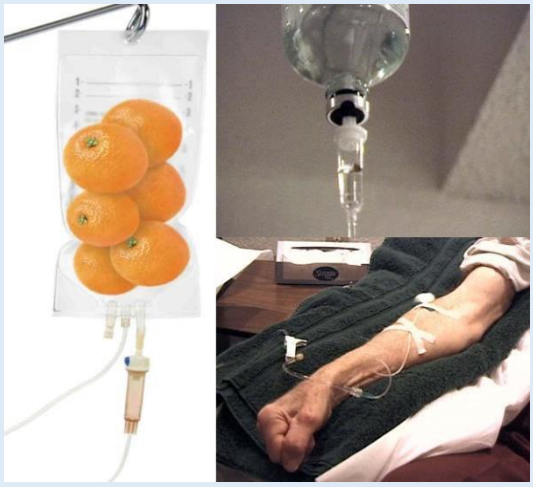
ABSTRACT



Objective: Cytotoxic effect of ascorbic acid on colon cancer cells has been demonstrated in pre-clinical models. In this study, we analyzed data of a previous clinical trial of the treatment of late stage colon cancer patients by continuous ascorbic acid infusions.

Design: The author analyzed the effect of continuous intravenous ascorbic acid (10 g–50 g) administered by injection pumps for 6-8 weeks. Adverse effects, hematologic and blood chemistry parameters, and time to survival were monitored during treatment.

Subjects: 17 terminal colon cancer patients.

Outcome measures: Blood was collected to measure ascorbic acid (AA), absolute lymphocyte count (ALC), neutrophil to lymphocyte ratio (NLR), lactate dehydrogenase concentration (LDH), glucose concentration, ratio of immature neutrophils to total white blood cells (IN/WBC), albumin and creatinine concentrations. Patients' survival time was correlated with measured biomarkers.

Results: The evaluation of the initial blood chemistry parameters as prognostic factors of patients' survival demonstrated strong correlation with survival for lactate dehydrogenase, creatinine, and albumin levels. Continuous ascorbate infusions demonstrated a regulatory effect on ALC, lymphopenia, and NLR, which suggested a benefit of using medium continuous ascorbate doses for improvement of immune functioning. The rate of

growth of LDH in patients with elevated initial levels was decreased in most cases. Treatments were accompanied by reduced serum glucose and uric acid concentrations. In addition, our data demonstrated that continuous IVC can be administered safely.

Conclusions: Continuous IVC infusions show potential to benefit colon cancer patients with minimal side effects. Further research and clinical studies investigating the efficacy of continuous IVC therapy for colon cancer are warranted.

Keywords: continuous infusion, ascorbic acid, colon cancer, survival, lymphopenia, lactate dehydrogenase, neutrophil to lymphocyte ratio.

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/740/1328

Biotic nutritional components in baby formula: possible solution for infantile colic management

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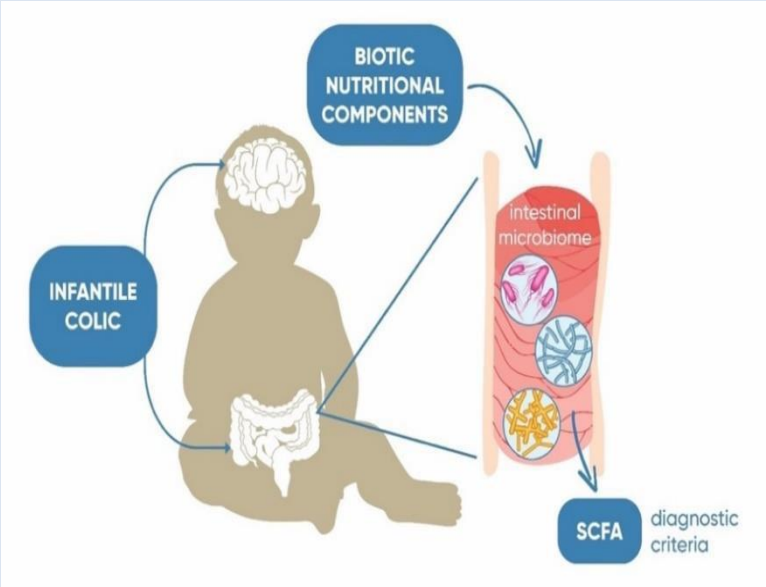
ABSTRACT



The etiology and pathogenesis of infantile colic are still unclear but are most likely determined by a range of behavioral and biological components. The diet contribution to the origin of infantile colic also remains controversial. The review considers the role of biotic nutritional components in the colic prevention and treatment, the role of the intestinal microbiome, as well as diagnostic methods based on objective parameters. The impact of prebiotics in the infant diet on the intestinal microbiome composition and its influence on the manifestation of infant colic is considered. The presence of various probiotic cultures in the diet and their relationship to colic symptoms is also discussed. The importance of examination of the bacterial markers composition, metabolites of the intestinal microbiome, in particular, short-chain fatty acids (SCFA), has been shown.

Keywords: infantile colic, infant formula, nutrient components, intestinal microbiota, short-chain fatty acids

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/737/1317

Influence of a food supplement on the gut microbiome in healthy overweight women

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Clinical Trial Registration: (BASEC (Business Administration System for Ethics Committees, Switzerland) ID 2016-02162; ClinicalTrials.gov NCT03223987, BS2016.1)

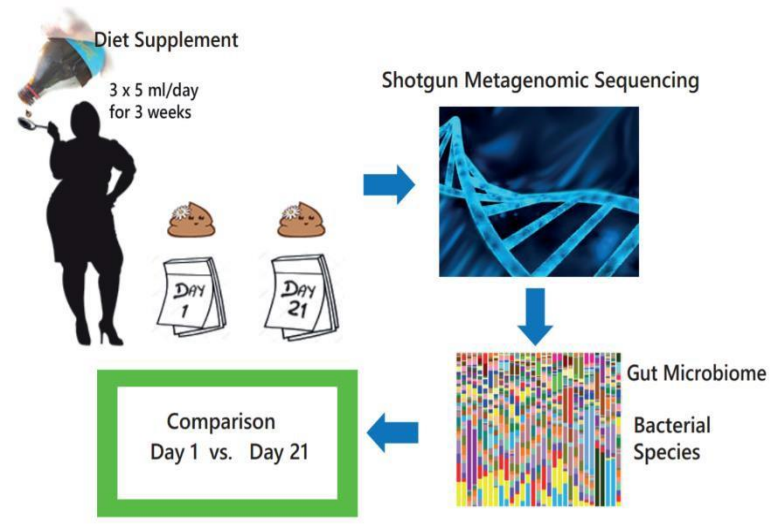
Submission Date: September 16th, 2020; **Acceptance Date:** October 23rd, 2020; **Publication Date:** October 28th, 2020

Please cite this article as: Joller P., Maurer S., Cabaset S. Influence of a Food Supplement on the gut Microbiome in Healthy Overweight Women. *Functional Foods in Health and Disease* 2020. 10(10): 428-438. DOI: https://www.doi.org/10.31989/ffhd.v10i10.750

ABSTRACT

Objectives: We attempted to influence the gut microbiome in 26 women with a BMI (Body Mass Index: kg/m^2) between 30 and 35, and aged 25 to 35 years with an herbal yeast-based dietary supplement (3 x 5ml/d) during 3 weeks in a first pilot trial.

Methods: Shotgun Metagenomic Sequencing in 2 stool samples of each participant.



Results: The majority of the bacteria in the gut microbiome were altered to an extent, which could have an impact on health. Five bacterial species found were identical to probiotic species known as good butyrate producers and described as beneficial for the gut.

Seventy percent of our study cohort showed an increase in the majority of these beneficial microbes during the

study. The ratio of Firmicutes to Bacteroidetes is an important parameter in analyzing overweight persons. Twelve of the participants initially showed a Firmicutes to Bacteroidetes ratio above 1.6. After three weeks, five of these women normalized. Overall, 14 of the 26 participants had a reduction of their F/B ratios.

Conclusions: A baker's yeast-based food supplement can modulate the gut microbiome of overweight young women within 3 weeks to an extent described in the literature as influencing well-being and health.

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/750/1337

Fasting and fasting mimetic supplementation address sirtuin expression, miRNA and microbiota composition

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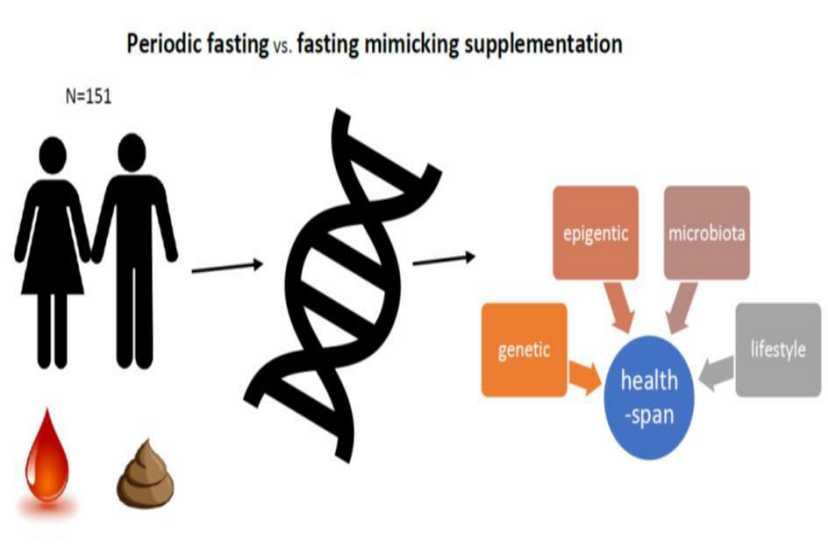
Abstract

Background: Fasting and fasting mimetics - bioactive compounds mimicking fasting effects, are of growing interest as potential means to slow down the aging process and increase health span. Sirtuins are known as enzymes that interfere with mitochondrial energy metabolism and molecular pathways involved in longevity. Although their activation is determined as a response to stress i.e. caloric restriction. Sirtuin activating nutraceuticals are believed to mimic the effects of nutrient deprivation, thus activating signaling pathways correlated to an improved health span. In this study, we compare 5 days periodic buchinger fasting intervention with 3 months shot supplementation, a drink formula, containing secondary plant ingredients considered to activate sirtuins.



Methods We analyzed pathways in response to fasting and a sirtuins activating drink. Genetic and epigenetic biomarkers including telomere length, *LINE1* methylation, and a set of mRNAs and miRNAs were assessed using qPCR analysis. Gut composition and metabolites were compared using Illumnia sequencing and mass spectrometry.

Results Fasting, but also the fasting mimetic could increase expression of *FoxO1, SIRT1,* and *MLH1* mRNA, all genes discussed in aspects of longevity. A positive correlation between telomere length and both *SIRT1,* and *SIRT6* was observed. Furthermore, a significant change in the gut composition was measured. *Actinobacteria* increased in the supplementation group, whereas after buchinger fasting a rise in the distribution of *Proteobacteria* could be observed. Firmicutes*/Bacteroidetes* ratio decreased and correlated with the body mass index (BMI).

Conclusions Our results confirm the effects of fasting on longevity associated mechanisms but also suggest that SIRTFOOD shot intervention addresses some of these effects.

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/752/1344

How does the food in the first 1000 days affect infant and toddler brain development?

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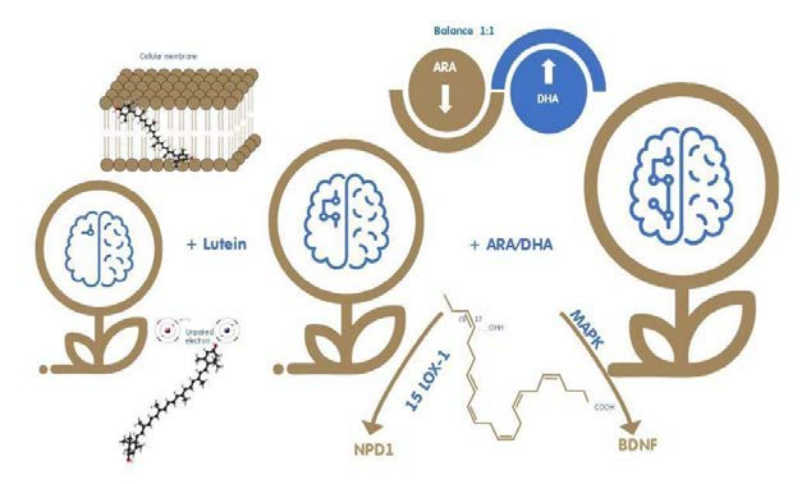
ABSTRACT



Today, hundreds of millions of children under the age of 5 fall short of their development potential. Advances in neuroscience have confirmed that adult health and well-being are based on the developmental conditions and opportunities they had in early childhood, from conception to 24 months (first 1000 days) and then to the age of 5 (second 1000 days). Young children, who eat a healthy balanced diet, who are treated with care and attention, and who have more opportunities to learn, have a better chance to thrive. Data from a survey of adopted children, as well as experimental and quasi-experimental studies, showed that prevention of stunting is most effective during the first 1000 days and developmental delays in both the first and second 1000 days. External factors affect cognitive development significantly less after this period, and the older a person becomes, the less effective educational programs are, and the longer it takes to learn a new skill. In this regard, it is necessary to identify the degree of influence of nutrient components, such as polyunsaturated fatty acids and lutein, on the cognitive

development of the child in the first year of life, as it determines the intellectual potential of the person throughout life. The goal of this review is to review the existing literature to find out how certain food components (polyunsaturated fatty acids and lutein) affect infant and toddler brain development.

Keywords: omega-3, omega-6, polyunsaturated fatty acids, lutein, cognitive development

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/738/1333

Solvent extraction and spectroscopy identification of bioactive compounds from medicinal shrub *Tamarix gallica*

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Submission Date: August 14th, 2020; **Acceptance Date:** October 28th, 2020; **Publication Date:** November 17th, 2020

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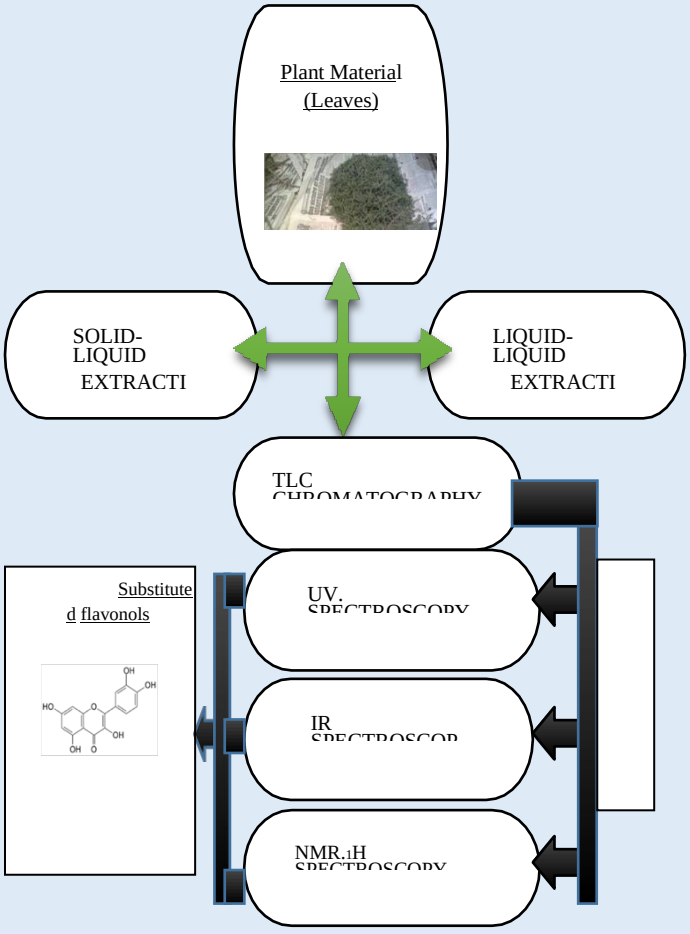
ABSTRACT

This research is interested in chemical valorization of the medicinal shrub called *Tamarix gallica*. The phytochemical study of the extracts of this plant showed that it is rich in phenolic compounds especially the flavonoids. The liquid-liquid extraction by n-butanol and acetate of ethyl of the leaves allowed to us the extraction of the secondary metabolites of class of the flavonoids.

The identification of the isolated flavonoids is made by the spectroscopy methods: UV, IR, NMRH, from where we extracted some structures of flavonols class.



Keywords: *Tamarix gallica*, chemical valorization, flavonoids extraction, spectroscopy methods, chromatography analysis

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/744/1348

Production and nutritional composition of juice powder from oyster mushroom *Pleurotus ostreatus* (Jacq.) Kummer

Lauretta Nwanneka Ofodile[1], Nwachukwu Viola A. Nicholas-Okpara[2], Emmanuel Ani[3], Emmanual Mmaduabuchi Ikegwu[4], Anjorin Saanu[1], Peace Chidinma Ezenwa[5] and Rafiat Titlope Osorinde[5]

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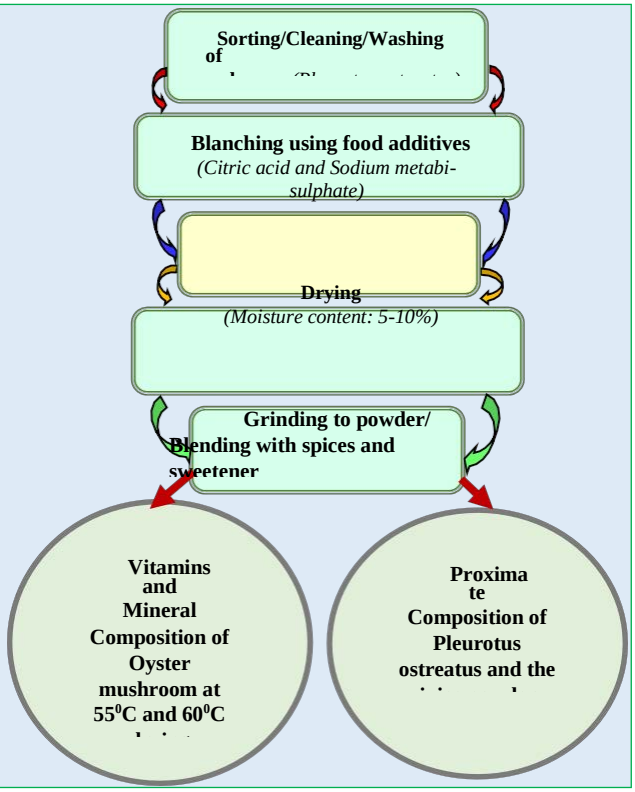
ABSTRACT

Background: Mushrooms have been used as functional foods, nutraceuticals and medicines for decades in Asian countries. Because of their vital roles in human health, nutrition, and well-being, they are described as treasures in the wild and have served as food supplements. In regard to their nutritional composition, they are relatively low in total fat, vitamins, minerals, and fiber, but rich in high quality proteins and polyunsaturated fatty acids.

Objective: To determine the nutritional value and proximate analysis of the oyster mushroom *Pleurotus ostreatus,* formulate mushroom juice powder, and determine its nutritional composition of the powder

Methods: Optimization of the processing condition of the mushroom *Pleurotus ostreatus* (Jacq.) Kummer



Was first conducted using four different drying temperatures; 55°C, 60°C, 65°C and 70°C hourly for 3 hours to determine the best drying temperature. The temperatures at which the juice retained 5-10% moisture were selected for preparation of condensate and analysis because they had the best nutrient composition. Stevia (plant sugar) was used as a sweetener and ginger as the flavor for the formulation of the juice powder. A nutritional composition analysis of the juice powder was also carried out.

Results*:* The nutritional composition of dried *P. ostreatus* at the chosen drying temperature (55 °C) were (8.71, 9.45, 7.07, 9.38, 51.81 and 13.3 mg/g) for iron, manganese, copper, zinc, magnesium and calcium respectively. Nutritional values Fe, Mn, Cu, Zn, Mg and Ca for the juice powder were 8.96 mg/g, 12.1mg/g, 7.94 mg/g, 11.88 mg/g, 59.0 mg/g and 42.0 mg/g respectively. The vitamin content of initial P*. ostreatus* raw material were Vitamin B1 (4.99) and B6 (0.74) while for the juice powder B1, B6 and C were 0.78mg/g, 0.035mg/g and 0.21mg/g respectively. Proximate analysis showed that the mushroom contained moisture (11.20±0.47%), fat (0.55±0.07%), protein (39.75±0.53%), fiber (3.30±1.04%), ash (8.65±0.52%) and carbohydrate (36.54±0.50%) while juice powder contained moisture (5.0%), fat (1.0%), protein(27.13%), fiber (16.00±2.52%), ash (2.83±0.12%) and carbohydrate(48.04±2.58%).

Conclusion: This work demonstrated that the nutrient composition of the mushroom improved when formulated into juice powder. The quantity of Zn and Ca significantly increased in the juice powder at $p<0.05$ and reached the recommended daily dietary allowances and adequate intakes.

Keywords: *Pleurotus ostreatus,* Juice powder, Nutritional value, formulation

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/751/1352

Functional Food Center's vision on functional food definition and science in comparison to FDA's health claim authorization and Japan's Foods for Specified Health Uses

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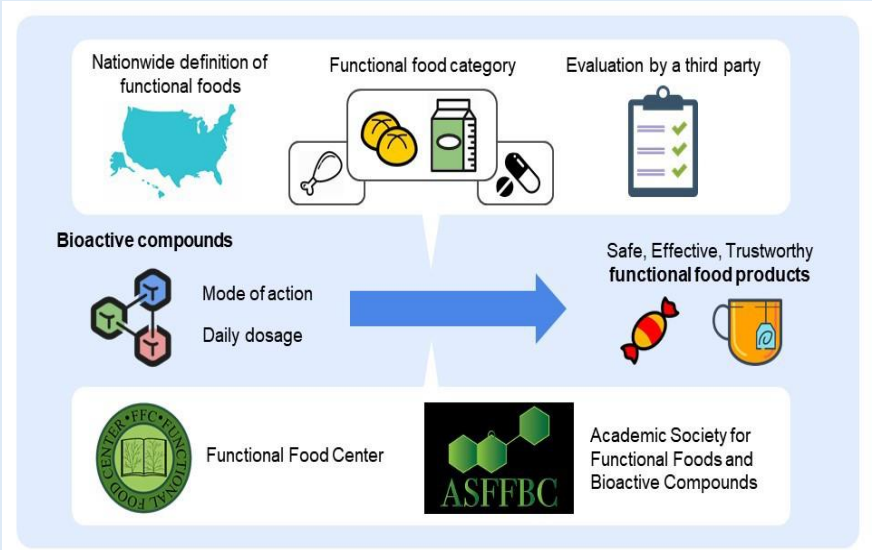
ABSTRACT



The aging population and skyrocketing medical costs are an urgent problem in some countries, which necessitates the prevention of diseases and postponement of disease progression with non-medical means. Functional foods are those that exhibit beneficial effects on human health and play a vital role in supporting part of normal diets. In order to produce functional foods with safe and effective active compounds, it is necessary to define functional foods and to identify the bioactive compounds, the mode(s) of action, and the proper daily dosage. Furthermore, functional foods should undergo a neutral evaluation by an independent organization to ensure only safe and effective products will be released to the market. Japan's Foods for Specified Health Uses (FOSHU) approval system will be described in this review as an example in which individual functional foods are evaluated with numerous criteria by a governmental agency. Whilst the Food and Drug Administration (FDA)

evaluates and authorizes health claim petitions, a definition of functional foods and a distinct functional food category are lacking in the U.S.. The Functional Food Center (FFC) has been supporting functional food scientists worldwide through research and the publishing of numerous educational materials on functional foods. Thus, the FFC and the Academic Society for Functional Foods and Bioactive Compounds (ASFFBC) can and are willing to help the FDA and other governmental agencies establish the category of functional foods and the field of functional food science, which needs to be highly collaborative and multidisciplinary. This review will also describe the current health claim authorization by the FDA and the FFC's vision on the definition of functional foods, bioactive compounds, and the establishment of functional food science that will eventually contribute to human health and well-being in the US and across the globe.

Keywords: functional food definition, functional foods, FOSHU, bioactive compounds, functional food science, health claim, foods for specified health uses

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/753/1350

Brazilian green propolis promotes the cytoprotective expression of heme oxygenase-1 against oxidative stress injury in murine myoblast cells

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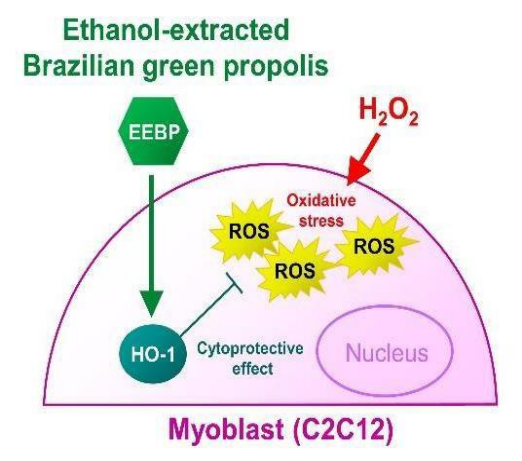
Please cite this article as: Chinen N., Otsu W., Ohuchi K., Ando S., Najkamura S., Kono H., Shimazawa M., Hara H. Brazilian green propolis promotes the cytoprotective expression of heme oxygenase-1 against oxidative stress injury in murine myoblast cells. *Functional Foods in Health and Disease* 2020. 10(12): 493-504. DOI: https://www.doi.org/10.31989/ffhd.v10i12.756

ABSTRACT

Background: Sarcopenia is a progressive skeletal muscle disorder characterized by the progressive loss of muscle mass and function, resulting in physical disability and mortality. Although sarcopenia impacts a large proportion of elderly individuals, no effective treatment for this disease has yet been identified. The excessive production of reactive oxygen species (ROS) can damage tissues and promote aging, and the daily use of dietary antioxidants can be effective for maintaining skeletal muscle health.



Propolis, a natural substance that is collected by honey bees, has been used as traditional medicine, and many reports have described its antioxidative properties. However, how propolis exhibits cytoprotective effects and antioxidative effects in skeletal muscles remains unclear. The purpose of this study was to investigate the

Antioxidative effects of ethanol-extracted Brazilian green propolis (EEBP, from *Baccharis dracunculifolia*) and its three constituents using an *in vitro* myoblast cell model.

Methods: Murine myoblast C2C12 cells were treated with either EEBP or its constituents, including caffeic acid, *trans*-ferulic acid, and *p*-coumaric acid, in the presence of 100 or 300 mM H2O2 to induce oxidative stress injury. The cell death ratio and cell viability were assessed by Hoechst 33342 and propidium iodide staining and the WST- 8 assay, respectively. Simultaneously, intracellular ROS production was measured by CM-H2DCFDA [5-(and-6)- chloromethyl-2',7'-dichlorodihydrofluorescein diacetate, acetyl ester] assay. Finally, immunoblotting was performed in myoblast cell lysates to assess the expression level of an antioxidative enzyme, heme oxygenase-1 (HO-1).

Results: We demonstrated that EEBP significantly reduced H2O2-induced cell death at a concentration of 3 µg/ml in myoblasts. Additionally, caffeic acid at 100 µM improved cell viability under oxidative stress conditions, but not *trans*-ferulic acid or *p*-coumaric acid. Both EEBP and caffeic acid inhibited the H2O2-induced increase in ROS production. Finally, HO-1 expression was increased by treatment with either EEBP or caffeic acid. The increase in HO-1 expression induced by H2O2 was enhanced in the presence of EEBP and caffeic acid.

Conclusions: These findings indicated that EEBP has protective effects against oxidative damage in the C2C12 murine myoblast cell line. Caffeic acid is an EEBP constituent that contributes to cytoprotective activity. EEBP may act as an inducer of HO-1 to prevent oxidative stress-induced myoblast death.

Keywords: C2C12 murine myoblast cells, heme oxygenase-1, oxidative stress, propolis, reactive oxygen species

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/756/1356

Nanoencapsulation and identification of phenolic compounds by UPLC-Q/TOF-MS^2 of an antioxidant extract from *Opuntia atropes*

Running title: Nanoencapsulation of phenolics from *Opuntia*

Eunice Tranquilino-Rodríguez[1], Héctor E. Martínez-Flores[2*], José O. Rodiles-López[2], Guillermo C. G. Martínez-Avila[3]

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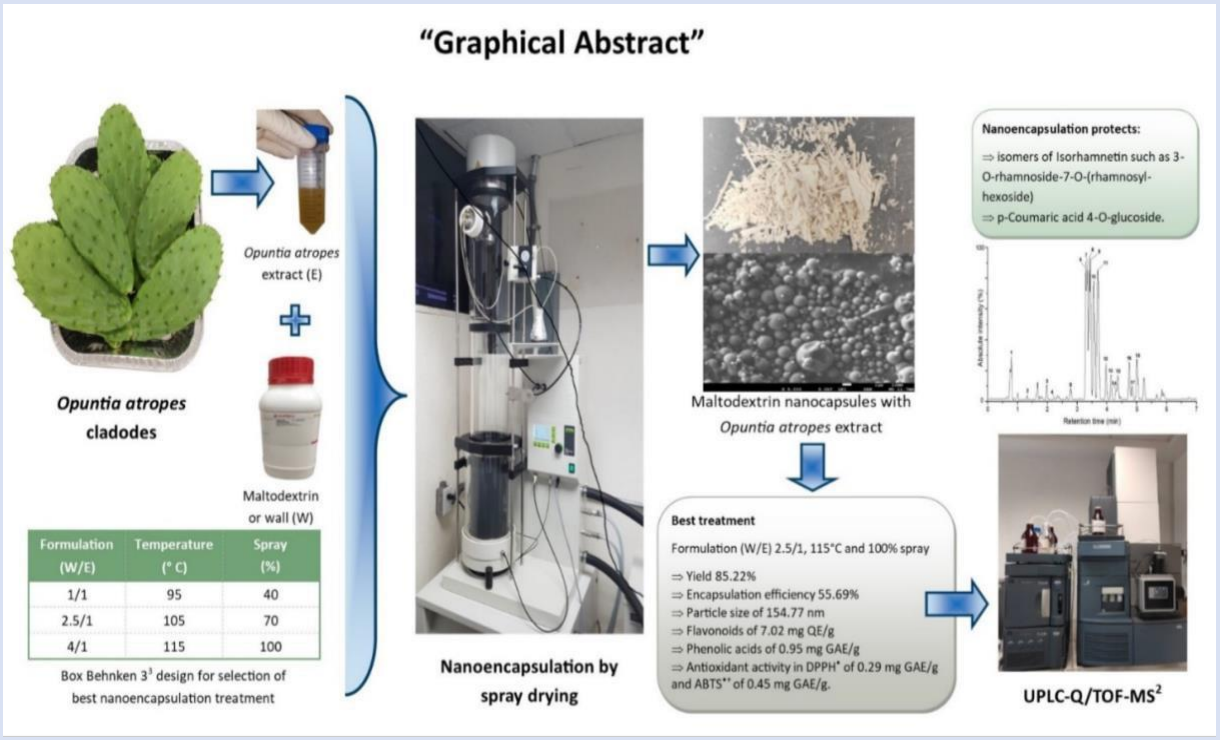
ABSTRACT

Background: Nanoencapsulation is a technique that protects bioactive compounds such as polyphenolic compounds from environmental factors, through a biopolymer that acts as a wall system. Cladodes of *O. atropes* are an important source of polyphenolic compounds, flavonoids being the most abundant, these are mainly in the form of glycosides and their consumption has been related to a decrease in glucose and lipid profile through the elimination of intracellular radicals.

Purpose of the study: To study the formulation and process parameters that allow for obtaining the best experimental conditions for nanoencapsulation and protect the polyphenolic compounds of the *O. atropes* extract.



Methods: Wall materials applied for nanoencapsulation include soy protein isolate, calcium caseinate , and maltodextrin. A 3^3 Box Behnken design was used: wall material extract of *O. atropes* (1/1, 2.5 / 1, 4/1), temperature (95, 105 and 115 ° C) and spray (40, 70 and 100%).Yield, feeding speed, particle size, encapsulation efficiency, phenolic acids, flavonoids, DPPH• (1,1-dipheny l-2-picrilhydrazyl) and ABTS•+(2,2'-azino-bis-3- ethylbenzothia-zolin acid-6-sulfonic) were evaluated. Polyphenolic compounds were identified by UPLC-Q / TOF- MS^2.

Results: Maltodextrin presented better properties in the encapsulation of the extract of *O. atropes*. The 3^3 Box Behnken design made it possible to identify the treatment with the appropriate quality characteristics for the nanoencapsulation process: Formulation 2.5 / 1 (maltodextrin / *O. atropes* extract), 115 ° C and 100% spray resulted in 85.22% yield, feeding speed of 9 mL / h, the particle size of 154.77 nm, 55.69 % encapsulation efficiency, phenolic acids of 0.95 mg GAE / g, flavonoids of 7.02 mg QE / g, and antioxidant activity in DPPH• of 0.29 mg GAE / g and ABTS•+ of 0.45 mg GAE / g. The polyphenolic profile was characterized, and it was confirmed that nanoencapsulation protects some isomers of isorhamnetin 3-*O*-rhamnosido-7-*O*- (rhamnosyl-hexoside) and p-coumaric acid 4-*O*-glucoside.

Conclusion: Maltodextrin is an excellent encapsulating material of the *O. atropes* extract. The formulation and process conditions that favored all the response variables were identified, and it was shown that nanoencapsulation protects the polyphenolic compounds.

Keywords: *O. atropes* extract, nanoencapsulation, polyphenolic profile, UPLC-Q / TOF-MS^2.

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/763/1406

Effect of cassava on proximate composition, insulin index,glycemic profile, load, and index in healthy individuals: a cross-sectional study

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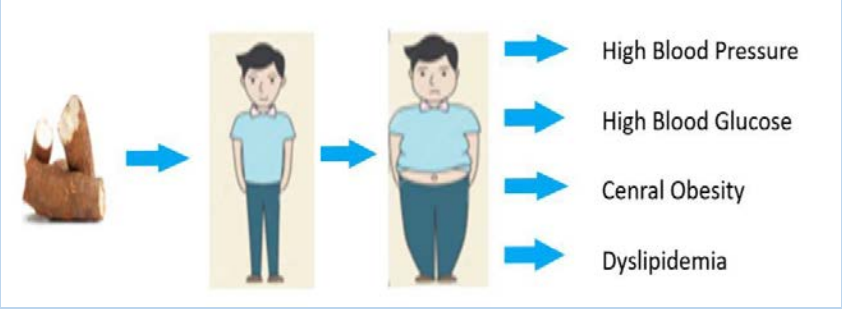
ABSTRACT



Background: The major challenge in Africa is the growing prevalence of metabolic syndrome which has been attributed to changing lifestyles in developing countries. The impact of the commonly available staple starchy food; eaten in this environment may also be a factor contributing to growing concerns of metabolic syndrome. Hence,the need to assess the affordable staple starchy foods. Cassava is the most consumed staple starchy food in our environment; therefore, our study evaluated its impact on glycaemic and insulin response in consumers.

Aim: To determine Insulin Index (II), glycaemic profile (GP), glycaemic load (GL) and Glycaemic Index (GI), incremental glucose peak value (IGPV), and glycaemic profile index (GPI) of cassava food meals.

Methods: Participants ingested three cassava processed products (cassava dough [fufu], chips [Abacha], andflakes [garri] (the equivalent of 50g glucose) and 50 g of reference meal (glucose solution). Fasting and post- prandial samples were taken for blood glucose and insulin however sample for glucose was taken at intervals of 30 mins to a maximum of 180mins and 120 mins for insulin, respectively.

Result: The GI for cassava dough, flakes and chips were 93.26; 95.92 and 91.94, respectively. Their glycaemic load was 46.62; 47.96 and 45.97, respectively. The glycaemic profile index was 37.34; 41.41 and 46.19, respectively. In addition, the insulin index was 55.83; 69.36 and 97.02. The proximate analysis showed protein, moisture, fibre, fat, ash, and carbohydrate content as follows the cassava **(%)** (crude form) 1.075%; 72.00%; 0.80%; 0.58%; 0.35%; 25.07%, Chips 1.44%; 59.13%; 0.73%; 1.71%; 36.83%, flakes 1.82%; 67.36%;

0.15%; 0.91%; 0.25%; 39.64% and dough 1.56%; 67.51%; 0.21%; 0.52%; 0.20%; 30.22% respectively.

Conclusion: II, GP, GL, and GI of cassava dough (fufu), cassava flakes(garri)and cassava chips (Abacha) were found to be high. Unregulated dietary intake in adults may lead to metabolic diseases.

Keywords: Glycaemic index, Glycaemic load, Glycaemic profile, Cassava, Makurdi

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/772/1371

Eryngium caeruleum essential oil as a promising natural additive: *in vitro* antioxidant properties and its effect on lipid oxidation of minced rainbow trout meat during storageat refrigeration temperature

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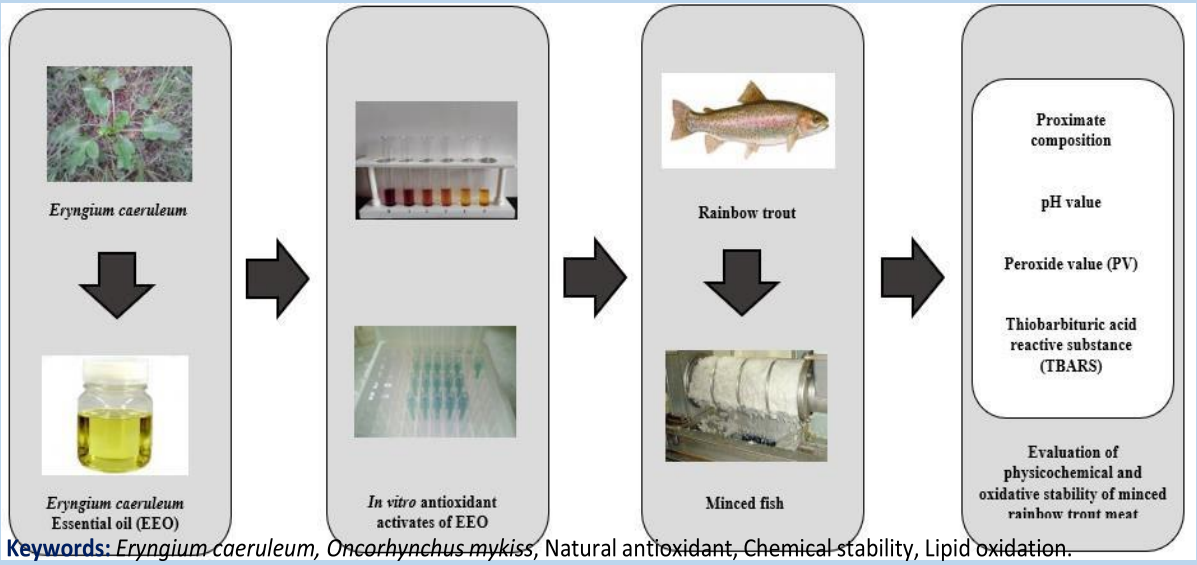
ABSTRACT

Background: One of the most common species of oily fish is rainbow trout. Chemical deterioration of oily fish species is principally caused by lipid oxidation. The adverse effects of various chemical preservatives caused consumer's attention to shift to natural alternatives. *Eryngium caeruleum* is an herbaceous plant that is native to the northern areas of Iran and is used in various local foods. The aim of the present study was to investigate the effects of different concentrations of *E. caeruleum* essential oil (EEO) on the physicochemical and oxidativestability of minced rainbow trout meat for 20 days storage at 4±1°C.

Methods: Firstly, the chemical compounds and total phenolic content of EEO were determined by gas chromatography-mass spectrometry and Folin–Ciocalteu reagent, respectively. Then, *in vitro* antioxidant capacity of EEO was evaluated using 2,2-Diphenyl-1-picrylhydrazyl (DPPH) and 2,2'-azino-bis (3- ethylbenzthiazoline-6-sulphonic acid) (ABTS) methods. Finally, the minced rainbow trout meat was mixed with different concentrations of EEO, and physicochemical and oxidative stability of treatments were investigated for 20 days storage at 4±1°C.

Results: According to the results, 0.4% EEO significantly improved the chemical stability of minced fish compared to control group at the end of storage period with the following scores (P<0.05): pH value (6.3),peroxide value (11.88 meq/kg of lipid) and thiobarbituric acid reactive substance (0.43 mg MDA/kg sample). **Conclusions:** In order to increase the chemical quality characteristics of minced fish, new ingredient systems that are associated with natural and organic foods are applied. The results of present study indicate that the use of EEO in the meat industry can develop the novel healthy fish products and improve its chemical stability.



Keywords: *Eryngium caeruleum, Oncorhynchus mykiss*, Natural antioxidant, Chemical stability, Lipid oxidation.

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/766/1372

Enhancing effect of glycine and tryptophan mixture on estimated glomerular filtration rate in healthy participants: Arandomized, double-blind, placebo-controlled parallel study

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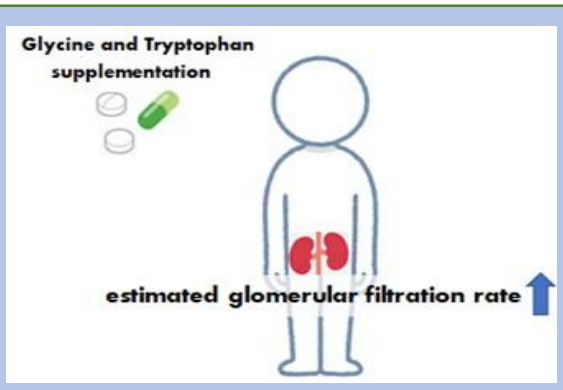
Please cite this article as: Oshima S., Shiiya S., Nakamura Y. Enhancing effect of glycine and tryptophan mixture onestimated glomerular filtration rate in healthy participants: A randomized, double-blind, placebo-controlled parallelstudy. *Functional Foods in Health and Disease* 2021. 11(1): 24-33. DOI: https://www.doi.org/10.31989/ffhd.v11i1.774

ABSTRACT

Background: The mixture of glycine and tryptophan exhibited serum uric acid-lowering effects in our previous clinical trial.



Objective: Using a randomized, double-blind, placebo-controlled, and parallel study design, this current study aimed to examine whether this mixture enhanced the estimated glomerular filtration rate (eGFR) as an indicator of renal function in healthy individuals.

Methods: Healthy Japanese adult males and females ingested a powder mixture containing 3.0 g of glycine and 0.2 g of tryptophan or a placebo powder once daily at bedtime for 8 weeks.

Results: After 8 weeks of continual ingestion, the combined glycine and tryptophan supplementation significantly enhanced eGFR. It also decreased serum uric acid levels, consistent with our previous reports. Meanwhile, thecontinual ingestion of the mixture had no influence on serum total or essential amino acids.

significantly elevated the eGFR of healthy participants. However, further investigation is required to elucidate the detailed mechanisms underlying the potential therapeutic or preventive effect of combined glycine and tryptophan supplementation. Nevertheless, the uric acid-lowering effect of glycine and tryptophan mixture hasthe potential to directly influence renal function.

Key words: glycine, tryptophan, estimated glomerular filtration rate, uric acid

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/774/1379

Flavonoids from the leaves and twigs of *Lindera sericea* (Seibold et Zucc.) Blume var. *sericea* (Lauraceae) from Japanand their bioactivities

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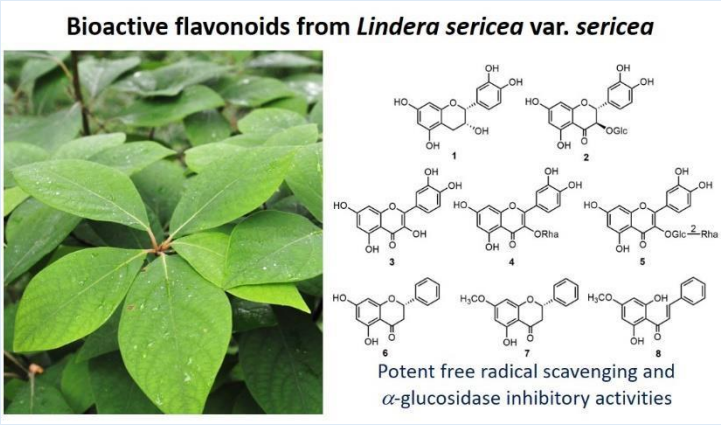
ABSTRACT



Background: The leaves and twigs of *Lindera sericea* (Seibold et Zucc.) Blume var. *sericea* (Lauraceae) are used as traditional medicines for treating indigestion, stomachache, anxiety, etc. In recent years, there has been a growing interest in these plant materials as a source of healthy drinks and functional foods. The main aim of this study was to characterize the major phenolic compounds from the leaves and twigs and to evaluate their free radical scavenging and α-glucosidase inhibitory activities.

Methods: The dried leaves and twigs were extracted with 70% methanol. The dried extract was then subjectedto repeated column chromatography to isolate eight flavonoids. The compounds were then evaluated for their 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging activity and *α*-glucosidase inhibitory activity.

Results: The isolated compounds were identified as (-)-epicatechin (**1**), taxifolin 3-*O*-glucoside (**2**), quercetin (**3**), quercitrin (**4**), quercetin 3-*O*-neohesperidoside (**5**), pinocembrin (**6**), pinostrobin (**7**) and pinostrobin chalcone (**8**) based on their nuclear magnetic resonance (NMR), spectroscopic data and comparison with literature values. All these compounds were isolated for the first time from this plant. All flavonoids except pinocembrin (**6**), pinostrobin (**7**) and pinostrobin chalcone (**8**) showed potent free radical scavenging activity. In *α*-glucosidase inhibitory activity assay, quercetin (**3**), quercitrin (**4**) and taxifolin 3-*O*-glucoside (**2**) showed potent activity.

Conclusions: Eight flavonoids were reported for the first time from the leaves and twigs of the title plant. Someof these compounds showed potent free radical scavenging and *α*-glucosidase inhibitory activities.

Keywords: *Lindera sericea* var. *sericea*; Lauraceae; Kekuromoji; free radical; α-glucosidase

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/769/1377

Effect of flavonoid-rich meals and low-flavonoid meals basedon the dietary reference intakes for Japanese, using basic foodstuffs on the gene expression of inflammatory cytokinesin the whole blood cells from adult men of normal or light overweight

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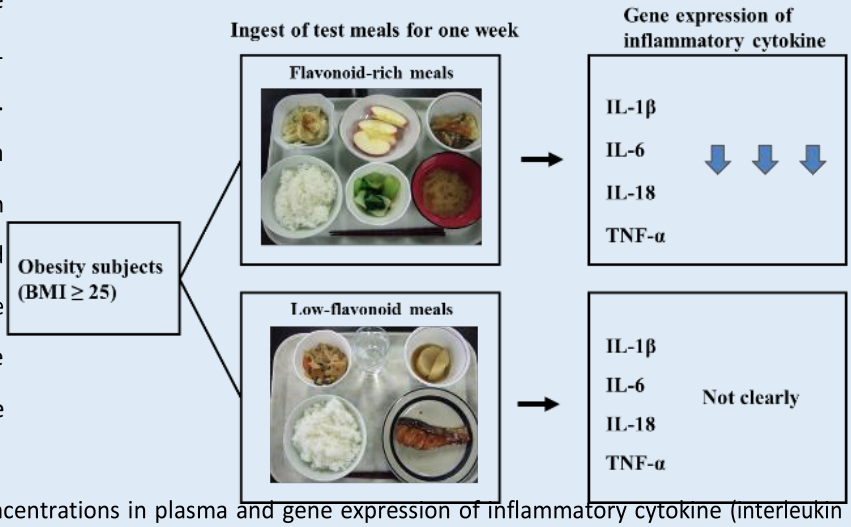
ABSTRACT

Introduction: Flavonoids have a variety of functions, such as antioxidant activity, and are expected to have adisease prevention effect. In order to verify the disease risk reduction effect of flavonoids, we carried out a crossover trial in seven adult men of normal or light overweight who ingested flavonoid-rich meals, with a diverse combination of basic foodstuffs, and low-flavonoid meals and compared blood disease-related inflammatory markers.

Methods: On the first two days of the study, seven male volunteers were provided with low-flavonoid meals (flavonoid content below the detection limit of HPLC: less than 0.24 mg/meal) three times a day as a washout.

For the next seven days, they were fed flavonoid-rich meals (46.9 ± 8.1 mg/meal) or low- flavonoid meals. Blood samples were collected from all the volunteers before breakfast on the third day, after the washout and before breakfast on the tenth day. The test was consisted of one cycle from the first day to the tenth day, and the participants carried out two cycles. Flavonoid concentrations in plasma and gene expression of inflammatory cytokine (interleukin 1 beta, interleukin 6, interleukin 18, and tumor necrosis factor-α) in whole blood cells were compared before and after the intervention. Gene expression in whole blood cells was measured using real time RT-PCR.



Results: We found a significant increase in plasma flavonoid concentration (quercetin, kaempferol, daidzein, and genistein) upon intervention with flavonoid-rich meals ($p < 0.05$). In addition, the inflammatory cytokine gene expression was reduced in the subjects with a body mass index of more than, but not less than, 25 kg/m^2 compared with that observed after the intake of low-flavonoid meals.

Conclusion: These results suggest that flavonoid-rich meals have an anti-inflammatory effect in obese persons who are likely to have chronic inflammation.

Keywords: Flavonoids, inflammatory cytokines, flavonoid-rich meal, human study

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/781/1386

Choosing Suitable Food Vehicles for Functional FoodProducts

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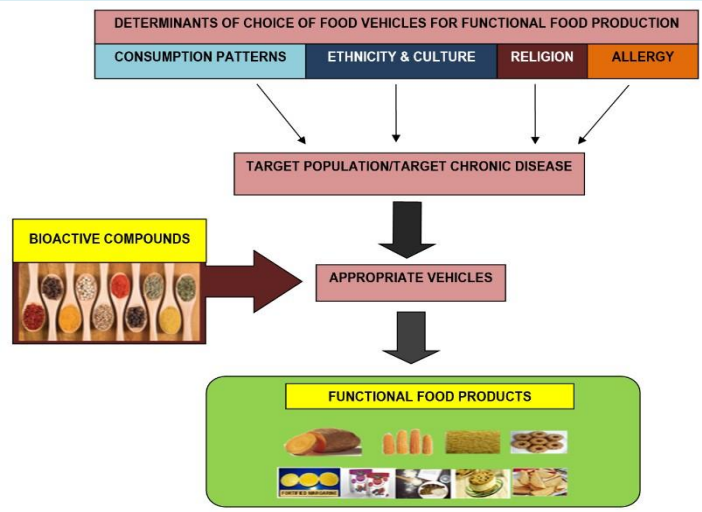
ABSTRACT



Globally, there is a growing demand for functional foods that provide health benefits without changing current dietary habits. However, the world is made up of diverse societies that consist of a wide range of individuals from different ethnic and cultural backgrounds associated with different food choices and preferences. Functional foods resemble traditional foods but have been designed andtailored to confer physiological and health benefits that go beyond their nutritional function. Of the seven-step cycle involved in functional food production, choosing a suitable food vehicle as a carrier of the bioactive components is essential. Therefore, this review explored the importance of food vehicles and how they can influence the acceptance of functional

foods. Relevant scientific literature was electronically sourced from Google Scholar, Google, PubMed, databases of the Journals of Functional Foods in Health and Disease (JFFHD) and Bioactive Compounds in Health and Disease (BCHD) based on their mention or discussion of food choice and preference and foodvehicles for food fortification or functional food production. These studies revealed that although functionalfoods are found virtually in all food categories, they are not homogeneously scattered over all segments ofthe growing market. Consumer demands and acceptance in terms of consumption patterns, ethnicity, culture, religion, and allergy, amongst others, need to be taken into consideration when choosing appropriate vehicles for functional food development.

Keywords: food vehicles, functional foods, food fortification, food choice, food preference, fortification, phytonutrients, bioactive compounds

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/764/1380

The green tea polyphenol EGCG is differentially associated with telomeric regulation in normal human fibroblasts versuscancer cells

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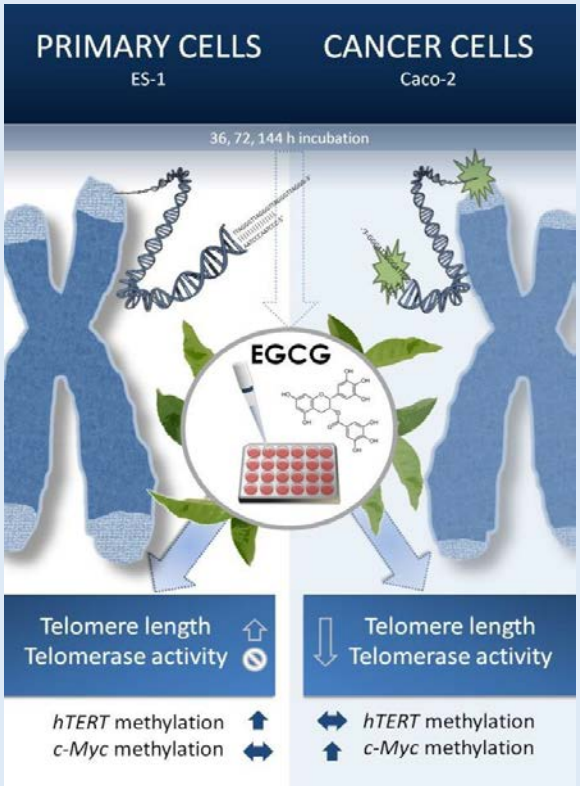
ABSTRACT

Introduction: Topical investigations have demonstrated that oxidative stress and inflammation play key roles in biological aging and determine incidence and course of age-related diseases. Lifestyle and environmental factors hugely impact epigenetic regulation and DNA stability with telomere attrition and epigenetic instability providing a potential record of the cumulative burden of endogenous and exogenous oxidative noxae. Certain physiologically active plant components exhibit antioxidative activities affecting epigenetic regulation of inflammation response and DNA repair.

Methods: Against this background, the present study investigated green tea polyphenol epigallocatechin gallate (EGCG) in the context of telomere regulation in Caco-2 colorectal adenocarcinoma cells vs. ES-1 primary skinfibroblasts. Cell lines were treated with 20 and 200 µM EGCG for 36, 72 and 144 hours, respectively. Telomerase

activity, relative telomere length as well as methylation status of *hTERT* and *c-Myc* from different culture conditions were assessed. Malondialdehyde (MDA) served as a surrogate marker of potential pro- oxidative effects of EGCG in a physiologically relevanttissue model.



Results: EGCG incubation was associated with telomere shortening and decreased telomerase activity in Caco-2 cells, and relatively longer telomeresalong with increased methylation of six 5'—C— phosphate—G—3' (CpG) sites in the promoter region of human Telomerase Reverse Transcriptase (*hTERT)* in fibroblasts. At low concentrations, EGCG significantly decreased oxidative damage to lipids in Caco-2 cells and attenuated H_2O_2 induced oxidation athigher concentrations.

Conclusion: These results suggest differential EGCG-mediated telomeric modulation in cancer vs. primary cells and a specific antioxidant activity of EGCG againstoxidative damage to lipids in abnormal cells.

Keywords: Caco-2, epigallocatechin gallate, telomeres, hTERT, DNA methylation, telomerase, oxidative stress, malondialdehyde

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/775/1387

Oil emulsion from *Plukenetia huayllabambana* (Sacha inchi) modifies nitric oxide and leptin in the liver and antioxidant and inflammation markers in the adipose tissue in obese rats

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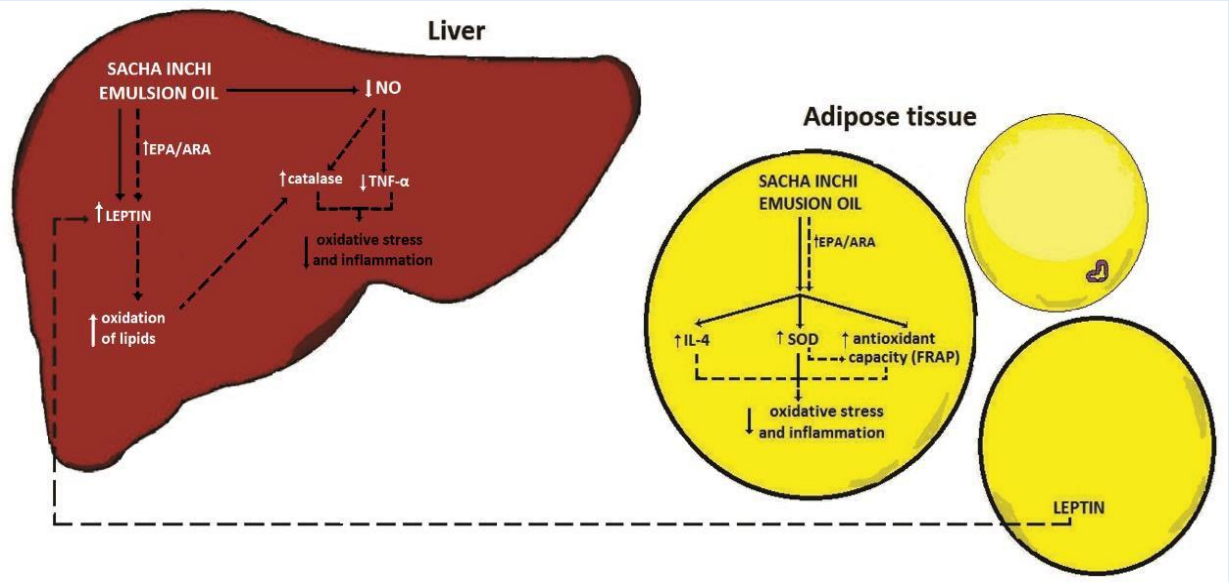
B.

ABSTRACT

Background: Obesity is characterized by excessive accumulation of adipose tissue and is associated with higher risk of metabolic diseases and other comorbidities. Efficacious strategies including a diet high in "functional foods" are promising. *Plukenetia huayllabambana* known as Sacha Inchi (SI), is a legume which seeds are rich in proteins, tocopherols, and fatty acids such as omega-3 (ω-3). The latter has emerged as a potential protective nutrient against the cardiometabolic risks associated with obesity. Omega-3 changes the membrane lipid profileof hepatic and adipose cells triggering the expression of antioxidant and anti-inflammatory genes. However,there are few reports in relation to the effect of these oils in inflammatory and stress response related to obesity. In this sense, the present study evaluated the effect of SI oil emulsion on nitric oxide and leptin levels in the liver

and some markers of oxidative stress and inflammation in adipose tissue from the rodent obesity model.



Methods: Six groups were formed: Not obese control group (Noc), obese control (Oc), two groups treated with the emulsion of SI oil (Os1:0.25g ω-3/day; Os2:0.5g ω-3/day), one obese group treated with atorvastatin (Oa)and one group treated with atorvastatin plus the emulsion of SI oil (Oas2).

Results: Os1 and Os2 lowered nitric oxide and increased liver leptin levels. In the adipose tissue, the superoxide dismutase and reducing antioxidant power increased significantly in Os1 and Os2 groups. The anti-inflammatory marker IL-4 was also increased in Os2, Oa and Oas2 compared to the Oc and IL-10 increased in Oas2 group.

Conclusion: Our study suggests that the emulsion of SI oil can modify the inflammatory and stress responses associated with obesity and it can be incorporated as a promising functional food.

Keywords: Inflammation, leptin, obesity, nitric oxide, oxidative stress, SI oil emulsion.

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/778/1389

The effect of consuming an anthocyanin-containing supplement derived from Bilberry (*Vaccinium myrtillus*) on eyefunction: A Randomized, Double-Blind, Placebo Controlled Parallel Study

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ABSTRACT

Objective: The purpose of this study was to determine the effects of 6-week consumption of anthocyanin- containing supplement on eye function.

Methods: This was a randomized, placebo-controlled, double-blind, parallel-group comparison study involving 32 healthy Japanese adults with eye fatigue after using visual display terminals (VDTs). Subjects were randomlyallocated into either the active group (bilberry-derived anthocyanin 43.2 mg per capsule) or placebo group using a random number generator. Subjects consumed either one active or placebo capsule once a day for 6 weeks.The primary outcome measured was the change in percentage of pupillary response pre- and post-VDT use,whereas the secondary outcomes were tear film break-up time, Schirmer's value, muscle hardness, and subjectivesymptoms. Experimental data was analyzed using Student's t-test, the two-way analysis of covariance, or Mann– Whitney U-test.

Results: Each group included 15 subjects in the efficacy analysis. The active group showed a significant

improvement in the logarithmic conversion values of the percentage of pupillary response (active group: 0.2 ±0.4, placebo group: 0.0 ± 0.3; P = 0.043) and pupillary response/near point (active group: 0.1 ± 0.4, placebo group: −0.1 ± 0.3; P = 0.049) pre- and post-VDT use at 6 weeks compared with the placebo group in a subgroup analysisper eye. No adverse events were reported.

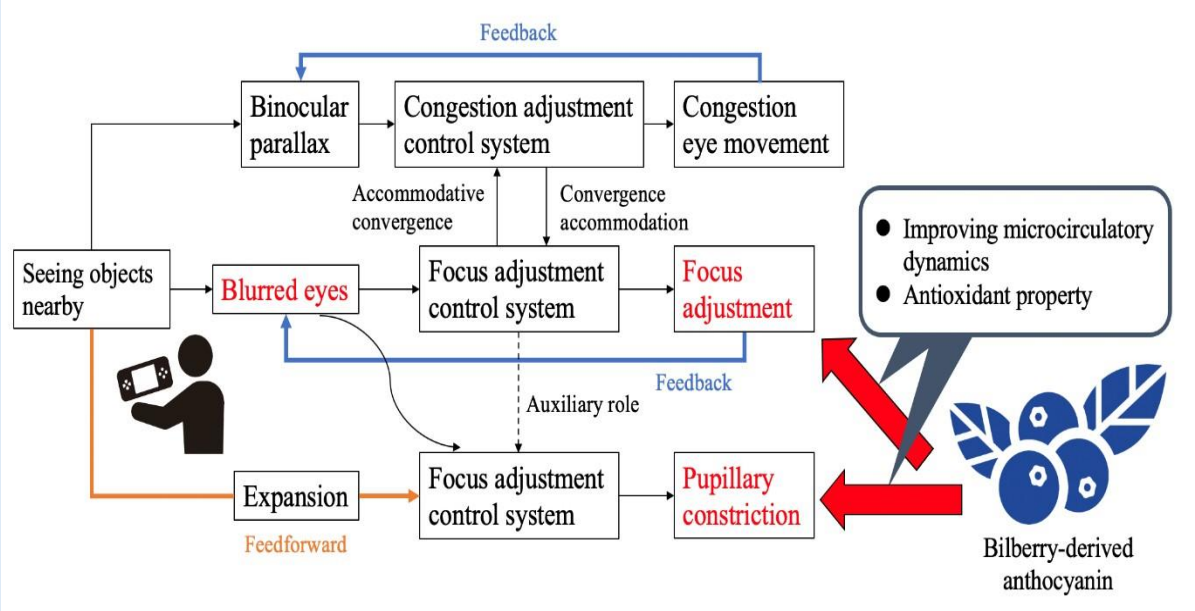
Conclusions: The consumption of the supplement containing anthocyanins extracted from bilberry for 6 weeksinhibited the decrease in the accommodative function caused by oxidative stress due to VDT use.

Trial registration: UMIN-CTR: UMIN000037039.

Foundation: BGG Japan Co., Ltd. and Arysta Health and Nutrition Sciences Corp.

Keywords: accommodative function; anthocyanin; bilberry; visual display terminals

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/782/1393



Cholesterol in virus entry into host cell: diet,phytosterols and statins

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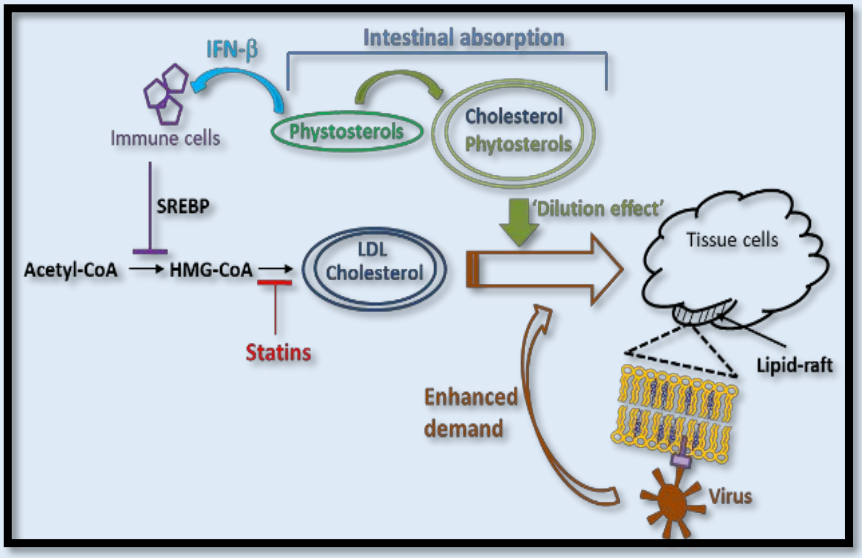
Please cite this article as: Montero O. Cholesterol in virus entry into host cell: diet, phytosterols and stains. *Functional Foods in Health and Disease* 2021. 11(3): 104-115 DOI: https://www.doi.org/10.31989/ffhd.v11i3.780

ABSTRACT



Cholesterol has been reported in a number of studies to play an essential role in the effectiveness of viral infection in mammalcells. The main characteristic of cholesterol that is involved in viral infection is its capability to afford negative curvature to the membrane. This faculty of cholesterol hasto do with the necessary steep curvature that the host cell membrane undergoes in the primary processes of viral infection. In particular, for RNA enveloped viruses, membrane curvature is involved in two mechanisms of the viral infection, which are virus and host cell membrane fusion for viral genome release and virus reproduction scaffold build-up. Low cholesterol diets have been shown to reduce or even suppress virus infection efficiency in murine models or cell cultures; but to what extent a diet-based lowering of the blood cholesterol level may help preventing virus infection still lacks enough scientific evidence. The use of statins in individuals with hypercholesterolemia has been recommended in the recent COVID-19 outbreak. The possibility of using sterols from natural sources in the

diet or in supplementary concentrates has been suggested to be an alternative to drop the circulating cholesterol.In this manuscript, the most relevant and recent bibliography on the aforementioned issues is reviewed.

Keywords: cholesterol, virus infection, membrane curvature, sterols, natural food sources

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/780/1392

Transcriptomic analysis reveals that combinations of vitamins A, D2, and D3 have synergistic effects in HCT-116 colon cancercells by altering the expression of genes involved in multiple canonical pathways including apoptosis, regulation of the epithelial mesenchymal transition and immunity

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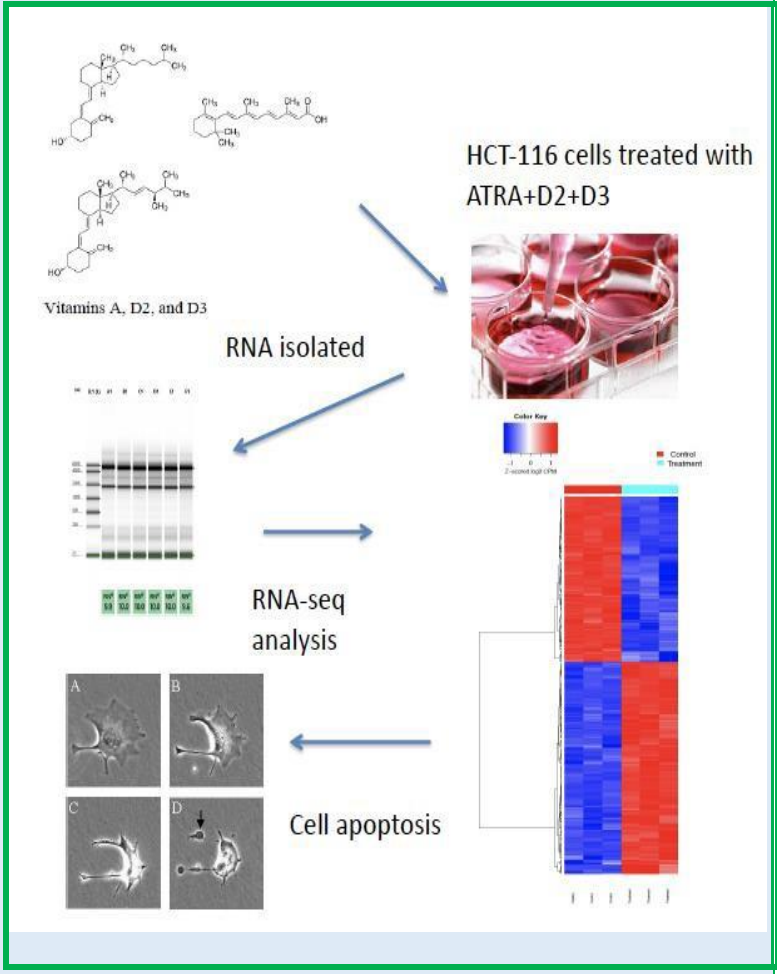
ABSTRACT

Integrated systems biology approaches suggest that combinations of nutrients may be more effective againstcancer due to the large number of signaling pathways associated with cancer initiation and promotion. In a previous work, we have reported that combinations of vitamins A (as all trans-retinoic acid, ATRA), D2, and D3act synergistically to induce apoptosis in colon and gastric cancer cells. In this work, we use whole-genome transcriptomic profiling to detect gene expression changes using RNA-seq to more comprehensively investigate the biological pathways affected by the combination of vitamin D2, D3 and ATRA. HCT-116 colon cancer cells were harvested, RNA was isolated and RNA-seq libraries were prepared using a Universal Plus mRNASeq kit. Sequencingwas carried out on NovaSeq 6000. General quality-control metrics were obtained using FastQC and raw reads

were aligned to human reference genome hg38 using STAR and BWA MEM. ENSEMBL genes were quantified using

FeatureCounts, and differential expression statistics were computed using EdgeR. Specific gene expression was validated using qPCR. Transcriptomic analysis showed that of 26,313 genes analyzed, the expression of 8,402 geneswas significantly altered (4030 up- regulated and 4373 down-regulated,FDR≤0.05) in the treated cells, of which,3,621 genes were differentially expressed (fold change ≤-1 or ≥+1 and an FDR <0.05). Ingenuity® Pathway analysis revealed the involvement of 97 canonical pathways, with the top pathways including: mechanisms of cancer, apoptosis, *myc*-mediated apoptosis, regulation of the epithelial mesenchymal transition, and immunity.

Keywords: apoptosis, cholcalciferol, colon cancer, caspase, CRMP1, ergocalciferol, IL-12, NOTCH1, RNA-seq, SMAD7, synergism, transcriptome



Link to full article: https://ffhdj.com/index.php/ffhd/article/view/784/1401

Tuna blood inhibits lipopolysaccharide-induced inflammatorymediators in RAW264.7 macrophages

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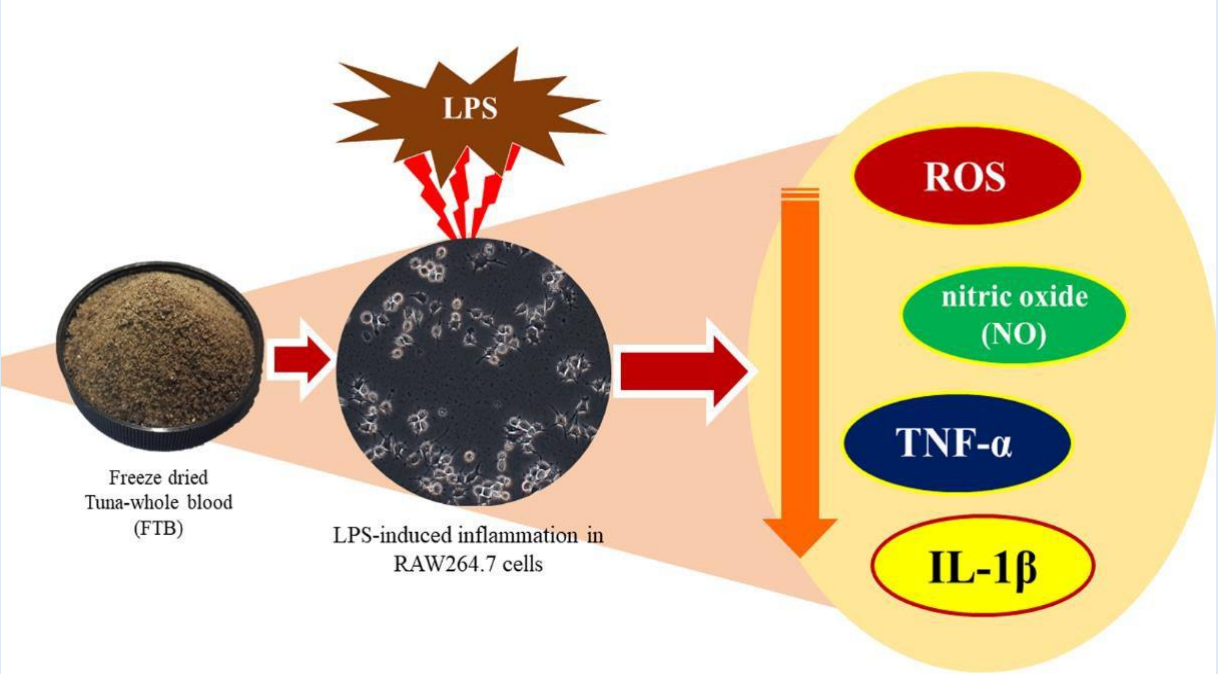
ABSTRACT

Background: This study aimed to evaluate the anti-inflammation effects of the freeze-dried tuna whole blood(FTB), and freeze-dried tuna blood cell (FTC) in LPS-induced RAW264.7 cells.

Methods: The RAW264.7 cells were pre-administered with FTB and FTC at different concentrations for 2 h and then stimulated with lipopolysaccharide (LPS) for 24 h. The production of reactive oxygen species (ROS), nitricoxide (NO), tumor necrosis factor-alpha (TNF-α), and interleukin-1 beta (IL-1β) in RAW 264.7 cells were thendetermined.

Results: The results showed that only FTB remarkably abolished LPS-induced ROS in RAW264.7 cells. FTB and FTC significantly decreased LPS-induced NO which IC50 values of FTB and FTC after 24 h were 78.58 and 22.47 µg/mL,respectively. TNF-α and IL-1β secretion were abolished by FTB and FTC in LPS-stimulated macrophages which IC50 values of both FTB and FTC after 24 h were more than 25 µg/mL, respectively. However, the efficacy of FTC against inflammatory mediators was due to cytotoxic effects on RAW 264.7 cells.



Conclusion: Tuna whole blood potentially inhibits inflammation through modulating the synthesis of several mediators and cytokines associated with the development of inflammation. These findings suggest a role of tuna blood on anti-inflammatory activity.

Keywords: Anti-inflammatory activity, RAW 264.7 cells, red blood cell, tuna blood, waste utilization

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/785/1411

Health Communication in Nutrition for Cancer Prevention inThailand

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ABSTRACT

Cancer has been ranked first of the Thai mortality causes. As dietary factors affect the risk of cancer, communication is crucial for providing beneficial nutritional knowledge for patients to change their daily diets accurately. The communication could be through the use of the internet, as there is currently media that could be easily accessed at a large scale. As a result, modern technology could facilitate the interaction between citizens and nutritionalprofessionals, leading to healthy lifestyles. For example, the nutritional labels of products could be read by using IoT, which is a mobile application. It is also believed that devices will be developed to help prevent cancer in the future.

Keywords: health communication, nutrition for cancer prevention, IoT, social media nutrition, nutrition labeling

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/792/1399

Plant-Based Polysaccharides and their Health Functions

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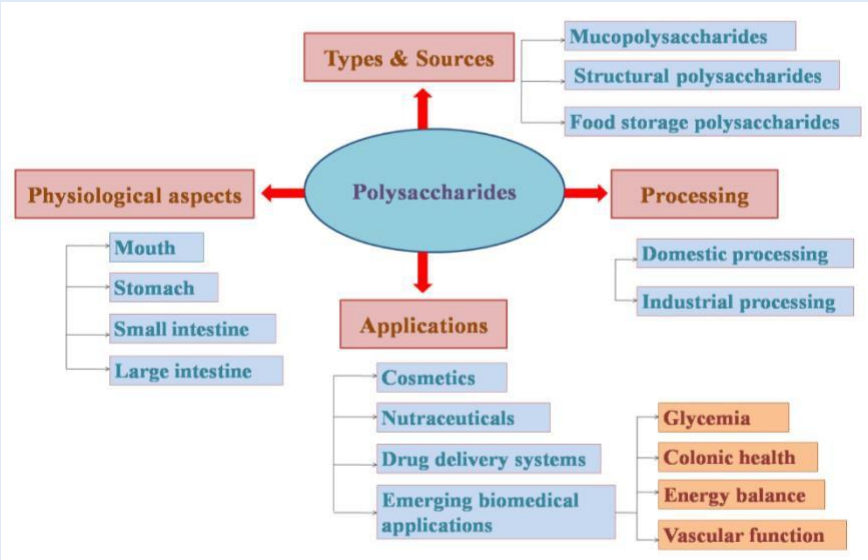
ABSTRACT

Plants are valuable source of polysaccharides that make a large portion of our daily diet. These are natural polymers thatare essential to sustain life. They provide high-value nutrition and positively help the immune system and improve the digestive properties. They also help in the elimination oftoxic by-products from the human body. Polysaccharides and human health are inextricably linked and intertwined. These are also important components of the cell wallthat provides its strength and integrity. Due to their indispensable role in human health, it is very important toknow the different modifications and loss of nutritional value during the processing of plant material. Nowadays, these plant-based polysaccharides are used for diverse applications including wound dressing, drug delivery, laxative, cosmetic and pharmaceutical preparations. As an emerging area of plant-based medicines to reduce the



side effects of synthetic sources, these polysaccharides are used to enhance the immunogenic response against a specific antigen. This review envisages some important polysaccharides (e.g.
mucilages and gums, glycosamine glycans and chitin/chitosan) and their medical, cosmetic, and pharmaceuticalapplications, with emphasis on the relationship between their structure and function.

Keywords: Polysaccharides; Nutrition; Health Functions; Cosmetics; Vaccine; Nutraceuticals

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/773/1405

Black tea decreases postprandial blood glucose levels in healthyhumans and contains high-molecular-weight polyphenols that inhibit α-glucosidase and α-amylase *in vitro:* a randomized, double blind, placebo-controlled, crossover trial

Yoshikazu Isono [1,] *, Hisako Watanabe [1], Masafumi Kumada [1], Tsuyoshi Takara [2], andShin-ichro Iio [3]

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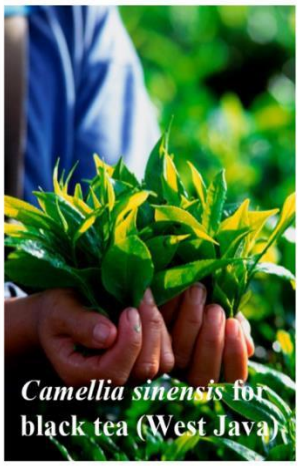
ABSTRACT

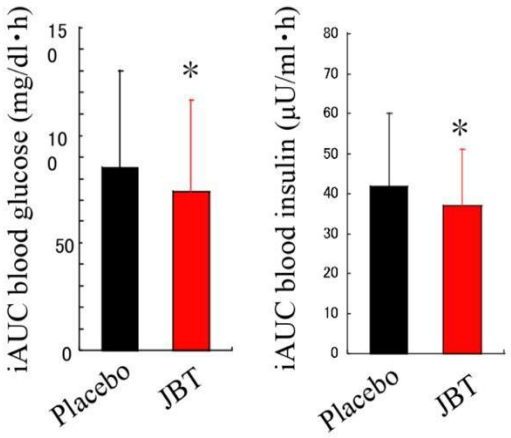
Background: To prevent diabetes, it is important to control postprandial glycemic levels. Studies have suggested that consuming black tea decreases the risk of type 2 diabetes; however, only a few studies have examined the effects of black tea on postprandial glycemic control after consuming starch-rich foods. In addition, the mechanism underlying the suppression of postprandial glucose levels remains unclear.

Objective: To investigate the effects of black tea on postprandial blood glucose levels in healthy humans and to identify the components of black tea that inhibit digestive enzymes.

Methods: The inhibitory activity of black tea on digestive enzymes was measured, and the inhibitory components

were fractionated. Healthy Japanese adults ingested 200 ml of black tea, and its effect on postprandial blood glucose and insulin levels were investigated.





The iAUC of blood glucose and insulin after ingestion of cooked rice with Java black tea (JBT) or placebo drink.

Results: Black tea dose-dependently inhibited α-glucosidase, sucrase, and α-amylase activity. The major components responsible for this inhibition were high–molecular-weight polyphenols. The galloyl moieties present in these compounds play an important role in their inhibitory activities. Two randomized, double-blind, placebo-controlled, crossover studies of healthy human subjects (total n = 46) were conducted to investigate the effect of black teaon blood glucose and insulin levels. Combined data from the two studies showed that black tea ingestion (200 mL)after cooked rice intake (200 g) significantly reduced the incremental area under the curve of glucose (*P* =.024)and insulin (*P* =.014) compared to placebo drink.

Conclusions: The high–molecular-weight polyphenols in black tea inhibited α-glucosidase, sucrase, and α-amylaseactivity in a dose-dependent manner. Furthermore, black tea ingestion after eating cooked rice significantly reduced the incremental area under the curve of glucose and insulin. These effects of black tea could be attributedto the inhibition of digestive enzymes by high–molecular-weight polyphenols containing galloyl groups.

Keywords: black tea, blood glucose, α-glucosidase, α-amylase, polyphenol

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/791/1423

Serum levels of vitamin D, calcium, phosphorus, and oxidativeparameters in healthy and diabetic people

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and 40 healthy individuals (female and male between 20-60 years old without comorbidities). The high- performance liquid chromatography (HPLC) method was adopted for measuring Vitamin D and for measuringother levels, the colorimetric method was used. Using SPSS 22, statistical analysis was performed. The Mann- Whitney U test for quantitative data was applied. P<0.05 was deemed significant.

Results: There was a statistically significant difference between the two groups when it came to the means ofvitamin D and MDA. In the diabetic group, vitamin D levels were lower (p=0.001) and MDA levels were higher(p<0.001). Comparing the level of calcium and phosphorus in diabetics and healthy people revealed no significant difference. This result was also true for the TAC test.

Conclusions: According to our results, the mean of vitamin D in T2DM was significantly lower than healthy peopleand MDA in T2DM significantly increased compared to the control group, suggesting that increasing the activity of this enzyme in the development of secondary complications in diabetic patients is a predisposing factor.

Keywords: Vitamin D, Diabetes mellitus, HPLC, Oxidative stress

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/787/1422

Can functional foods reduce the risk of disease? Advancementof functional food definition and steps to create functional food products

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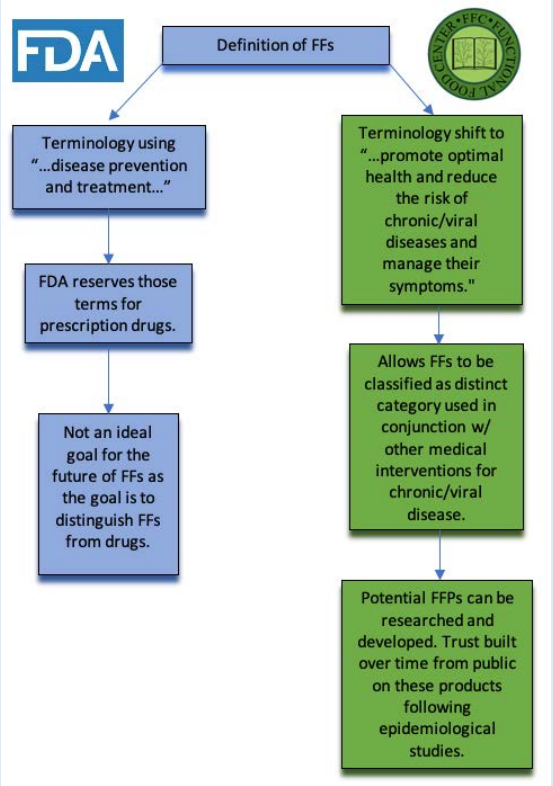
ABSTRACT

The definition of functional foods (FFs) has been in development for many years by the Functional Food Scientists of the Functional Food Institute/Functional Food Center (FFC). The status of the FFC's definition is currently unrecognized by the Food and Drug Administration (FDA),but recognition is important for the safe, uniform development and disbursement of functional food products(FFPs) that could improve the health of Americans and people around the world struggling with chronic and viral diseases. If functional foods were to be properly termed using the FFC's current definition, they would be classified asa drug according to the FDA. Thus, the FFC is in communication with governmental representatives to determine the next steps for functional foods to be properly acknowledged. To that end, the FFC is revising its current definition of functional foods to fit a more accurate and encompassing idea of the nature of what functional foods do. This includes a shift to stressing how functional foods promote optimal health, reduce the risk of chronic/viral disease, and manage their symptoms.



Additionally, the process of developing a functional food product must be standardized to ensure the safety of administering bioactive compounds as a health optimization tool. This process follows the methodology of functional food science, which is a potential new form of life science proposed by the Functional Food Center.Over time, the FFC has been developing the appropriate steps to create a functional food product, however, inthis article, new steps are emphasized, such as epidemiological studies and after-market research—vital steps to ensuring the safest and most efficacious product is released to the public. Functional foods are not meant to take the place of conventional medicine. They can, however, be used in conjunction with Western medicine and serve as an aid to health optimization for people with chronic/viral diseases and prioritize the management of symptoms associated with those diseases.

Keywords: functional foods, bioactive compounds, biomarkers, functional food science, functional food products, epidemiological studies

Link to full article: https://ffhdj.com/index.php/ffhd/article/view/788/1416

Health benefits of olive oil and by-products and possible innovative applications for industrial processes

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**Corresponding Author: Grazia Tamma, PhD, Professor, Department of Biosciences, Biotechnologies and Biopharmaceutics, University of Bari, Aldo Moro, Bari, Italy.

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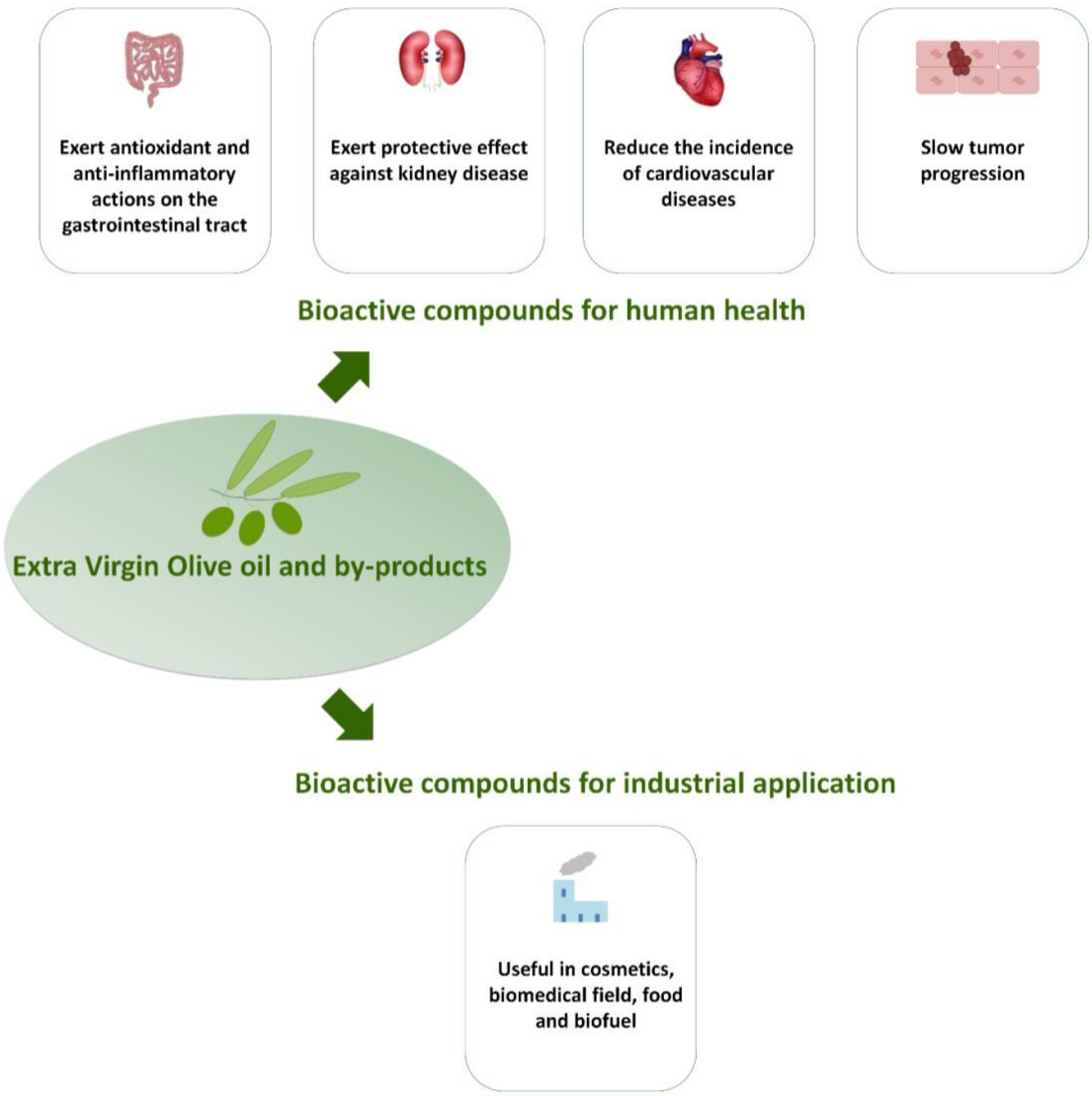
ABSTRACT

In the last few years, the production of olive oil has incredibly increased due to its beneficial properties on human health. On the other hand, the amount of waste and by-products derived from the olive oil industry has increased as well, prompting the development of new fields of research aiming to reduce disposal costs and valorize bioactive compounds from the viewpoint of the green economy. Interestingly, olive oil and by-products contain numerous molecules, including phenols, exhibiting pleiotropic effects in both *in vitro* and *in vivo* studies. This review aims to describe the more recent studies focusing to identify and describe the potential roles and the new applications of extracts isolated from wastes and by-products or specific compounds, such as hydroxytyrosol (HT) and oleuropein. Extracts or bioactive molecules from olive oil and by-products have been proposed as a food additive, to produce biofuel, for animal feeding, and to create new matrices in bioremediation protocols. Moreover, bio-compounds have been described to have numerous beneficial effects on human health as they reduce the risk of developing certain chronic diseases. Despite the already published studies, more research is necessary to valorize bioactive compounds in olive oil and by-products, as well as their potential use to improve human health and green applications in different industrial processes.

Keywords: extra virgin olive oil, by-products, olive leaf extract, bioactive compounds, human health, and industrial application



The effect of electron beam on oxidative stress and inflammatory factors in diabetes mellitus: An in vitro and in vivo study

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ABSTRACT

Background: The main purpose of this study was to investigate whether or not electron beam therapy (EBT) was an effective method in terms of moderating oxidative stress by reducing free radicals in BALB/c mice with type 1 diabetes mellitus.

Methods: The study was performed on thirty BALB/c mice in three groups including normal control, diabetic control, and EBT treated. Before studying the effect of electron beam on the studied groups, optimal level of constant source-to-surface distance, as well as the effects of EBT on glutathione reductase (GR) structure and function were determined. After studying the structure and the function of GR protein with three methods including fluorometry, circular dichroism (CD), and activity assay methods, SSD 100 was selected for EBT. Glucose, advanced glycation end-products, GR, oxidative stress factors such as hydrogen peroxide, malondialdehyde, advanced oxidation protein products, oxidized low-density lipoprotein, and inflammatory factors were measured in the serum of all groups.

Results: The results of in vitro study showed that electron beam therapy could increase glutathione reductase activity, which was not significant. Also, the results were compared between and within groups using one-way analysis of variance. Significant differences were observed for all variables measured between the normal control group and the other groups ($P < 0.05$). There was also no significant difference in blood glucose levels between the electron beam therapy treated group and the diabetic one ($P > 0.05$).

Conclusion: The results suggested that electron beam therapy could be effective in reducing free radicals and oxidative stress. Electron beam therapy, as a complementary method, might aid in moderating the complications of diabetes mellitus.

Keywords: Diabetes mellitus, Electron beam, Inflammatory factors, Oxidative stress

Effects of the consumption of proanthocyanidins derived from acacia bark on blood pressure in healthy Japanese adults: A randomized, double-blind, placebo-controlled, parallel-group comparison study

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Submission Date: June 11th, 2021; **Acceptance Date:** July 12th, 2021; **Publication Date:** July 16th, 2021

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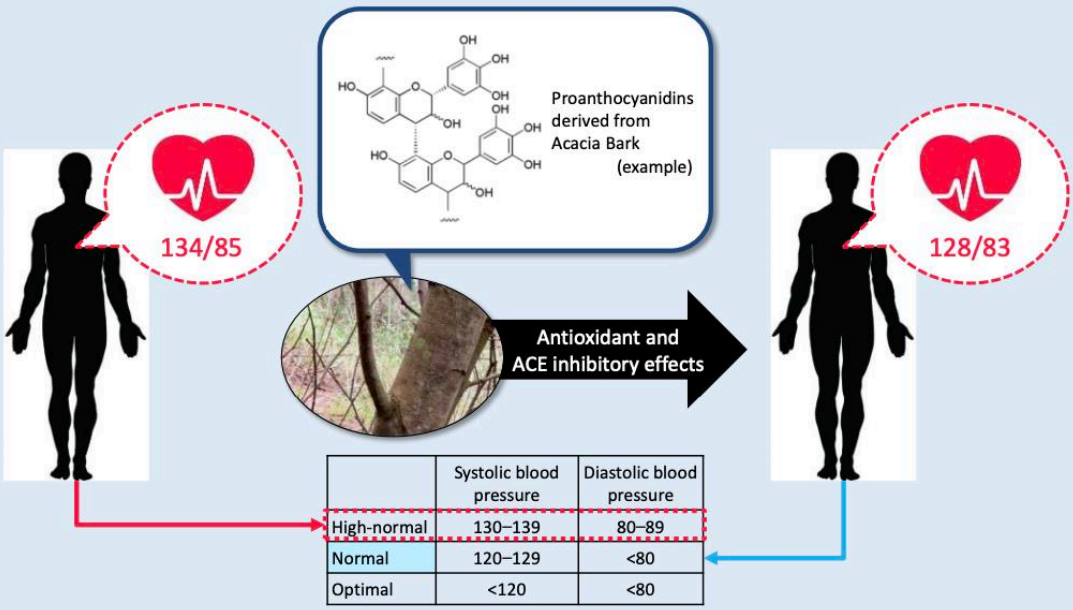
Objective: The aim of this study is to verify the effects of consuming proanthocyanidins derived from acacia bark on improving blood pressure and blood circulation in healthy Japanese adult subjects.

Methods: This was a randomized, double-blind, placebo-controlled, parallel-comparison study involving 66 healthy Japanese adults. Subjects were allocated into either acacia or placebo group (n = 33 each) using a random number generator. Subjects consumed six tablets/day of either acacia bark extract tablets or placebo for 12 weeks. The primary outcome was the measured value of sitting systolic blood pressure at 12 weeks, whereas the secondary outcomes were sitting systolic and diastolic blood pressures, superoxide dismutase activity in blood, and blood flow.

ABSTRACT



	Systolic blood pressure	Diastolic blood pressure
High-normal	130–139	80–89
Normal	120–129	<80
Optimal	<120	<80

Results: The number of subjects analyzed as full analysis set was 33 (20 men and 13 women) in the Acacia group and 31 (23 men and 8 women) in the placebo group. Compared with the placebo group, the measured values and changes from baseline at 4, 8, and 12 weeks of the sitting systolic blood pressure were significantly lower in the Acacia group. Furthermore, “the ratio of the number of subjects whose sitting systolic blood pressure <130 mmHg and diastolic blood pressure ≤89 mmHg at 12 weeks” of the Acacia group was significantly higher than that of the placebo group. No adverse event was observed.

Conclusions: Proanthocyanidins derived from acacia bark showed a hypotensive effect.
Trial registration: UMIN-CTR: UMIN000039416.
Foundation: Acacia-No-Ki Co., Ltd.

Keywords: Acacia bark extract, Proanthocyanidins, Systolic blood pressure, Diastolic blood pressure

Adherence to the Mediterranean diet: An online questionnaire based-study in a Spanish population sample just before the Covid-19 lockdown

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ABSTRACT

Background: The Mediterranean Diet (MD) has been associated with a reduced risk of developing several pathologies, such as cardiovascular diseases. Despite this, adherence to MD in the general population has decreased in the past years. Due to COVID-19 crisis, eating habits of the population are being affected, thus data assessing these habits just before lockdown are important to determine how they are modified. The Mediterranean Diet Quality Index (KIDMED) questionnaire was used to evaluate adherence to MD just before COVID-19 lockdown.

Methods: The KIDMED survey was launched through the Google platform for surveys, from 2/20/20 until 3/13/20. Additionally, questions about gender, weight and height for body mass index (BMI) calculation, academic degree, and nationality were included. Multivariate linear regression was performed for data analysis.

Results: A total of 861 completed surveys were collected. Some surveys were discarded because data was missing (18), the participants were not of Spanish nationality (18), or because they did not belong to the age groups

included in the study (19). The remaining 804 surveys were divided into the following age groups: 15-24 (n=160), 25-34 (n=158), 35-54 (n=363) and 55-69 (n=123). In the 15–24-year-old group, 71.9% had a BMI between 18-24.9, but only 28.1% reached an index ≥8 in the KIDMED questionnaire. Adherence to MD improved as the age in the groups increased, but so did the BMI, especially in the oldest group. In all adult groups, approximately 50% had a university education. Overall, lower BMI was significantly related to females, younger age and a higher degree of studies. On the other hand, the higher adherence to MD was related to older age and a higher degree of education.

Conclusions: The improved adherence to MD was not associated with a reduced BMI. Maybe other factors, like sedentary life or hormonal changes, known to impact people while aging, have influenced our results. Possibly, adherence to MD might have played a protective role, at least partially, against an even higher BMI. More research is needed to fully determine the impact of adherence to MD in the Spanish population, also after COVID-19 lockdown.

Keywords: Mediterranean diet, KIDMED, Body mass index, Spain.

Suppressive effect of a single dose of monoglucosyl rutin on postprandial blood glucose elevation: A randomized, placebo-controlled, double-blind crossover study

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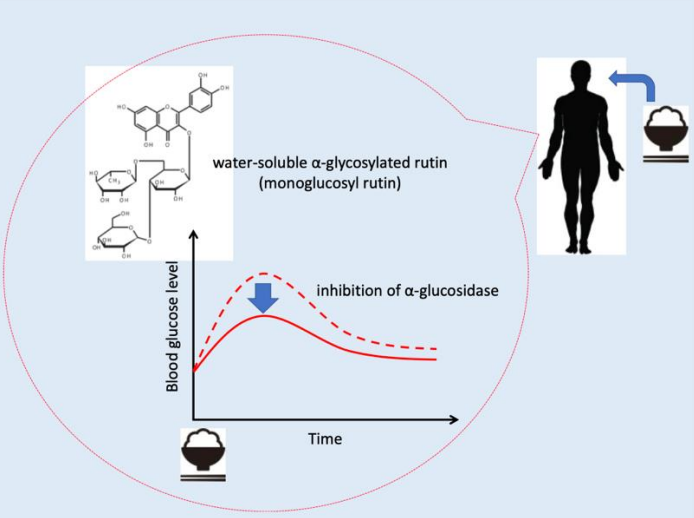
ABSTRACT

Objective: This study aimed to investigate the suppressive effect of a single dose of water-soluble α- glycosylated rutin (monoglucosyl rutin; MR) on postprandial blood glucose elevation in healthy subjects with relatively high fasting blood glucose levels.



Methods: This randomized, placebo-controlled, double-blind crossover study enrolled 34 healthy Japanese adult subjects with relatively high fasting blood glucose levels. The study period ran from November 13, 2019, to March 19, 2020. All subjects were randomly allocated to either sequence A or sequence B (n = 17 per group) using a computerized random number generator. The washout period was at least one week between periods I and II. In period I, the subjects took either MR or placebo tablets. In period II, subjects took different tablets from the ones they had taken in period I. We evaluated their blood glucose and insulin levels after glucose loading (150 g of cooked rice). The incremental area under the curve (IAUC) of the postprandial blood glucose level was determined as the primary outcome. The blood glucose and insulin levels at maximum (maximum blood concentration; Cmax), each measurement point, and IAUC of the blood insulin level after glucose loading were the secondary outcomes.

Results: Out of 33 subjects, 16 in sequence A (11 men and 5 women, 54.5 ± 9.8 years) and 17 in sequence B (9 men and 8 women, 58.8 ± 9.4 years) were analyzed as a per-protocol dataset. The glucose IAUC after MR consumption was significantly lower than that of the placebo (P = 0.034). Results of the other outcomes were not observed with significant treatment effects. There were no adverse events attributable to the test foods.

Conclusions: We suggest that MR has a suppressive effect on the elevation of postprandial blood glucose in healthy adults with relatively high fasting blood glucose levels.

Trial registration: UMIN-CTR: UMIN000038515. **Foundation:** Toyo Sugar Refining Co., Ltd.

Keywords: monoglucosyl rutin, blood glucose level, incremental area under the curve, α-amylase, α-glucosidase, crossover study

Effects of Theracurmin® consumption on liver function, fatigue, and sleep: a randomized, double-blind, placebo- controlled, parallel-comparison study

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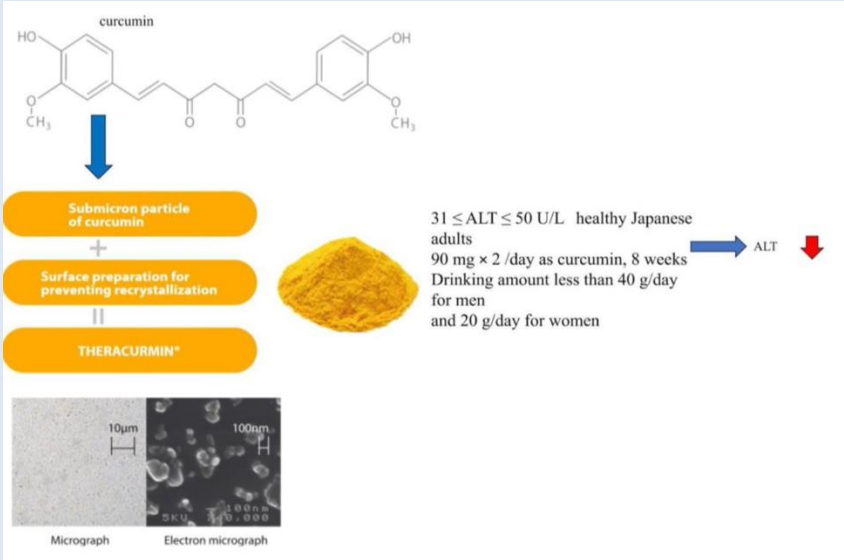
ABSTRACT

Objective: To evaluate the effects of the eight-week consumption of Theracurmin® on liver function, fatigue, and sleep.

Methods: This was a randomized, double-blind, placebo-controlled, parallel-comparison study involving 68 healthy Japanese adults. Subjects were allocated into either the active (Theracurmin®) or placebo group (*n* = 34 each) using a random number generator. Subjects consumed two capsules per day of either the active or placebo food for eight weeks. The primary outcome was the serum alanine aminotransferase (ALT) levels at eight weeks, whereas the secondary outcomes were the biomarkers of liver function, comparison of the percentages of improvement in liver function based on the decision criteria, OSA sleep inventory MA version (OSA-MA), and visual analog scale of fatigue.



Results: Each group included 33 subjects in the full analysis set. ALT levels in the per protocol set analysis, except for subjects drinking quantities of alcohol that increase the risk of lifestyle-related disease onset, showed a

significant decrease in ALT compared to the placebo group ($P < 0.05$). The subjective symptom in the fatigue recovery factor of OSA-MA was significantly improved through the intervention ($P < 0.05$). The fatigue recovery effect of Theracurmin® was prominent in the subjects aged ≤ 45 years, the age group defined by the Ministry of Health, Labour and Welfare as middle-aged and older persons in the Act on Stabilization of Employment of Elderly. No adverse event was observed.

Conclusions: These results suggest that the consumption of Theracurmin® or eight weeks improved liver function and fatigue recovery at awakening in healthy Japanese adults.

Trial registration: UMIN-CTR: UMIN000039319. **Foundation:** Theravalues Corporation

Keywords: highly bioavailable curcumin, liver function, alanine aminotransferase (ALT), OSA sleep inventory MA version, fatigue recovery

BCHD

Protective effect of Zingiber zerumbet Smith extract on thermotolerance

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ABSTRACT

Background: Global warming causes severe heat conditions. Heat stress contributes to higher morbidity of heatstroke in human and mortality in livestock. To protect them from heat stress, thermotolerance mechanisms were widely studied, and some studies suggest relationship between heat shock proteins (HSPs) and thermotolerance. HSPs were not induced by only heat shock but also some stimulations including bioactive compounds from plants. Zingiber zerumbet is a perennial herb found in many tropical countries, including Thailand. The rhizome of Zingiber zerumbet contains zerumbone that is a bioactive compound to induce HSPs expression in animal cells.

Objective: To prevent higher morbidity of heatstroke in human and mortality in livestock by the heat stress, we investigated the effect of zerumbone, the extract of Zingiber zerumbet Smith, on thermotolerance, using a cell line and mice.

Methods: The murine liver hepatoma cell line, Hepa1c1c7 cells, were incubated in medium supplemented with extract from rhizome of Zingiber zerumbet Simith containing zerumbone, and then the expression of heat shock proteins (HSP) 40, 70 and 90 were investigated by western blotting. Furthermore, we established the evaluation system of thermotolerance using mice, and studied the effect of the extract on the growth rate of mice under the heat shock treatment. Briefly, 4 weeks old C57BL6 mice were fed that with the extract (or vehicle) for a week before the first heat shock treatment (38 °C for an hour). Before and after five days heat treatment, body weights were measured. The protein expressions of heat shock proteins in liver were measured by western blotting using HSPs antibodies.

Results: The extract of Zingiber zerumbet rhizome, equivalent to 50 μM zerumbone, significantly increased the expression of heat shock proteins (HSP40, HSP70, HSP90). The growth rate of the mice under the heat treatment were lower than control. The feeding with the extract containing 25 ppm zerumbone have significantly attenuated the decline of the growth rate led by the heat treatment, whereas there was little effect on mouse growth rate grown under normal conditions. The protein expression of HSP70 in the liver of zerumbone-fed mice was upregulated compared with control mice, equivalent to heat treatment without zerumbone. On the other hand, both treatments of zerumbone and heat resulted in highest HSP70 expression among four groups.

Conclusion: Our study demonstrated that oral administration of the extract of Zingiber zerumbet Smith led to the attenuation of decline of growth rate induced by heat treatment. HSP70 expression in murine liver was enhanced by either feeding the extract or heat treatment. More interestingly, HSP70 expression was further enhanced by both treatments of zerumbone and heat. These results suggested that zerumbone may contribute to thermotolerance via, at least, HSP70 expression.

Keywords: Zingiber zerumbet, thermotolerance, heat shock protein

Link to Full Article: https://ffhdj.com/index.php/BioactiveCompounds/article/view/777/1368

FFHD

Effect of cassava on proximate composition, insulin index, glycemic profile, load, and index in healthy individuals: a cross-sectional study

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ABSTRACT

Background: The major challenge in Africa is the growing prevalence of metabolic syndrome which has been attributed to changing lifestyles in developing countries. The impact of the commonly available staple starchy food; eaten in this environment may also be a factor contributing to growing concerns of metabolic syndrome. Hence, the need to assess the affordable staple starchy foods. Cassava is the most consumed staple starchy food in our environment; therefore, our study evaluated its impact on glycaemic and insulin response in consumers.

Aim: To determine Insulin Index (II), glycaemic profile (GP), glycaemic load (GL) and Glycaemic Index (GI), incremental glucose peak value (IGPV), and glycaemic profile index (GPI) of cassava food meals.

Methods: Participants ingested three cassava processed products (cassava dough [fufu], chips [Abacha], and flakes [garri] (the equivalent of 50g glucose) and 50 g of reference meal (glucose solution). Fasting and post- prandial samples were taken for blood glucose and insulin however sample for glucose was taken at intervals of 30 mins to a maximum of 180mins and 120 mins for insulin, respectively.

Result: The GI for cassava dough, flakes and chips were 93.26; 95.92 and 91.94, respectively. Their glycaemic load was 46.62; 47.96 and 45.97, respectively. The glycaemic profile index was 37.34; 41.41 and 46.19, respectively. In addition, the insulin index was 55.83; 69.36 and 97.02. The proximate analysis showed protein, moisture, fibre, fat, ash, and carbohydrate content as follows the cassava (%) (crude form) 1.075%; 72.00%; 0.80%; 0.58%; 0.35%; 25.07%, Chips 1.44%; 59.13%; 0.73%; 1.71%; 36.83%, flakes 1.82%; 67.36%; 0.15%; 0.91%; 0.25%; 39.64% and dough 1.56%; 67.51%; 0.21%; 0.52%; 0.20%; 30.22% respectively.

Conclusion: II, GP, GL, and GI of cassava dough (fufu), cassava flakes(garri)and cassava chips (Abacha) were found to be high. Unregulated dietary intake in adults may lead to metabolic diseases.

Keywords: Glycaemic index, Glycaemic load, Glycaemic profile, Cassava, Makurdi

Link to Full Article: https://ffhdj.com/index.php/ffhd/article/view/772/1371

FFHD

Eryngium caeruleum essential oil as a promising natural additive: in vitro antioxidant properties and its effect on lipid oxidation of minced rainbow trout meat during storage at refrigeration temperature

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ABSTRACT

Background: One of the most common species of oily fish is rainbow trout. Chemical deterioration of oily fish species is principally caused by lipid oxidation. The adverse effects of various chemical preservatives caused consumer's attention to shift to natural alternatives. Eryngium caeruleum is an herbaceous plant that is native to the northern areas of Iran and is used in various local foods. The aim of the present study was to investigate the effects of different concentrations of E. caeruleum essential oil (EEO) on the physicochemical and oxidative stability of minced rainbow trout meat for 20 days storage at 4±1°C.

Methods: Firstly, the chemical compounds and total phenolic content of EEO were determined by gas chromatography-mass spectrometry and Folin–Ciocalteu reagent, respectively. Then, in vitro antioxidant capacity of EEO was evaluated using 2,2-Diphenyl-1-picrylhydrazyl (DPPH) and 2,2'-azino-bis (3-ethylbenzthiazoline-6-sulphonic acid) (ABTS) methods. Finally, the minced rainbow trout meat was mixed with different concentrations of EEO, and physicochemical and oxidative stability of treatments were investigated for 20 days storage at 4±1°C.

Results: According to the results, 0.4% EEO significantly improved the chemical stability of minced fish compared to control group at the end of storage period with the following scores ($P<0.05$): pH value (6.3), peroxide value (11.88 meq/kg of lipid) and thiobarbituric acid reactive substance (0.43 mg MDA/kg sample). Conclusions: In order to increase the chemical quality characteristics of minced fish, new ingredient systems that are associated with natural and organic foods are applied. The results of present study indicate that the use of EEO in the meat industry can develop the novel healthy fish products and improve its chemical stability.

Keywords: Eryngium caeruleum, Oncorhynchus mykiss, Natural antioxidant, Chemical stability, Lipid oxidation.

Link to Full Article: https://ffhdj.com/index.php/ffhd/article/view/766/1372

BCHD

No evidence of allergenic reactions to soy lecithin phospholipids used in Membrane Lipid Replacement studies

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ABSTRACT

Abstract: Membrane Lipid Replacement (MLR) is the functional use of dietary supplements containing cell membrane glycerolphospholipids and antioxidants to safely replace and remove damaged membrane phospholipids that accumulate during various chronic and acute illnesses and during aging. Some products used in MLR are obtained from soy lecithin extracts that contain cell membrane glycerolphospholipids. Thus the soybean source has been questioned because of concerns related to genetic engineering (GMO) and the potential presence of hormone-like components and soy allergens. There is a complete absence of proteins, glycoproteins or carbohydrates in soy lecithins and MLR supplements that could be allergenic. One lecithin ingredient that contains purified membrane phospholipids (NTFactor Lipids®) has been shown to produce significant positive health benefits in clinical trials. NTFactor Lipids® are fractionated and purified from non-GMO soy lecithin, but this formulation does not contain detectable amounts of protein or glycoprotein allergens or other components that could elicit allergic or non- allergic adverse reactions. In addition, allergenic and non-allergenic reactions have not been found in multiple clinical trials and studies that have utilized this dietary supplement. NTFactor Lipids® are manufactured in certified Good Manufacturing Practices (cGMP) facilities using established allergen-control strategies to minimize any cross-contact with food allergens.

Keywords: Phospholipids, Clinical trials, Allergies, Cellular membranes

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FFHD

Enhancing effect of glycine and tryptophan mixture on estimated glomerular filtration rate in healthy participants: A randomized, double-blind, placebo-controlled parallel study

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ABSTRACT

Background: The mixture of glycine and tryptophan exhibited serum uric acid-lowering effects in our previous clinical trial.

Objective: Using a randomized, double-blind, placebo- controlled, and parallel study design, this current study aimed to examine whether this mixture enhanced the estimated glomerular filtration rate (eGFR) as an indicator of renal function in healthy individuals.

Methods: Healthy Japanese adult males and females ingested a powder mixture containing 3.0 g of glycine and 0.2 g of tryptophan or a placebo powder once daily at bedtime for 8 weeks.

Results: After 8 weeks of continual ingestion, the combined glycine and tryptophan supplementation significantly enhanced eGFR. It also decreased serum uric acid levels, consistent with our previous reports. Meanwhile, the continual ingestion of the mixture had no influence on serum total or essential amino acids.

Conclusions: The current study demonstrated that the combined oral administration of glycine and tryptophan significantly elevated the eGFR of healthy participants. However, further investigation is required to elucidate the detailed mechanisms underlying the potential therapeutic or preventive effect of combined glycine and tryptophan supplementation. Nevertheless, the uric acid-lowering effect of glycine and tryptophan mixture has the potential to directly influence renal function.

Key words: glycine, tryptophan, estimated glomerular filtration rate, uric acid

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FFHD

Flavonoids from the leaves and twigs of *Lindera sericea* (Seibold et Zucc.) Blume var. *sericea* (Lauraceae) from Japan and their bioactivities

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ABSTRACT

Background: The leaves and twigs of Lindera sericea (Seibold et Zucc.) Blume var. sericea (Lauraceae) are used as traditional medicines for treating indigestion, stomachache, anxiety, etc. In recent years, there has been a growing interest in these plant materials as a source of healthy drinks and functional foods. The main aim of this study was to characterize the major phenolic compounds from the leaves and twigs and to evaluate their free radical scavenging and α-glucosidase inhibitory activities.

Methods: The dried leaves and twigs were extracted with 70% methanol. The dried extract was then subjected to repeated column chromatography to isolate eight flavonoids. The compounds were then evaluated for their 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging activity and α-glucosidase inhibitory activity.

Results: The isolated compounds were identified as (-)-epicatechin (1), taxifolin 3-O-glucoside (2), quercetin (3), quercitrin (4), quercetin 3-O-neohesperidoside (5), pinocembrin (6), pinostrobin (7) and pinostrobin chalcone (8) based on their nuclear magnetic resonance (NMR), spectroscopic data and comparison with literature values. All these compounds were isolated for the first time from this plant. All flavonoids except pinocembrin (6), pinostrobin (7) and pinostrobin chalcone (8) showed potent free radical scavenging activity. In α-glucosidase inhibitory activity assay, quercetin (4), quercitrin (5) and taxifolin 3-O-glucoside (2) showed potent activity.

Conclusions: Eight flavonoids were reported for the first time from the leaves and twigs of the title plant. Some of these compounds showed potent free radical scavenging and α-glucosidase inhibitory activities.

Keywords: Lindera sericea var. sericea; Lauraceae; Kekuromoji; free radical; α-glucosidase

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FFHD

Choosing Suitable Food Vehicles for Functional Food Products

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ABSTRACT

Abstract: Globally, there is a growing demand for functional foods that provide health benefits without changing current dietary habits. However, the world is made up of diverse societies that consist of a wide range of individuals from different ethnic and cultural backgrounds associated with different food choices and preferences. Functional foods resemble traditional foods but have been designed and tailored to confer physiological and health benefits that go beyond their nutritional function. Of the seven-step cycle involved in functional food production, choosing a suitable food vehicle as a carrier of the bioactive components is essential. Therefore, this review explored the importance of food vehicles and how they can influence the acceptance of functional foods. Relevant scientific literature was electronically sourced from Google Scholar, Google, PubMed, databases of the Journals of Functional Foods in Health and Disease (JFFHD) and Bioactive Compounds in Health and Disease (BCHD) based on their mention or discussion of food choice and preference and food vehicles for food fortification or functional food production. These studies revealed that although functional foods are found virtually in all food categories, they are not homogeneously scattered over all segments of the growing market. Consumer demands and acceptance in terms of consumption patterns, ethnicity, culture, religion, and allergy, amongst others, need to be taken into consideration when choosing appropriate vehicles for functional food development.

Keywords: food vehicles, functional foods, food fortification, food choice, food preference, fortification, phytonutrients, bioactive compounds

Link to Full Article: https://ffhdj.com/index.php/ffhd/article/view/764/1380

FFHD

Effect of flavonoid-rich meals and low-flavonoid meals based on the dietary reference intakes for Japanese, using basic foodstuffs on the gene expression of inflammatory cytokines in the whole blood cells from adult men of normal or light overweight

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ABSTRACT

Introduction: Flavonoids have a variety of functions, such as antioxidant activity, and are expected to have a disease prevention effect. In order to verify the disease risk reduction effect of flavonoids, we carried out a crossover trial in seven adult men of normal or light overweight who ingested flavonoid-rich meals, with a diverse combination of basic foodstuffs, and low-flavonoid meals and compared blood disease-related inflammatory markers.

Methods: On the first two days of the study, seven male volunteers were provided with low-flavonoid meals (flavonoid content below the detection limit of HPLC: less than 0.24 mg/meal) three times a day as a washout. For the next seven days, they were fed flavonoid-rich meals (46.9 ± 8.1 mg/meal) or low-flavonoid meals. Blood samples were collected from all the volunteers before breakfast on the third day, after the washout and before breakfast on the tenth day. The test was consisted of one cycle from the first day to the tenth day, and the participants carried out two cycles. Flavonoid concentrations in plasma and gene expression of inflammatory cytokine (interleukin 1 beta, interleukin 6, interleukin 18, and tumor necrosis factor-α) in whole blood cells were compared before and after the intervention. Gene expression in whole blood cells was measured using real time RT-PCR.

Results: We found a significant increase in plasma flavonoid concentration (quercetin, kaempferol, daidzein, and genistein) upon intervention with flavonoid-rich meals ($p < 0.05$). In addition, the inflammatory cytokine gene expression was reduced in the subjects with a body mass index of more than, but not less than, 25 kg/m2 compared with that observed after the intake of low-flavonoid meals.

Conclusion: These results suggest that flavonoid-rich meals have an anti-inflammatory effect in obese persons who are likely to have chronic inflammation.

Keywords: Flavonoids, inflammatory cytokines, flavonoid-rich meal, human study

Link to Full Article: https://ffhdj.com/index.php/ffhd/article/view/781/1386

BCHD

The effect of cold plasma on antioxidant enzymes, minerals, and some of the levels of the biochemical parameters in the subjects with type 2 diabetes mellitus samples

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ABSTRACT

Introduction: Hyperglycemia in people with diabetes mellitus and its lack of control are associated with irreversible consequences. Glycation of proteins and enzymes, especially antioxidant enzymes in uncontrolled diabetes mellitus, affects these consequences. Consumption of bioactive compounds containing antioxidants and minerals as well as the use of adjunct therapies, such as cold atmospheric plasma therapy, can be effective in preventing and controlling the consequences of diabetes mellitus.

Objective: In this research, we investigated whether cold plasma treatment of diabetic samples was effective in altering the activity of oxidative enzymes, some biochemical elements, and biochemical parameters.

Methods: Thirty individuals with type 2 diabetes mellitus and 30 healthy individuals, as controls, participated in the study. The samples were exposed to cold argon plasma jet for 10 minutes (by a 10 kHz pulsed DC power supply with an amplitude up to 20.0 kV). The following contents of the serum samples of all participants were evaluated according to the instructions of the used kits before and after the cold argon plasma jet treatment: the activity of catalase, superoxide dismutase, and glutathione peroxidase enzymes; the concentration of glucose, hydrogen peroxide, and selenium binding protein 1 (as an indicator of blood selenium); and the concentration of copper, zinc, iron, and magnesium.

Results: The activity of antioxidant enzymes and minerals significantly increased in diabetic samples treated with cold plasma (P value < 0.05). No significant changes were observed in the concentrations of glucose, hydrogen peroxide, or selenium binding protein 1 in diabetic samples treated with cold plasma.

Conclusions: Using cold argon plasma jet as an adjunct method, which will reduce the glycation of enzymes and improve some minerals, can reduce the risk of diabetes complications in patients with diabetes mellitus.

Keywords: Antioxidant enzymes, Cold plasma, Diabetes mellitus, Minerals.

Link to Full Article: https://ffhdj.com/index.php/BioactiveCompounds/article/view/783/1382

FFHD

The green tea polyphenol EGCG is differentially associated with telomeric regulation in normal human fibroblasts versus cancer cells

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ABSTRACT

Introduction: Topical investigations have demonstrated that oxidative stress and inflammation play key roles in biological aging and determine incidence and course of age-related diseases. Lifestyle and environmental factors hugely impact epigenetic regulation and DNA stability with telomere attrition and epigenetic instability providing a potential record of the cumulative burden of endogenous and exogenous oxidative noxae. Certain physiologically active plant components exhibit antioxidative activities affecting epigenetic regulation of inflammation response and DNA repair.

Methods: Against this background, the present study investigated green tea polyphenol epigallocatechin gallate (EGCG) in the context of telomere regulation in Caco-2 colorectal adenocarcinoma cells vs. ES-1 primary skin fibroblasts. Cell lines were treated with 20 and 200 µM EGCG for 36, 72 and 144 hours, respectively. Telomerase activity, relative telomere length as well as methylation status of hTERT and c-Myc from different culture conditions were assessed. Malondialdehyde (MDA) served as a surrogate marker of potential pro- oxidative effects of EGCG in a physiologically relevant tissue model.

Results: EGCG incubation was associated with telomere shortening and decreased telomerase activity in Caco-2 cells, and relatively longer telomeres along with increased methylation of six 5'—C— phosphate—G—3' (CpG) sites in the promoter region of human Telomerase Reverse Transcriptase (hTERT) in fibroblasts. At low concentrations, EGCG significantly decreased oxidative damage to lipids in Caco-2 cells and attenuated H2O2 induced oxidation at higher concentrations.

Conclusion: These results suggest differential EGCG-
mediated telomeric modulation in cancer vs. primary cells and a specific antioxidant activity of EGCG against oxidative damage to lipids in abnormal cells.

Keywords: Caco-2, epigallocatechin gallate, telomeres, hTERT, DNA methylation, telomerase, oxidative stress, malondialdehyde

Link to Full Article: https://ffhdj.com/index.php/ffhd/article/view/775/1387

FFHD

Oil emulsion from *Plukenetia huayllabambana* (Sacha inchi) modifies nitric oxide and leptin in the liver and antioxidant and inflammation markers in the adipose tissue in obese rats

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ABSTRACT

Background: Obesity is characterized by excessive accumulation of adipose tissue and is associated with higher risk of metabolic diseases and other comorbidities. Efficacious strategies including a diet high in "functional foods" are promising. Plukenetia huayllabambana known as Sacha Inchi (SI), is a legume which seeds are rich in proteins, tocopherols, and fatty acids such as omega-3 (ω-3). The latter has emerged as a potential protective nutrient against the cardiometabolic risks associated with obesity. Omega-3 changes the membrane lipid profile of hepatic and adipose cells triggering the expression of antioxidant and anti-inflammatory genes. However, there are few reports in relation to the effect of these oils in inflammatory and stress response related to obesity. In this sense, the present study evaluated the effect of SI oil emulsion on nitric oxide and leptin levels in the liver and some markers of oxidative stress and inflammation in adipose tissue from the rodent obesity model.

Methods: Six groups were formed: Not obese control group (Noc), obese control (Oc), two groups treated with the emulsion of SI oil (Os1:0.25g ω-3/day; Os2:0.5g ω-3/day), one obese group treated with atorvastatin (Oa) and one group treated with atorvastatin plus the emulsion of SI oil (Oas2).

Results: Os1 and Os2 lowered nitric oxide and increased liver leptin levels. In the adipose tissue, the superoxide dismutase and reducing antioxidant power increased significantly in Os1 and Os2 groups. The anti-inflammatory marker IL-4 was also increased in Os2, Oa and Oas2 compared to the Oc and IL-10 increased in Oas2 group.

Conclusion: Our study suggests that the emulsion of SI oil can modify the inflammatory and stress responses associated with obesity and it can be incorporated as a promising functional food.

Keywords: Inflammation, leptin, obesity, nitric oxide, oxidative stress, SI oil emulsion.

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FFHD

Cholesterol in virus entry into host cell: diet, phytosterols and statins

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ABSTRACT

Abstract: Cholesterol has been reported in a number of studies to play an essential role in the effectiveness of viral infection in mammal cells. The main characteristic of cholesterol that is involved in viral infection is its capability to afford negative curvature to the membrane. This faculty of cholesterol has
to do with the necessary steep curvature that the host cell membrane undergoes in the primary processes of viral infection. In particular, for RNA enveloped viruses, membrane curvature is involved in two mechanisms of the viral infection, which are virus and host cell membrane fusion for viral genome release and virus reproduction scaffold build-up. Low cholesterol diets have been shown to reduce or even suppress virus infection efficiency in murine models or cell cultures; but to what extent a diet-based lowering of the blood cholesterol level may help preventing virus infection still lacks enough scientific evidence. The use of statins in individuals with hypercholesterolemia has been recommended in the recent COVID-19 outbreak. The possibility of using sterols from natural sources in the diet or in supplementary concentrates has been suggested to be an alternative to drop the circulating cholesterol. In this manuscript, the most relevant and recent bibliography on the aforementioned issues is reviewed.

Keywords: cholesterol, virus infection, membrane curvature, sterols, natural food sources

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BCHD

Bioactive compounds in functional food and their role as therapeutics

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ABSTRACT

Abstract: Bioactive food ingredients are non-essential substances found in foods that can modulate one or more metabolic processes, resulting in enhanced health. Functional diets have attracted more critical than ever as an alternative to conventional treatments of many diseases. The medicinal potential of functional foods and nutraceuticals are due to some unique functional groups produced due to food metabolism and their molecular variants. Phytochemicals are biologically active, naturally occurring chemical compounds in plants with various biological properties and therapeutic benefits. While functional foods and natural bioactive compounds have been used as conventional medicines to treat chronic diseases for decades, recent scientific findings identify functional foods' health advantages and present the basic mechanisms of their behaviors. Phytochemicals have essential bioactive roles in the prevention and treatment of oxidative and inflammatory diseases. Plant-derived bioactive compounds can help suppress inflammation by inhibiting oxidative damage and communicating with the immune system. Many bioactive components are capable of binding to intestinal tract toxins or carcinogens. These bioactive peptides control diet-related medical conditions such as obesity, cardiovascular diseases, and other metabolic diseases. Various bioactive compounds in common food and their therapeutic role is discussed in this review.

Keywords: Functional food, phytochemicals, bioactive peptides, therapeutic effects.

Link to Full Article: https://ffhdj.com/index.php/BioactiveCompounds/article/view/786/1395

FFHD

The effect of consuming an anthocyanin-containing supplement derived from Bilberry (Vaccinium myrtillus) on eye function: A Randomized, Double-Blind, Placebo Controlled Parallel Study

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ABSTRACT

Objective: The purpose of this study was to determine the effects of 6-week consumption of anthocyanin-containing supplement on eye function.

Methods: This was a randomized, placebo-controlled, double-blind, parallel-group comparison study involving 32 healthy Japanese adults with eye fatigue after using visual display terminals (VDTs). Subjects were randomly allocated into either the active group (bilberry-derived anthocyanin 43.2 mg per capsule) or placebo group using a random number generator. Subjects consumed either one active or placebo capsule once a day for 6 weeks. The primary outcome measured was the change in percentage of pupillary response pre- and post-VDT use, whereas the secondary outcomes were tear film break-up time, Schirmer's value, muscle hardness, and subjective symptoms. Experimental data was analyzed using Student's t-test, the two-way analysis of covariance, or Mann– Whitney U-test.

Results: Each group included 15 subjects in the efficacy analysis. The active group showed a significant improvement in the logarithmic conversion values of the percentage of pupillary response (active group: 0.2 ± 0.4, placebo group: 0.0 ± 0.3; P = 0.043) and pupillary response/near point (active group: 0.1 ± 0.4, placebo group: −0.1 ± 0.3; P = 0.049) pre- and post-VDT use at 6 weeks compared with the placebo group in a subgroup analysis per eye. No adverse events were reported.

Conclusions: The consumption of the supplement containing anthocyanins extracted from bilberry for 6 weeks inhibited the decrease in the accommodative function caused by oxidative stress due to VDT use.

Trial registration: UMIN-CTR: UMIN000037039.

Foundation: BGG Japan Co., Ltd. and Arysta Health and Nutrition Sciences Corp. Keywords: accommodative function; anthocyanin; bilberry; visual display terminals

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BCHD

Vitamin D and COVID-19: Partial Evidence

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ABSTRACT

Abstract: The COVID-19 pandemic, now in its second year, has created challenges for health maintenance. Lockdowns, working from home and social distancing have all created changes to the way we live, increasing stress, anxiety and depression and impacting our lifestyle habits such as diet and exercise. This may be particularly concerning considering the association between obesity and adverse outcomes of COVID infection including hospitalization, invasive ventilation, and death. While vaccines are now available, they were not an option earlier in the pandemic, and researchers and clinicians alike sought interventions to prevent infection and reduce risk of adverse outcomes. Among these are nutrition supplementation with vitamin D. This nutrient plays an important role in maintaining the integrity of the immune system; however, it is essential to examine its performance on a population level to assess its efficacy, and to consider findings in the context of the hierarchy of evidence.

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FFHD

Health Communication in Nutrition for Cancer Prevention in Thailand

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ABSTRACT

Abstract: Cancer has been ranked first of the Thai mortality causes. As dietary factors affect the risk of cancer, communication is crucial for providing beneficial nutritional knowledge for patients to change their daily diets accurately. The communication could be through the use of the internet, as there is currently media that could be easily accessed at a large scale. As a result, modern technology could facilitate the interaction between citizens and nutritional professionals, leading to healthy lifestyles. For example, the nutritional labels of products could be read by using IoT, which is a mobile application. It is also believed that devices will be developed to help prevent cancer in the future.

Keywords: health communication, nutrition for cancer prevention, IoT, social media nutrition, nutrition labeling

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FFHD

Transcriptomic analysis reveals that combinations of vitamins A, D2, and D3 have synergistic effects in HCT-116 colon cancer cells by altering the expression of genes involved in multiple canonical pathways including apoptosis, regulation of the epithelial mesenchymal transition and immunity

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ABSTRACT

Abstract: Integrated systems biology approaches suggest that combinations of nutrients may be more effective against cancer due to the large number of signaling pathways associated with cancer initiation and promotion. In a previous work, we have reported that combinations of vitamins A (as all trans-retinoic acid, ATRA), D2, and D3 act synergistically to induce apoptosis in colon and gastric cancer cells. In this work, we use whole-genome transcriptomic profiling to detect gene expression changes using RNA-seq to more comprehensively investigate the biological pathways affected by the combination of vitamin D2, D3 and ATRA. HCT-116 colon cancer cells were harvested, RNA was isolated and RNA-seq libraries were prepared using a Universal Plus mRNASeq kit. Sequencing was carried out on NovaSeq 6000. General quality-control metrics were obtained using FastQC and raw reads were aligned to human reference genome hg38 using STAR and BWA MEM. ENSEMBL genes were quantified using FeatureCounts, and differential expression statistics were computed using EdgeR. Specific gene expression was validated using qPCR. Transcriptomic analysis showed that of 26,313 genes analyzed, the expression of 8,402 genes was significantly altered (4030 up- regulated and 4373 down-regulated, FDR<0.05) in the treated cells, of which, 3,621 genes were differentially expressed (fold change <-1 or >+1 and an FDR <0.05). Ingenuity Pathway analysis revealed the involvement of 97 canonical pathways, with the top pathways including: mechanisms of cancer, apoptosis, myc-mediated apoptosis, regulation of the epithelial mesenchymal transition, and immunity.

Keywords: apoptosis, cholcalciferol, colon cancer, caspase, CRMP1, ergocalciferol, IL-12, NOTCH1, RNA-seq, SMAD7, synergism, transcriptome

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FFHD

Plant-Based Polysaccharides and their Health Functions

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ABSTRACT

Abstract: Plants are valuable source of polysaccharides that make a large portion of our daily diet. These are natural polymers that are essential to sustain life. They provide high-value nutrition and positively help the immune system and improve the digestive properties. They also help in the elimination of toxic by-products from the human body. Polysaccharides and human health are inextricably linked and intertwined. These are also important components of the cell wall that provides its strength and integrity. Due to their indispensable role in human health, it is very important to know the different modifications and loss of nutritional value during the processing of plant material. Nowadays, these plant-based polysaccharides are used for diverse applications including wound dressing, drug delivery, laxative, cosmetic and pharmaceutical preparations. As an emerging area of plant-based medicines to reduce the side effects of synthetic sources, these polysaccharides are used to enhance the immunogenic response against a specific antigen. This review envisages some important polysaccharides (e.g.
mucilages and gums, glycosamine glycans and chitin/chitosan) and their medical, cosmetic, and pharmaceutical applications, with emphasis on the relationship between their structure and function.

Keywords: Polysaccharides; Nutrition; Health Functions; Cosmetics; Vaccine; Nutraceuticals

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FFHD

Tuna blood inhibits lipopolysaccharide-induced inflammatory mediators in RAW264.7 macrophages

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ABSTRACT

Background: This study aimed to evaluate the anti-inflammation effects of the freeze-dried tuna whole blood (FTB), and freeze-dried tuna blood cell (FTC) in LPS-induced RAW264.7 cells.

Methods: The RAW264.7 cells were pre-administered with FTB and FTC at different concentrations for 2 h and then stimulated with lipopolysaccharide (LPS) for 24 h. The production of reactive oxygen species (ROS), nitric oxide (NO), tumor necrosis factor-alpha (TNF-α), and interleukin-1 beta (IL-1β) in RAW 264.7 cells were then determined.

Results: The results showed that only FTB remarkably abolished LPS-induced ROS in RAW264.7 cells. FTB and FTC significantly decreased LPS-induced NO which IC50 values of FTB and FTC after 24 h were 78.58 and 22.47 µg/mL, respectively. TNF-α and IL-1β secretion were abolished by FTB and FTC in LPS-stimulated macrophages which IC50 values of both FTB and FTC after 24 h were more than 25 µg/mL, respectively. However, the efficacy of FTC against inflammatory mediators was due to cytotoxic effects on RAW 264.7 cells.

Conclusion: Tuna whole blood potentially inhibits inflammation through modulating the synthesis of several mediators and cytokines associated with the development of inflammation. These findings suggest a role of tuna blood on anti-inflammatory activity.

Keywords: Anti-inflammatory activity, RAW 264.7 cells, red blood cell, tuna blood, waste utilization

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BCHD

Japan's health food industry: An analysis of the efficacy of the FOSHU system

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ABSTRACT

Abstract: Health claims and their regulations have been a contended topic globally with varying degrees of standardization. Japan is one of the most advanced countries in terms of their view on the regulation of health claims and their role in the food industry. With the introduction of functional foods in 1984, Japan put health claims to use by informing consumers of specific health benefits of food products marketed and sold to them, while also cutting down on inflated and false claims made by food manufacturers. This was done with the establishment of Foods for Specified Health Uses (FOSHU) a few years later. Although extremely strict and sometimes problematic, the FOSHU system has served as a model of what functional foods could be if given the chance. Regulations in the United States differ in their beliefs that health claims should be approved based on a disease-food relationship rather than on an individual product basis. This, along with the lack of definition for functional foods, leads to a poorly organized health food sector in the United States. FOSHU is highly regarded and well trusted in Japan; so much so that FOSHU products and packaging helps promote non-FOSHU products with similar appearance. Yet, despite the system's tightly controlled mechanism, its efficacy and comprehensiveness to the average consumer has come under question. Due to tight regulations and the high costs and long wait times of developing FOSHU products, many small businesses find it difficult to apply for them. Subsequently, this trickles down to consumers and inhibits lower-income populations from purchasing these products. Additionally, the effectiveness of FOSHU products outside of a clinical setting has come into question from the scientific community. Factors including poor consumer education regarding FOSHU, as well as clinical settings that do not mimic the daily life of consumers have produced unsatisfactory results in the general public.

Keywords: FOSHU, Health Claims, Functional foods, After market research, Clinical setting, functional/active ingredient, FOSHU seal

Link to Full Article: https://ffhdj.com/index.php/BioactiveCompounds/article/view/795/1414

BCHD

Increased Sirtuin expression, senescence regulating miRNAs, mtDNA, and bifidobacteria correlate with wellbeing and skin appearance after Sirtuin- activating drink

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ABSTRACT

Background: Sirtuins attract high attention considering their properties to reverse molecular hallmarks of aging and age-related disorders. Many secondary plant ingredients (SPI) are known for their sirtuin-activating activities as well as epigenetic regulation of telomers, autophagy, senolysis, DNA repair but also improvement of gut microbiota. Furthermore, prebiotics enhanced butyrate and was shown to interact with SIRT pathways. This study investigated the effects of a drink containing a mix of different SPIs in combination with galactooligosaccharides (GOS) and their effect on SIRT activation, markers of aging relevant mechanisms, and gut microbiota composition in correlation with subjective wellbeing and skin structure appearance.

Methods: We analyzed gene expression, mtDNA amount, and microbial composition in response to a sirtuin-activating drink in humans compared to a control group consuming a placebo. Food frequency, beauty, and general health questionnaires were asked, and a set of mRNAs and miRNAs were assessed using qPCR analysis. The gut composition was analyzed using Illumnia sequencing.

Results: SPI increased SIRT1, SIRT3, and modulated cell cycle relevant miR16 and senescence regulating miR34 expression. Additionally, mtDNA amount was higher in the group consuming the active supplement indicating an improved mitochondrial activity. The combined effect of SPI and GOS lead to an increase of Actinobacteria, especially Bifidobacterium, but also Veillonellaceae which was not observed in the control group. Significant correlations between SIRT3 expression and the gut microbiota Bifidobacterium and Veillonellaceae were observed. Additionally, statistical analysis of subjects self-reporting indicated beneficial effects regarding beauty and wellbeing.

Conclusion: Our results show that the combination of sirtuins inducing SPI and prebiotic GOS influences molecular pathways counteracting aging, senescence, inflammation, and enhanced groups of gut microbiota which are known to improve the innate and adaptive immune system.

Keywords: secondary plant ingredients, prebiotic, Sirtuins, subjective wellbeing, Bifidobacterium

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FFHD

Can functional foods reduce the risk of disease? Advancement of functional food definition and steps to create functional food products

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ABSTRACT

Background: The definition of functional foods (FFs) has been in development for many years by the Functional Food Scientists of the Functional Food Institute/Functional Food Center (FFC). The status of the FFC's definition is currently unrecognized by the Food and Drug Administration (FDA), but recognition is important for the safe, uniform development and disbursement of functional food products
(FFPs) that could improve the health of Americans and people around the world struggling with chronic and viral diseases. If functional foods were to be properly termed using the FFC's current definition, they would be classified as a drug according to the FDA. Thus, the FFC is in communication with governmental representatives to determine the next steps for functional foods to be properly acknowledged. To that end, the FFC is revising its current definition of functional foods to fit a more accurate and encompassing idea of the nature of what functional foods do. This includes a shift to stressing how functional foods promote optimal health, reduce the risk of chronic/viral disease, and manage their symptoms. Additionally, the process of developing a functional food product must be standardized to ensure the safety of administering bioactive compounds as a health optimization tool. This process follows the methodology of functional food science, which is a potential new form of life science proposed by the Functional Food Center. Over time, the FFC has been developing the appropriate steps to create a functional food product, however, in this article, new steps are emphasized, such as epidemiological studies and after-market research—vital steps to ensuring the safest and most efficacious product is released to the public. Functional foods are not meant to take the place of conventional medicine. They can, however, be used in conjunction with Western medicine and serve as an aid to health optimization for people with chronic/viral diseases and prioritize the management of symptoms associated with those diseases.

Keywords: functional foods, bioactive compounds, biomarkers, functional food science, functional food products, epidemiological studies

Link to Full Article: https://ffhdj.com/index.php/ffhd/article/view/788/1416

FFHD

Black tea decreases postprandial blood glucose levels in healthy humans and contains high-molecular-weight polyphenols that inhibit α-glucosidase and α-amylase in vitro: a randomized, double blind, placebo-controlled, crossover trial

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ABSTRACT

Background: To prevent diabetes, it is important to control postprandial glycemic levels. Studies have suggested that consuming black tea decreases the risk of type 2 diabetes; however, only a few studies have examined the effects of black tea on postprandial glycemic control after consuming starch-rich foods. In addition, the mechanism underlying the suppression of postprandial glucose levels remains unclear.

Objective: To investigate the effects of black tea on postprandial blood glucose levels in healthy humans and to identify the components of black tea that inhibit digestive enzymes.

Methods: The inhibitory activity of black tea on digestive enzymes was measured, and the inhibitory components were fractionated. Japanese adults ingested 200 ml of black tea, and its effect on postprandial blood glucose and insulin levels were investigated.

Results: Black tea dose-dependently inhibited α-glucosidase, sucrase, and α-amylase activity. The major components responsible for this inhibition were high–molecular-weight polyphenols. The galloyl moieties present in these compounds play an important role in their inhibitory activities. Two randomized, double-blind, placebo-controlled, crossover studies of healthy human subjects (total n = 46) were conducted to investigate the effect of black tea on blood glucose and insulin levels. Combined data from the two studies showed that black tea ingestion (200 mL) after cooked rice intake (200 g) significantly reduced the incremental area under the curve of glucose (P =.024) and insulin (P =.014) compared to placebo drink.

Conclusions: The high–molecular-weight polyphenols in black tea inhibited α-glucosidase, sucrase, and α-amylase activity in a dose-dependent manner. Furthermore, black tea ingestion after eating cooked rice significantly reduced the incremental area under the curve of glucose and insulin. These effects of black tea could be attributed to the inhibition of digestive enzymes by high–molecular-weight polyphenols containing galloyl groups.

Keywords: black tea, blood glucose, α-glucosidase, α-amylase, polyphenol

Link to Full Article: https://ffhdj.com/index.php/ffhd/article/view/791/1423

FFHD

Serum levels of vitamin D, calcium, phosphorus, and oxidative parameters in healthy and diabetic people

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ABSTRACT

Introduction: Diabetes mellitus is a metabolic disease that is a primary public health consideration. Low Vitamin D levels are linked to type 2 diabetes (T2DM), diminished insulin release, and enhanced insulin resistance in humans and animals. Vitamin D is also involved in the regulation of calcium and phosphorus homeostasis. Oxidative stress and antioxidant imbalances are important for the progression of diabetes as well. In this endeavor, the levels of vitamin D, calcium, phosphorus, and evaluation of the oxidant- antioxidant factors of malondialdehyde (MDA) and total antioxidant capacity (TAC) in healthy and diabetic people were compared.

Methods: This descriptive-analytical study was conducted in 2020 in Shiraz, Fars province, Iran. The population included 40 T2DM patients (with HbA1c equivalent 6-8) without comorbidities, 20-60 years old for both genders, and 40 healthy individuals (female and male between 20-60 years old without comorbidities). The high-performance liquid chromatography (HPLC) method was adopted for measuring Vitamin D and for measuring other levels, the colorimetric method was used. Using SPSS 22, statistical analysis was performed. The Mann- Whitney U test for quantitative data was applied. $P<0.05$ was deemed significant.

Results: There was a statistically significant difference between the two groups when it came to the means of vitamin D and MDA. In the diabetic group, vitamin D levels were lower ($p=0.001$) and MDA levels were higher ($p<0.001$). Comparing the level of calcium and phosphorus in diabetics and healthy people revealed no significant difference. This result was also true for the TAC test.

Conclusions: According to our results, the mean of vitamin D in T2DM was significantly lower than healthy people and MDA in T2DM significantly increased compared to the control group, suggesting that increasing the activity of this enzyme in the development of secondary complications in diabetic patients is a predisposing factor.

Keywords: Vitamin D, Diabetes mellitus, HPLC, Oxidative stress

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BCHD

FOSHU-approved Fibersol®-2 product review

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ABSTRACT

Abstract: Fibersol®-2 is manufactured by Matsutani Chemical Industry Co., Ltd. and is sold as a tasteless powder or liquid to be added to foods or beverages. It is approved by the Japanese Ministry of Health, Labour, and Welfare as a "Standardized FOSHU (Food for Specified Health Uses)" ingredient that contains the bioactive compound, digestion-resistant maltodextrin. Its current designated functions under FOSHU are as a dietary fiber for improving intestinal regularity and for controlling postprandial blood glucose and triglyceride levels. Furthermore, clinical trials have been done in human and animal subjects to investigate other potential health benefits. This product review focuses on English-language publications of studies that tested Fibersol-2 on human subjects. From these studies, there is evidence that Fibersol-2 plays a role in controlling fasting blood glucose levels, improving intestinal function and metabolic syndrome, and increasing satiety in human subjects. However, more studies are needed to draw definite conclusions about the amounts of Fibersol-2 that are needed to observe each health benefit and to confirm the efficacy and significance of Fibersol-2's benefits in the larger population, particularly the benefits that aren't designated under FOSHU.

Keywords: Fibersol-2, FOSHU, glucose control, metabolic syndrome, intestinal benefit, microbiome, dietary fiber, satiety

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BCHD

Saffron and depression

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ABSTRACT

Abstract: Throughout the centuries, people have used the dried stigma of Crocus sativus that is known as "saffron" for medicinal and nutritional purposes. Studies have shown that not only is saffron well worth the money, but also, its bioactive compounds (including crocin, precrocin, and safranal that are responsible for color, taste and fragrance respectively) play a crucial role in the central nervous system to positively affect conditions such as anxiety and depression. Saffron compounds are also neuroprotective and anxiolytic and can benefit learning and memory impairments.

Link to Full Article: https://ffhdj.com/index.php/BioactiveCompounds/article/view/808/1426

FFHD

Effects of Theracurmin® consumption on liver function, fatigue, and sleep: a randomized, double-blind, placebo-controlled, parallel-comparison study

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ABSTRACT

Objective: To evaluate the effects of the eight-week consumption of Theracurmin® on liver function, fatigue, and sleep.

Methods: This was a randomized, double-blind, placebo-controlled, parallel-comparison study involving 68 healthy Japanese adults. Subjects were allocated into either the active (Theracurmin®) or placebo group (n = 34 each) using a random number generator. Subjects consumed two capsules per day of either the active or placebo food for eight weeks. The primary outcome was the serum alanine aminotransferase (ALT) levels at eight weeks, whereas the secondary outcomes were the biomarkers of liver function, comparison of the percentages of improvement in liver function based on the decision criteria, OSA sleep inventory MA version (OSA-MA), and visual analog scale of fatigue.

Results: Each group included 33 subjects in the full analysis set. ALT levels in the per protocol set analysis, except for subjects drinking quantities of alcohol that increase the risk of lifestyle-related disease onset, showed a significant decrease in ALT compared to the placebo group ($P < 0.05$). The subjective symptom in the fatigue recovery factor of OSA-MA was significantly improved through the intervention ($P < 0.05$). The fatigue recovery effect of Theracurmin® was prominent in the subjects aged ≤ 45 years, the age group defined by the Ministry of Health, Labour and Welfare as middle-aged and older persons in the Act on Stabilization of Employment of Elderly. No adverse event was observed.

Conclusions: These results suggest that the consumption of Theracurmin® or eight weeks improved liver function and fatigue recovery at awakening in healthy Japanese adults.

Trial registration: UMIN-CTR: UMIN000039319. Foundation: Theravalues Corporation

Keywords: highly bioavailable curcumin, liver function, alanine aminotransferase (ALT), OSA sleep inventory MA version, fatigue recovery

Link to Full Article: https://ffhdj.com/index.php/ffhd/article/view/794/1430

FFHD

Suppressive effect of a single dose of monoglucosyl rutin on postprandial blood glucose elevation: A randomized, placebo- controlled, double-blind crossover study

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ABSTRACT

Objective: This study aimed to investigate the suppressive effect of a single dose of water-soluble α- glycosylated rutin (monoglucosyl rutin; MR) on postprandial blood glucose elevation in healthy subjects with relatively high fasting blood glucose levels.

Methods: This randomized, placebo-controlled, double-blind crossover study enrolled 34 healthy Japanese adult subjects with relatively high fasting blood glucose levels. The study period ran from November 13, 2019, to March 19, 2020. All subjects were randomly allocated to either sequence A or sequence B (n = 17 per group) using a computerized random number generator. The washout period was at least one week between periods I and II. In period I, the subjects took either MR or placebo tablets. In period II, subjects took different tablets from the ones they had taken in period I. We evaluated their blood glucose and insulin levels after glucose loading (150 g of cooked rice). The incremental area under the curve (IAUC) of the postprandial blood glucose level was determined as the primary outcome. The blood glucose and insulin levels at maximum (maximum blood concentration; Cmax), each measurement point, and IAUC of the blood insulin level after glucose loading were the secondary outcomes.

Results: Out of 33 subjects, 16 in sequence A (11 men and 5 women, 54.5 ± 9.8 years) and 17 in sequence B (9 men and 8 women, 58.8 ± 9.4 years) were analyzed as a per-protocol dataset. The glucose IAUC after MR consumption was significantly lower than that of the placebo (P = 0.034). Results of the other outcomes were not observed with significant treatment effects. There were no adverse events attributable to the test foods.

Conclusions: We suggest that MR has a suppressive effect on the elevation of postprandial blood glucose in healthy adults with relatively high fasting blood glucose levels.

Trial registration: UMIN-CTR: UMIN000038515. Foundation: Toyo Sugar Refining Co., Ltd.

Keywords: monoglucosyl rutin, blood glucose level, incremental area under the curve, α-amylase, α-glucosidase, crossover study

Link to Full Article: https://ffhdj.com/index.php/ffhd/article/view/793/1435

BCHD

Nutrition communication about low FODMAP diet in irritable bowel syndrome (IBS) and small intestinal bacterial overgrowth (SIBO) in Thai healthcare practitioners

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ABSTRACT

Abstract: Nowadays, communication is influential regarding the various communication channels that make the information spreading effectively to the audiences. Additionally, the senders are also another factor creating credibility to the receivers, particularly to the healthcare-related issue which is necessary to be guaranteed by the medical specialists. The Low FODMAP is a therapeutic diet which is recommended for Irritable Bowel Syndrome (IBS) and Small Intestinal Bacterial Overgrowth (SIBO) patients. However, this diet has not been practiced widespread among Thai healthcare practitioners. As a matter of fact, these practitioners are familiar with a great number of diseases and closely well-educated with healthcare issues, they would significantly hold credibility affecting the medical usage to the society. Consequently, this article aims to educate all the staff in the healthcare and medical industry to gain sufficient knowledge of low FODMAP and be able to apply for further development.

Keywords: nutrition communication, Low FODMAP, IBS, SIBO

Link to Full Article: https://ffhdj.com/index.php/BioactiveCompounds/article/view/798/1438

FFHD

Adherence to the Mediterranean diet: An online questionnaire based-study in a Spanish population sample just before the Covid-19 lockdown

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ABSTRACT

Background: The Mediterranean Diet (MD) has been associated with a reduced risk of developing several pathologies, such as cardiovascular diseases. Despite this, adherence to MD in the general population has decreased in the past years. Due to COVID-19 crisis, eating habits of the population are being affected, thus data assessing these habits just before lockdown are important to determine how they are modified. The Mediterranean Diet Quality Index (KIDMED) questionnaire was used to evaluate adherence to MD just before COVID-19 lockdown.

Methods: The KIDMED survey was launched through the Google platform for surveys, from 2/20/20 until 3/13/20. Additionally, questions about gender, weight and height for body mass index (BMI) calculation, academic degree, and nationality were included. Multivariate linear regression was performed for data analysis.

Results: A total of 861 completed surveys were collected. Some surveys were discarded because data was missing (18), the participants were not of Spanish nationality (18), or because they did not belong to the age groups included in the study (19). The remaining 804 surveys were divided into the following age groups: 15-24 (n=160), 25-34 (n=158), 35-54 (n=363) and 55-69 (n=123). In the 15–24-year-old group, 71.9% had a BMI between 18-24.9, but only 28.1% reached an index ≥8 in the KIDMED questionnaire. Adherence to MD improved as the age in the groups increased, but so did the BMI, especially in the oldest group. In all adult groups, approximately 50% had a university education. Overall, lower BMI was significantly related to females, younger age and a higher degree of studies. On the other hand, the higher adherence to MD was related to older age and a higher degree of education.

Conclusions: The improved adherence to MD was not associated with a reduced BMI. Maybe other factors, like sedentary life or hormonal changes, known to impact people while aging, have influenced our results. Possibly, adherence to MD might have played a protective role, at least partially, against an even higher BMI. More research is needed to fully determine the impact of adherence to MD in the Spanish population, also after COVID-19 lockdown.

Keywords: Mediterranean diet, KIDMED, Body mass index, Spain.

Link to Full Article: https://ffhdj.com/index.php/ffhd/article/view/806/1441

BCHD

COVID-19: human immune response and the influence of food ingredients and active compounds

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ABSTRACT

Abstract: The human immune system is the first line of defense in the prevention of viruses and diseases, and several immune response mechanisms are engaged at the onset of a pathogenic attack. In this review, we elucidate the human immune system as a critical element in protecting humans from COVID-19 by describing the immune process, explaining how the immune system functions, and highlighting the immune system's global importance in fighting infections. Potential challenges that limit the proper functioning of the immune system are also discussed. In addition, we address the impact of nutrition on boosting the body's defenses against COVID-19. For example, some foods and active compounds from food ingredients have been suggested as a way to strengthen the immune system. Physical exercise has also been encouraged as an important way to support the immune response to viral infections. The aim of this review is thus to outline holistic self-defense immunity mechanisms that can help to reduce the risk of viral infections in humans. This review could therefore be used as a comprehensive resource for educating consumers and the general public about measures that can enhance the body's immune support system as we continue to fight COVID-19 and its variants.

Keywords: Immunity, Covid-19 COVID-19, Nutrition, Bioactive compounds, Food Ingredients

Link to Full Article: https://ffhdj.com/index.php/BioactiveCompounds/article/view/802/1439

BCHD

Effect of preoperative feeding with germinated brown rice supplement on clinical outcome of orthopaedic and gastrointestinal surgery patients

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ABSTRACT

Background: Malnutrition prior to surgery can lead to inflammation, increased length of hospital stay, bed sores, muscle weakness, poor quality of life and mortality post-surgery in patients. Therefore, preoperative drinks that have been enriched with vitamins, easily digestible carbohydrates and amino acids have been necessitated by ESPEN. Health benefits of brown rice, which is a good source of phytonutrients like GABA, Ferulic acid Oryzanol and B-complex, BCAA and maltodextrin, have been well researched.

Methods: In the present study, a nutritious product was developed using germinated brown rice, salt and micronutrient mix (GBR Mix), analysed quantitatively (Proximate composition) and qualitatively (Phytochemicals). Major orthopaedic and gastrointestinal surgical patients in the age group of 40-65 years (n=124) were supplemented with GBR Mix in bouts of 3 meals (20gms x 3meals) namely lunch, mid-evening and bedtime time snack, 8 hrs prior to surgery unlike other patients who fasted for 12-16 hours prior to surgery. They were assessed for nutritional status, Serum Albumin, inflammatory markers (CRP and WBC), post-surgery complications and length of hospital stay.

Results: Supplementation was found to improve blood sugar ($p<0.05$) in gastroenterology patients, reduce inflammatory markers like CRP($p=0.053$) and WBC ($p<0.001$), reduced nausea and vomiting, improved food and fluid intake post-surgery in the patients. Additionally, length of hospital stay was also reduced ($p=0.001$).

Conclusion: Thus, germinated brown rice could be recommended as an economical nutritious and anti-inflammatory pre surgery feed.

Keywords: GBR, LOS, MUST, SGA, CRP, Micronutrient Mix

Link to Full Article: https://ffhdj.com/index.php/BioactiveCompounds/article/view/799/1451

FFHD

Health benefits of olive oil and by-products and possible innovative applications for industrial processes

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ABSTRACT

Abstract: In the last few years, the production of olive oil has incredibly increased due to its beneficial properties on human health. On the other hand, the amount of waste and by-products derived from the olive oil industry has increased as well, prompting the development of new fields of research aiming to reduce disposal costs and valorize bioactive compounds from the viewpoint of the green economy. Interestingly, olive oil and by-products contain numerous molecules, including phenols, exhibiting pleiotropic effects in both in vitro and in vivo studies. This review aims to describe the more recent studies focusing to identify and describe the potential roles and the new applications of extracts isolated from wastes and by-products or specific compounds, such as hydroxytyrosol (HT) and oleuropein. Extracts or bioactive molecules from olive oil and by-products have been proposed as a food additive, to produce biofuel, for animal feeding, and to create new matrices in bioremediation protocols. Moreover, bio-compounds have been described to have numerous beneficial effects on human health as they reduce the risk of developing certain chronic diseases. Despite the already published studies, more research is necessary to valorize bioactive compounds in olive oil and by-products, as well as their potential use to improve human health and green applications in different industrial processes.

Keywords: extra virgin olive oil, by-products, olive leaf extract, bioactive compounds, human health, and industrial application

Link to Full Article: https://ffhdj.com/index.php/ffhd/article/view/800/1455

FFHD

Effects of the consumption of proanthocyanidins derived from acacia bark on blood pressure in healthy Japanese adults: A randomized, double-blind, placebo-controlled, parallel-group comparison study

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ABSTRACT

Objective: The aim of this study is to verify the effects of consuming proanthocyanidins derived from acacia bark on improving blood pressure and blood circulation in healthy Japanese adult subjects.

Methods: This was a randomized, double-blind, placebo-controlled, parallel-comparison study involving 66 healthy Japanese adults. Subjects were allocated into either acacia or placebo group (n = 33 each) using a random number generator. Subjects consumed six tablets/day of either acacia bark extract tablets or placebo for 12 weeks. The primary outcome was the measured value of sitting systolic blood pressure at 12 weeks, whereas the secondary outcomes were sitting systolic and diastolic blood pressures, superoxide dismutase activity in blood, and blood flow.

Results: The number of subjects analyzed as full analysis set was 33 (20 men and 13 women) in the Acacia group and 31 (23 men and 8 women) in the placebo group. Compared with the placebo group, the measured values and changes from baseline at 4, 8, and 12 weeks of the sitting systolic blood pressure were significantly lower in the Acacia group. Furthermore, "the ratio of the number of subjects whose sitting systolic blood pressure <130 mmHg and diastolic blood pressure ≤89 mmHg at 12 weeks" of the Acacia group was significantly higher than that of the placebo group. No adverse event was observed.

Conclusions: Proanthocyanidins derived from acacia bark showed a hypotensive effect.

Trial registration: UMIN-CTR: UMIN000039416.

Foundation: Acacia-No-Ki Co., Ltd.

Keywords: Acacia bark extract, Proanthocyanidins, Systolic blood pressure, Diastolic blood pressure

Link to Full Article: https://ffhdj.com/index.php/ffhd/article/view/814/1449

FFHD

The effect of electron beam on oxidative stress and inflammatory factors in diabetes mellitus: An in vitro and in vivo study

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ABSTRACT

Background: The main purpose of this study was to investigate whether or not electron beam therapy (EBT) was an effective method in terms of moderating oxidative stress by reducing free radicals in BALB/c mice with type 1 diabetes mellitus.

Methods: The study was performed on thirty BALB/c mice in three groups including normal control, diabetic control, and EBT treated. Before studying the effect of electron beam on the studied groups, optimal level of constant source-to-surface distance, as well as the effects of EBT on glutathione reductase (GR) structure and function were determined. After studying the structure and the function of GR protein with three methods including fluorometry, circular dichroism (CD), and activity assay methods, SSD 100 was selected for EBT. Glucose, advanced glycation end-products, GR, oxidative stress factors such as hydrogen peroxide, malondialdehyde, advanced oxidation protein products, oxidized low-density lipoprotein, and inflammatory factors were measured in the serum of all groups.

Results: The results of in vitro study showed that electron beam therapy could increase glutathione reductase activity, which was not significant. Also, the results were compared between and within groups using one-way analysis of variance. Significant differences were observed for all variables measured between the normal control group and the other groups ($P < 0.05$). There was also no significant difference in blood glucose levels between the electron beam therapy treated group and the diabetic one ($P > 0.05$).

Conclusion: The results suggested that electron beam therapy could be effective in reducing free radicals and oxidative stress. Electron beam therapy, as a complementary method, might aid in moderating the complications of diabetes mellitus.

Keywords: Diabetes mellitus, Electron beam, Inflammatory factors, Oxidative stress

Link to Full Article: https://ffhdj.com/index.php/ffhd/article/view/803/1459

FFHD

Marketing strategies for functional food products

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ABSTRACT

Abstract: Functional foods are experiencing a growing demand worldwide as consumers seek ways to take control of their health. Despite this growing demand, the lack of a standard definition for functional food for formal categorization and regulation results in many functional food products run into hurdles for consumer acceptance, as many people are not familiar with the concept, and scientific evidence that could increase legitimacy of these products is not widely available. Of the 15 steps the Functional Food Center has outlined for development of functional food products, marketing a product to educate people is closely related to consumer acceptance and is therefore an important step to study to increase success of functional food products. This review article will focus on recent studies that examine carrier/ingredient combinations, information channels, credibility, and consumer targeting and how they can impact consumer intent to purchase or accept functional foods. These studies build off hypotheses tested in pre-existing studies or bring in novel determinants to consider. Finally, advice on marketing based on the results in the included papers and from an industry expert will be discussed.

Keywords: Functional Food Marketing, Carrier/Ingredient Combinations, Perceived Fit, Information Channels, Credibility, Consumer Targeting, Advertising, Consumer Acceptance, Purchase Intent

Link to Full Article: https://ffhdj.com/index.php/ffhd/article/view/817/1461

FFS

Effect of brewing method on quality parameters and antioxidant capacity of black tea

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ABSTRACT

Introduction: The traditional method for brewing tea in Turkey involves use of a two-vessel apparatus known as a "caydanlik." The caydanlik allows for tea to be brewed for a longer time than typical brewing methods and involves introducing boiling water to tea leaves and steeping them in a teapot as the temperature declines over 15 minutes. In comparison, the typical tea brewing method used in other parts of the world involves steeping tea leaves in a single vessel teapot for 5 minutes. This study evaluated the effects of these two methods of brewing using two brands of tea.

Results: Results of this experiment indicate that use of the caydanlik and the accompanying longer brewing time significantly changed key quality parameters and increased the antioxidant capacity of the brewed black tea beverage. Use of the caydanlik method resulted in significantly higher ($P < 0.05$) theaflavins, thearubigins, theabrownins, and total polyphenols in the resultant tea than in tea brewed in a traditional teapot. Additionally, analysis of color values of the brewed tea indicated the L and b-values were significantly ($P < 0.05$) lower in the caydanlik brewed tea while a and hue values were significantly higher ($P < 0.05$). However, chroma values were not significantly different ($P < 0.05$) between the two methods.

Conclusions: In addition to influencing color, flavor and aroma, the brewing method also influenced the functional properties of prepared black tea. Use of the traditional two-vessel caydanlik for tea preparation increased concentrations of beneficial functional components in the tea.

Keywords: Black tea, Caydanlik, Brewing, Camelia sinensis, ORAC, Total Phenolic Content

Link to Full Article: https://ffhdj.com/index.php/FunctionalFoodScience/article/view/807/1463

FFHD

The effect of vitamin D deficiency state on oxidized low-density lipoprotein alteration in patients with type 2 diabetes

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ABSTRACT

Introduction: The aim of this study was to compare oxidized low-density lipoprotein (oxLDL) and blood glucose in very low and low levels of vitamin D.

Methods: A total of 25 type-2 diabetic patients with very low serum levels of 25-hydroxy vitamin D (severe deficiency – <10 ng/ml); and 25 type-2 diabetic patients with low serum levels of 25-hydroxy vitamin D (deficient – 10 to 30 ng/ml) were recruited in this cross-sectional study. Fasting plasma glucose (FBS), postprandial glucose (PPG), HbA1C, oxLDL, and high- sensitivity C-reactive protein (hs-CRP) were measured. Diagnostic accuracies were determined by receiver- operating characteristic (ROC) curve analysis and measuring the area under the curve (AUC).

Results: Patients with severe vitamin D deficiency had higher FBS, PPG, HbA1C, and oxLDL than the vitamin D deficient group ($P<0.05$). We showed that the AUC of FBS, PPG, HbA1C, and oxLDL were in the range of 0.7-0.9, which indicates moderate accuracies in differentiating severe vitamin D deficiency from deficiency condition.

Conclusion: In conclusion, diabetic patients with severe vitamin D deficiency had higher FBS, PPG, and oxLDL levels compared with deficient ones. ROC curve analysis of FBS, PPG, HbA1C, and oxLDL showed these markers are independent predictors of severe vitamin D deficiency and significantly discriminate between very low and low levels of vitamin D deficiency in patients with diabetes.

Keywords: Type 2 diabetes mellitus. Vitamin D deficiency. OxLDL. Fasting blood glucose.

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FFHD

Anti-salmonella potential and antioxidant activity of fermented fruit-based juice by lactic acid bacteria and its biotransformation

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ABSTRACT

Background: Lactic acid bacteria-based fermentation clearly contributes to improving nutritional value and exhibits various health benefits. The demand for non-dairy functional beverages, such as fruit beverages, as an alternative vehicle for probiotics is increasing because of lifestyle choices or health conditions. Therefore, the objective of this study was to evaluate the anti-Salmonella potential and antioxidant activity of fermented fruit- based juice by lactic acid bacteria and its biotransformation.

Methods: In this study, to produce the fermented fruit-based juice (FFJ), the mixed fruit juice (MFJ) was fermented by Lactobacillus plantarum TISTR 1465 and Lactobacillus salivarius TIST 1112 for 72 hrs. The potential function, anti-Salmonella by the minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC), and antibiofilm activities of FFJ against Salmonella Typhi DMST 22842 was evaluated. The antioxidative capacity was determined by DPPH and FRAP assay. The active volatile compounds were identified by GC-MS.

Results: A novel functional FFJ showed excellent growth capacity with 8 log CFU/mL of probiotics Lactobacillus plantarum TISTR 1465 and Lactobacillus salivarius TIST 1112. MIC and MBC values in the FFJ were 500 mg/mL after 72 hrs of fermentation. After 48hrs of fermentation, biofilm formation inhibition was significant ($p < 0.05$) with 95.27% ± 2.26% inhibition; biofilm metabolic activity inhibition was also significant ($p < 0.05$) with 89.25% ± 0.18% inhibition. The volatile compounds present in the FFJ were fruity flavors and aromas, most of have antimicrobial and antioxidant properties. These compounds comprise various classes, including alcohols, organic acid, ester, and ketone. In both LAB fermentations, the most abundant volatile alcohol was isoamyl alcohol, followed by 1-hexanol and 2,3-Butanolone; acetic acid was only present in L. plantarum fermentation. In addition, DPPH radical scavenging and FRAP assay showed the mixed fruit juice had dramatically increased antioxidant activity after 48 hrs of fermentation.

Conclusion: The findings of this work indicate that the obtained fermented fruit-based juice (FFJ) showed excellent growth capacity of probiotics, Lactobacillus plantarum TISTR 1465 and Lactobacillus salivarius TIST 1112, and produced the volatile compounds from biotransformation. This not only improved fruit flavor and aroma, but also influenced antibacterial activity against the pathogen Salmonella Typhi DMST 22842, as well as increased antioxidant activity. Therefore, the FFJ could be a novel functional fermented drink for vegan and non-diary consumption.

Keywords: Lactic acid bacteria, Probiotics, Biotransformation, Non-dairy functional beverage, Anti-Salmonella.

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BCHD

Study of the effect of gallic acid and cold plasma on the levels of inflammatory factors and antioxidants in the serum sample of subjects with type 2 diabetes mellitus

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ABSTRACT

Background: Uncontrolled type 2 diabetes mellitus can have devastating consequences. The role of functional foods in controlling and even preventing diabetes mellitus is prominent, and adjunct therapies can help control some of the consequences of diabetes.

Objective: This study aimed to investigate whether gallic acid (as a functional food) and cold atmospheric plasma (as an adjunct therapy) influence the levels of some antioxidant enzymes, inflammatory factors, and the levels of an oxidizing agent and blood glucose.

Methods: In this study, 30 healthy individuals, as the control group, and 30 individuals with type 2 diabetes mellitus were selected. Samples of people with diabetes were examined before and after treatment with gallic acid and cold atmospheric plasma (cold argon plasma jet for 10 minutes). Levels of inflammatory factors (interleukin 2, 13 and NF-κB), antioxidants (glutathione reductase, paraoxonase, and lipoprotein lipase) as well as hydrogen peroxide and blood glucose, were assessed in untreated and treated diabetic groups and the control group according to kit instructions.

Results: A comparison of the results of the levels of inflammatory factors, antioxidants, blood glucose, and hydrogen peroxide showed a significant difference (P value < 0.05) between the diabetic and control groups. Treatment of diabetic subjects with plasma and gallic acid showed a significant increase (P value < 0.05) in glutathione reductase, paraoxonase, and NF-κB levels compared to the untreated diabetic group.

Conclusion: The results showed that concomitant use of gallic acid with plasma therapy, could be effective on NF-κB, glutathione reductase, and paraoxonase levels, yet the data suggest little or no effect. The results of the study showed that cold plasma treatment along with gallic acid supplementation can have a synergistic effect on the regulation of oxidative stress and inflammatory cytokine secretion in the patients with type 2 Diabetes mellitus.

Keywords: Diabetes mellitus, Cold plasma, Inflammatory factors, Gallic acid

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BCHD

Medicinal plants and the communication on precautionary use of herbs during COVID-19 outbreak in Thailand

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ABSTRACT

Abstract: COVID-19 has become a new global health issue that spreads easily and has high mortality rates across the world. Consequently, it is essential to discover new treatments rapidly. According to Integrative Medicine, certain herbs are useful for treating COVID-19 when taken with standard treatments. Thailand is one of the countries experiencing outbreaks and treating patients with herbs. For instance, some Thai patients are treated with Fah Talai Jone (Andrographis paniculata) at a different quantity limit used for treating fever and sore throats. Fah Talai Jone must be used with high precaution in renal insufficiency, hepatitis, or drug induced liver damage patients. In addition, finger root (Boesenbergia rotunda) and ginger (Zingiber officinale) are also used for managing COVID-19, but there is insufficient evidence about quantity limits and side effects of using them. Therefore, specialists need to do more research about the herbs to ensure the efficiency and safety of treatments.

Keywords: herb in COVID, Fah Talai Jone, andrographolide, finger root, ginger, COVID, herb communication

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FFS

Pycnogenol - extract from French maritime pine bark (Pinus pinaster), as an effective antioxidant against superoxide radical

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ABSTRACT

Background: Interest in the positive impact of naturally occurring polyphenols is still increasing in the scientific community. Research is focused mainly on their antioxidant properties, due to their significant effects in the prevention of diseases associated with oxidative stress. Pycnogenol is an extract from French maritime pine bark (Pinus pinaster), which is composed of a mixture of phenolic compounds: monomers (catechin, epicatechin, taxifolin), flavonoids (classed as procyanidins/proanthocyanidins), phenolic or cinnamic acids and their glycosides. Due to its composition, it has a high antioxidant capacity, and is used in traditional folk medicine, cosmetics and medicine.

Purpose of the study: The aim is to study the antioxidant properties of pycnogenol in order to obtain experimental information on the antioxidant effect of pycnogenol in terms of concentration dependence and pH conditions.

Methods: In our study, we used a methionine-riboflavin superoxide generator, and focused on determining the antioxidant capacity of Pycnogenol against the superoxide radical in different pH values (range 6.5 – 8) using the spectroscopic method.

Results: Our results showed that the antioxidant properties increased with a higher concentration of the tested compound in the tested pH range. Amongst all tested pH values, the most appropriate for pycnogenol antioxidant capacity is slightly basic pH (pH 8).

Conclusion: Information on the antioxidant and prooxidant properties of naturally occurring compounds is very important for understanding their activity and their proper use in prevention, disease treatment, and detection of pathological processes. The antioxidant activity of pycnogenol depends on the structure and concentration of antioxidants; it only slightly changes at different pH values. Increasing concentration of pycnogenol enhances its antioxidant properties.

Keywords: Pycnogenol, reactive oxygen species, spectrophotometry, pH dependency

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