

## 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 eating 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, cravings 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 =  $56.8 \pm 1.8$ ; 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  $6.11 \pm 0.28$  pounds ( $2.77 \pm 0.12$  Kg) ( $p < 0.001$ ) along with average reductions of  $2.51 \pm 0.05$  inches ( $6.4 \pm 0.13$  cm) ( $p < 0.0001$ ) and  $1.5 \pm 0.04$  inches ( $3.8 \pm 0.10$  cm) ( $p < 0.0001$ ) from waist and hip circumferences, respectively. The entire

group lost an average of  $3.63 \pm 0.13$  pounds ( $1.65 \pm 0.11$  Kg) ( $p < 0.001$ ) with average reductions of  $1.59 \pm 0.03$  inches ( $4.04 \pm 0.06$  cm) ( $p < 0.0001$ ) and  $1.13 \pm 0.02$  inch ( $2.87 \pm 0.05$  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

### **Background:**

Although obesity can lead to serious health problems, dieting can be difficult because dieters often have a constant feeling of hunger and cravings associated with reduced caloric intake [1-3]. Another problem associated with dieting is the feeling of fatigue or loss of energy and stamina [4]. Chronic or intractable fatigue that is not reversed by sleep occurs naturally during aging and in many degenerative diseases [5, 6], and it is also associated with obesity [7]. It is the most common complaint of patients seeking general medical care in North America [5, 6].

### **INTRODUCTION:**

Among the many approaches to restrict food intake and increase weight loss in obese individuals, lifestyle and behavioral modifications, restrictive diets, increased physical activity and use of pharmacological drugs or nutraceutical formulations have all been used with various degrees of success [8, 9]. However, there has been a tendency to use pharmacological drugs to treat obesity, such as use of lipase inhibitors, serotonergic agents, noradrenergic agents, among others, but use of such drugs can have undesirable side effects, including hypertension, seizures, headaches, insomnia, sexual dysfunction, fecal incontinence and cardiac disease [10, 11]. Therefore, finding alternative agents to weight loss drugs with undesirable side effects is an important goal.

An alternative strategy has been to develop natural products for weight loss that do not have the undesirable side effects found in pharmacologic drugs [11]. For example, certain plant products with weight loss potential have been widely used to treat obesity [11, 12]. Han and his colleagues [11] have divided these into five categories based on their mechanism of action: (1) decreased lipid absorption, (2) decreased energy/carbohydrate intake, (3) decreased pre-adipocyte differentiation and proliferation

and (5) decreased lipogenesis and increased lipolysis. In addition, natural products that increase cellular energy and decrease fatigue without undesirable side effects could also be added to this list [13].

Layer et al. [14, 15] initiated an important weight loss approach that utilizes the natural ability of white kidney bean (*Phaseolus vulgaris*) extracts containing alpha-amylase inhibitor to block digestion and uptake of carbohydrates. This has been developed further into a product that appears to be effective in weight loss studies [16, 17]. In the current study this formulation has been added to a phospholipid extract containing various membrane phosphatidyl lipids (NT Factor®). The rationale for this was that in previous studies we noted that NT Factor® reduced cravings for sweets and fats while reducing fatigue that was associated with reductions in mitochondrial function [13, 18]. Here we have used NT Factor plus *Phaseolus vulgaris* alpha-amylase inhibitor (Healthy Curb®) in an open label weight loss program to reduce girth and weight while also reducing fatigue associated with dieting without adding stimulants, herbs, dietary restrictions or a physical exercise program [13, 19, 20].

## **SUBJECTS AND METHODS:**

**Subjects.** Participants (n = 30) were adult male (6) and female (24) patients at a medical clinic. Subjects were asked if they used any prescription medications to see if this might exclude them from the study, as determined previously [21]. The mean age of the participants was  $56.8 \pm 1.8$  years.

**Study Design:** Subjects 18 or older signed an informed consent document and were admitted into a two-month open label study on weight reduction if they were overweight and had measurable fatigue levels (2-6) using the Piper Fatigue Scale (PFS). The study followed previous IRB-approved clinical studies. The PFS is a validated instrument for measuring fatigue using a survey questionnaire [22, 23]. Subjects filled out a routine medical history form and were weighed, their waist and hips measured, and a blood sample was taken for routine chemistry and blood lipid analysis. The participants also completed forms that measured their appetite (hunger index) and cravings for sweets and fats according to Arumugam et al. [24]. The participants were given a two-month supply of the test supplement along with instructions to take two tablets containing 500 mg NT Factor® and 500 mg alpha-amylase inhibitor preparation 30 min before each meal. Subjects were scheduled for clinic visits each two weeks for duration of the trial. During the final visit another blood sample was taken for routine chemistry and lipid analysis. Participants agreed to maintain their normal diets and exercise routines and to limit their intake of alcohol to NIH guidelines for consumption of alcohol during clinical trials.

All of the forms were checked for verification, completion and scoring accuracy [25]. There were no ethical questions raised on the design or execution of the study.

**Materials and Methods:** The supplement test product, Healthy Curb® (Nutritional Therapeutics, Inc., Commack, NY), contains a patent-pending proprietary product containing an exogenous source of polyunsaturated phosphatidyl lipids and other membrane phospholipids (NT Factor®) and an alpha-amylase inhibitor extract (Table 1). The participants initiated the study after being measured, weighed and completion of the PFS and appetite evaluation instruments. In addition, a blood sample was taken

for a standard Chem20 profile and lipid analysis. Body Mass Index (BMI) and Basal Metabolic Rate (BMR) were calculated according to established criteria [26]. BMI was calculated as weight (in pounds) times 703 divided by height (in inches) squared. BMR was calculated using the variables of height, weight, age and gender as follows: Female BMR =  $655 + (9.6 \times \text{weight in Kg}) + (1.8 \times \text{height in cm}) - (4.7 \times \text{age})$ ; male BMR =  $66 + (13.7 \times \text{weight in Kg}) + (3 \times \text{height in cm}) - (6.8 \times \text{age})$ . Appetite and cravings for sweets and fats were assessed as described [24].

**Table 1. Test Supplement (Healthy Curb®)**

Component	Amount Per Serving	% Daily Value*
NT Factor® <sup>#</sup> (includes phosphoglycolipids from soy)	500 mg	**
White Kidney Bean ( <i>Phaseolus vulgaris</i> ) Extract	500 mg	**
OptiMSM® <sup>^</sup>	46 mg	**
Phosphorus (as dicalcium phosphate)	60 mg	6%
Calcium (as dicalcium phosphate, calcium borogluconate calcium ascorb)	79 mg	7.9%

Other ingredients: dicalcium phosphate, calcium borogluconate, microcrystalline cellulose, vegetable stearic acid, vegetable magnesium stearate, sodium croscarmellose, silicon dioxide, pharmaceutical glaze

\*Daily values are based on a 2,000 calories per day diet

\*\*Daily values not established

<sup>#</sup>NT Factor® and Healthy Curb® are registered trademarks of Nutritional Therapeutics Inc., Commack, NY.

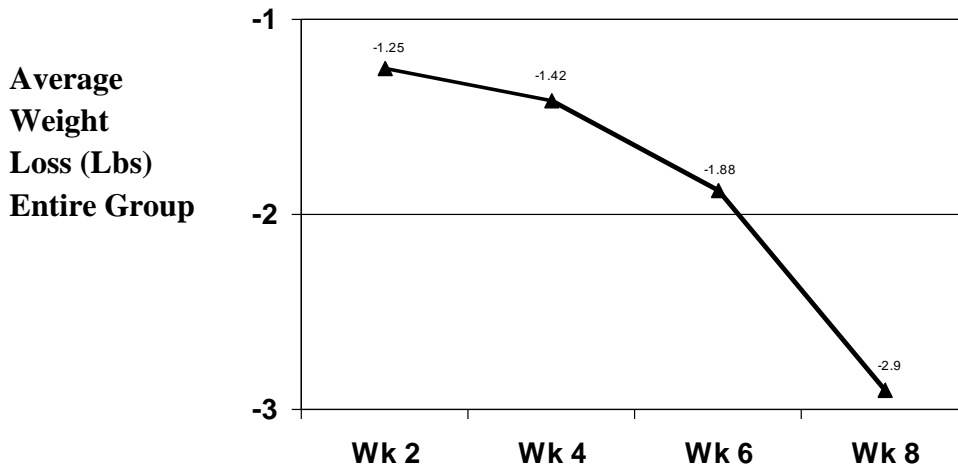
<sup>^</sup>OptiMSM® is a registered trademark of Bergstrom Nutrition, Inc.

The PFS form is composed of 22 numerically scaled questions rated from 0 (no fatigue) to 10 (severe fatigue) [18]. These items measure four dimensions of fatigue: behavioral/severity (6 items); affective/meaning (5 items); sensory (5 items); and cognitive/mood (6 items). These are used to calculate four sub-scale/dimensional scores and the overall fatigue levels of subjects. The standardized alpha (Cronbach's alpha) did not drop below 0.90 for any of the subscales, and the standard alpha for the entire scale of 22 questions was 0.96, indicating excellent reliability for an established, validated instrument [25].

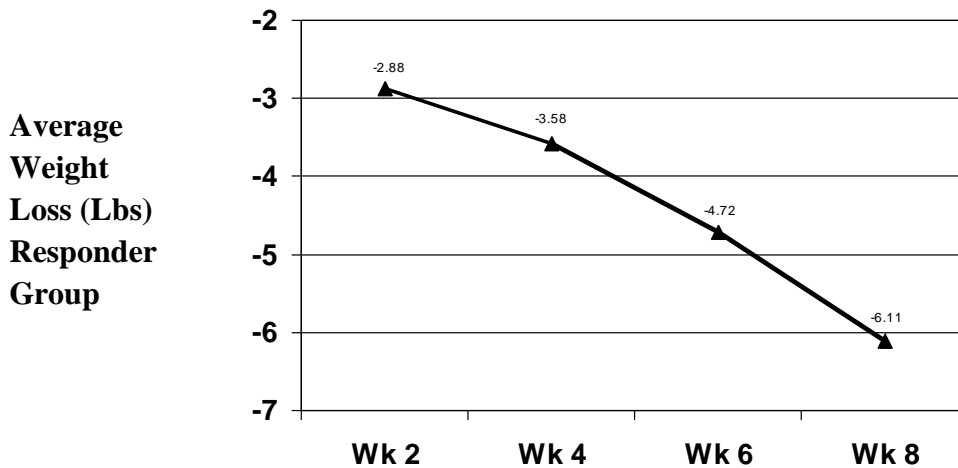
**Statistical Analyses.** Data were analyzed by ANOVA, with significance defined as  $p < 0.05$ . Further data analysis was performed with Tukey test and linear regression analysis, with significance defined as  $p < 0.05$ .

**RESULTS:**

**Weight and Girth Reduction.** The entire group of participants lost an average of  $3.63 \pm 0.13$  pounds ( $1.65 \pm 0.11$  Kg) ( $p < 0.001$ ) with average reductions of  $1.59 \pm 0.03$  inches ( $4.04 \pm 0.06$  cm) ( $p < 0.0001$ ) and  $1.13 \pm 0.02$  inch ( $2.87 \pm 0.05$  cm) ( $p < 0.0001$ ) in waist and hip circumference, respectively (Figs. 1 and 2). Most of the participants (63%) were in a high-responder group and lost an average of  $6.11 \pm 0.28$  pounds ( $2.77 \pm 0.12$  Kg) along with average reductions in waist and hip circumference of  $2.51 \pm 0.05$  inches ( $6.4 \pm 0.13$  cm) ( $p < 0.0001$ ) and  $1.5 \pm 0.04$  inches ( $3.8 \pm 0.10$  cm) ( $p < 0.0001$ ), respectively (Figs 3 and 4).



**Figure 1. Average weight loss for entire group on Healthy Curb®.**



**Figure 2. Average weight loss for the responder subgroup (n=19) on Healthy Curb®.**

**Body Mass Reduction.** The entire group showed reductions in average BMI of 0.18 ( $p < 0.05$ ), whereas the 63% responder group showed reductions in average BMI of 0.49 ( $p < 0.02$ ) (Figs. 5 and 6). In addition, we calculated differences in BMR, which uses the variables of height, weight, age and

gender to calculate a rate of resting metabolism. We found improvements in average BMR of 14.15 ( $p<0.09$ ) and 20.57 ( $p<0.01$ ) for the entire group and the responder group, respectively, by the end of the trial (Figs. 7 and 8).

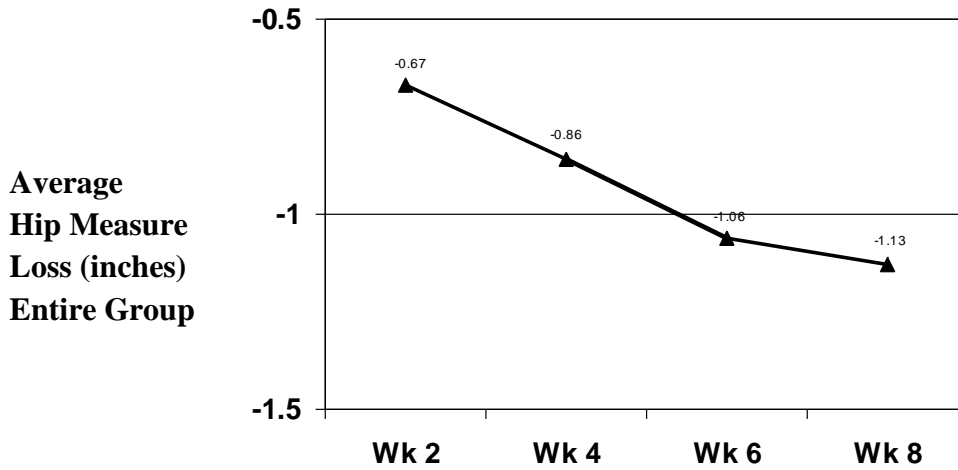


Figure 3. Average reduction in hip measurements for the entire group on Healthy Curb®

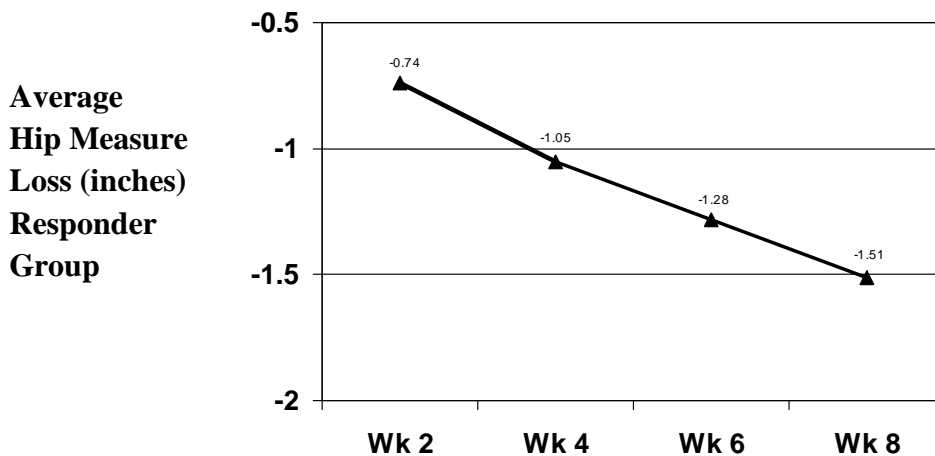
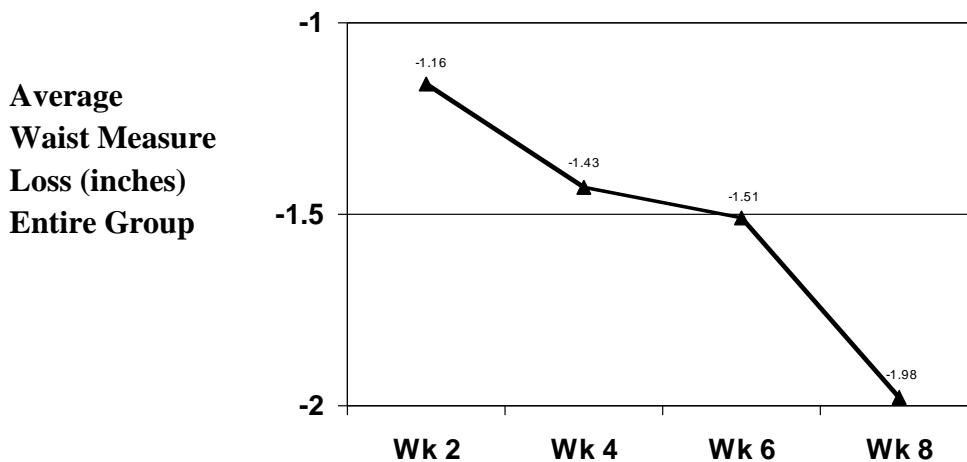
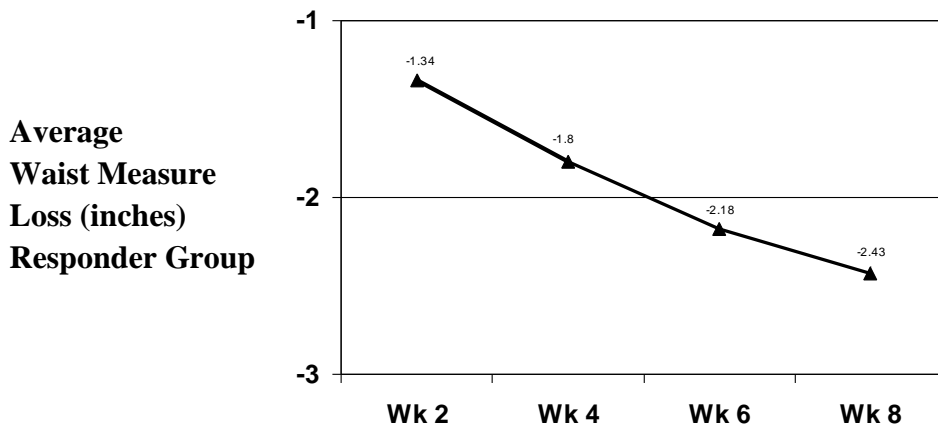


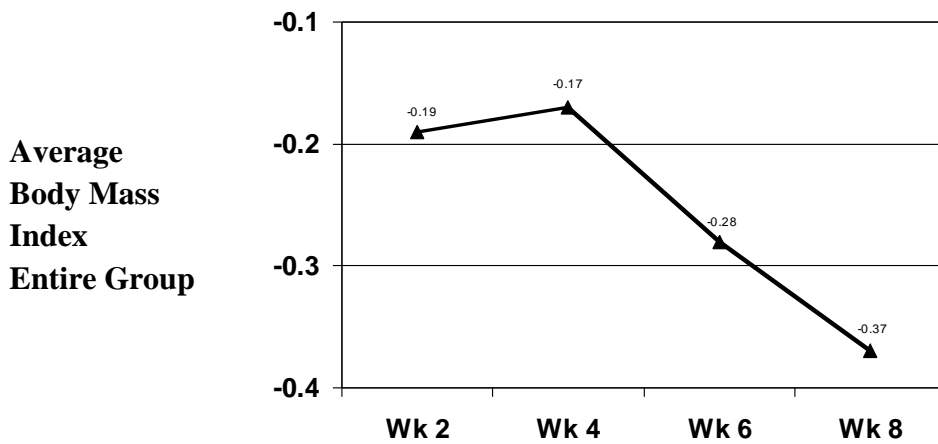
Figure 4. Average reduction in hip measurements for the responder group (n=19) on Healthy Curb®.



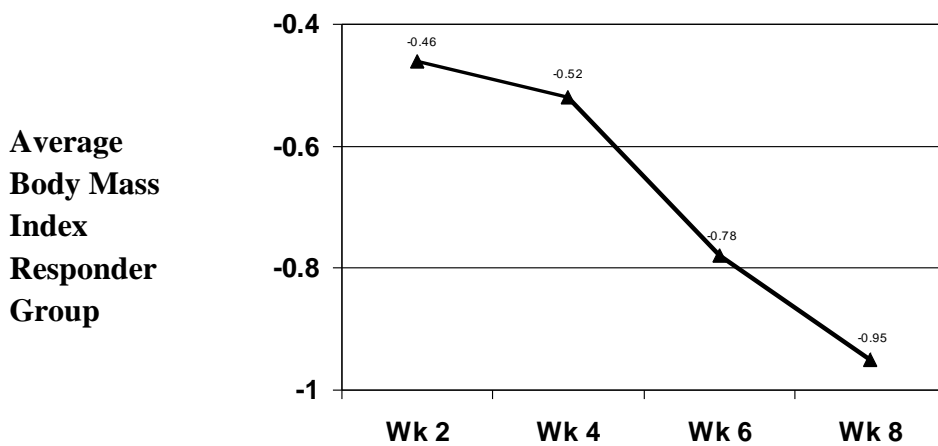
**Figure 5. Average reduction in waist measurements for entire group on Healthy Curb®.**



**Figure 6. Average reduction in waist measurements for responder group (n=19) on Healthy Curb®.**



**Figure 7. Average reduction in BMI measurements for entire group on Healthy Curb®.**



**Figure 8. Average reduction in BMI measurements for responder group on Healthy Curb®.**

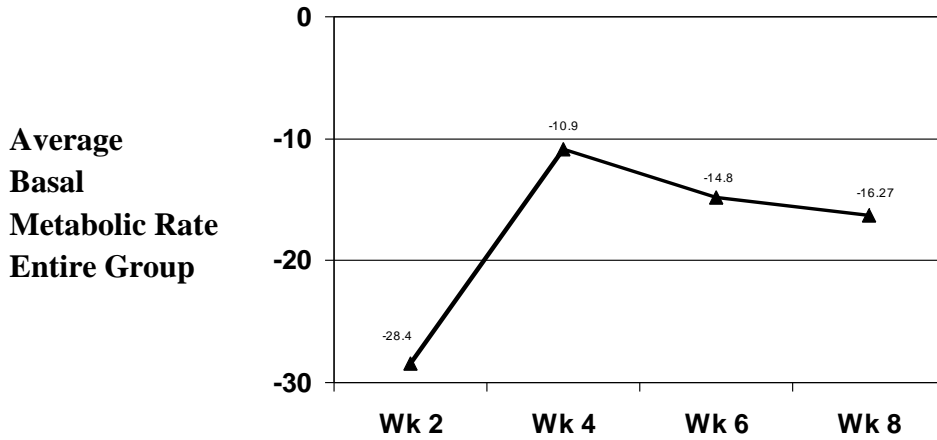


Figure 9. Average change in BMR measurements for entire group on Healthy Curb®.

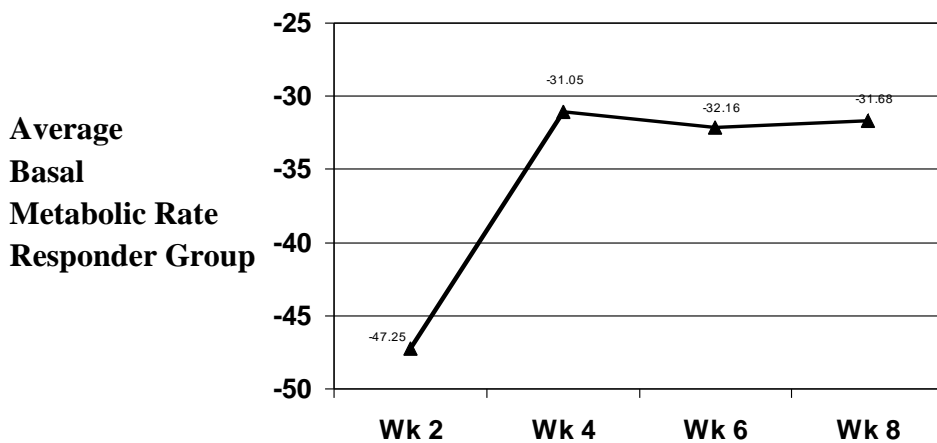


Figure 10. Average change in BMR measurements for responder group on Healthy Curb®.

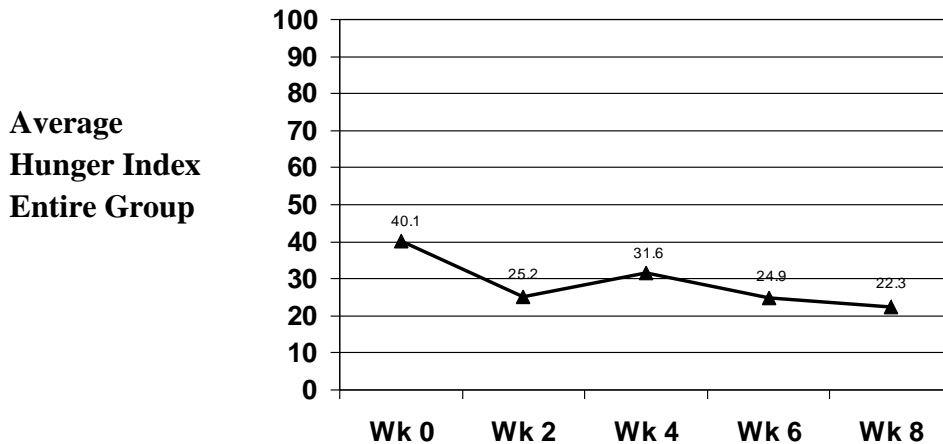


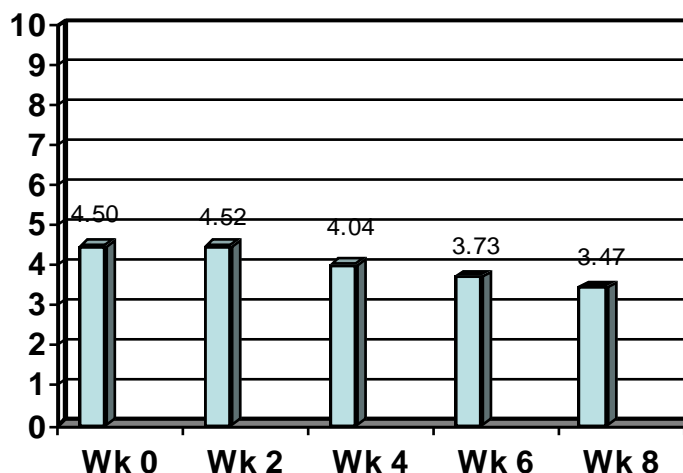
Figure 11. Overall hunger index change for entire group on Healthy Curb®.

**Appetite Suppression.** By the end of the trial there was an average suppression of appetite of 44.5% in the entire group on Healthy Curb® (Fig. 11) ( $p < 0.001$ ), with decreases in cravings for sweets and fatty foods (data not shown). In addition, there was a 38.9% improvement in fullness by the end of the



trial; thus participants felt more full and satisfied while on Healthy Curb® (data not shown).

**Reduction in Fatigue.** The overall PFS fatigue scores during the trial are shown in Fig. 12). There was a reduction in overall fatigue for the entire group of 23.9% by the end of the 8 week trial ( $p < 0.009$ ).



**Figure 11. Overall fatigue change (PFS scores) for entire group on Healthy Curb®.**

Fatigue is a multidimensional phenomenon, and the PFS evaluation can be further dissected into subcategories that include: overall fatigue, behavior/severity, affective meaning, sensory and cognitive/mood (Table 2). All of these subcategories showed mean reductions at the end of the trial: 20.3% reduction ( $p < 0.009$ ) in the Behavior/Severity category, 18.4% reduction ( $p < 0.01$ ) in the Affective/Meaning category, 28.4% reduction ( $p < 0.005$ ) in the Sensory category and 26.8% reduction ( $p < 0.004$ ) in the Cognitive/Mood category. This indicated that there were improvements in all subcategories of fatigue. The cognitive/mood improvements indicated that there was a 26.8% perceived improvement ( $p < 0.004$ ) in cognition and ability to concentrate, remember and think clearly at the end of the 8 week trial (Table 2).

**Table 2. Results From Overall Fatigue and Subcategories of the Piper Fatigue Scale Survey**

Category	Mean Fatigue Level $\pm$ S.E.M.		Percent Reduction	t-test
	Week 0	Week 8		
Overall Fatigue	4.56 $\pm$ 0.34	3.47 $\pm$ 0.40	23.9	$p < 0.009$
Behavior/Severity	3.59 $\pm$ 0.46	2.86 $\pm$ 0.42	20.3	$p < 0.01$
Affective/Meaning	4.73 $\pm$ 0.52	2.86 $\pm$ 0.52	18.4	$p < 0.01$

Sensory	5.43 ± 0.36	3.89 ± 0.42	28.4	p<0.005
Cognitive/Mood	4.47 ± 0.26	3.27 ± 0.36	26.8	p<0.004

**Blood Chemistry Profiles.** There were few significant changes in blood chemistry during the trial; however, there were changes in blood lipids (Table 3). Average HDL increased during the trial, whereas average LDL and cholesterol amounts in blood decreased (Table 3). There was a significant decrease in cholesterol/HDL ratio (p<0.0019) and significant increase in HDL/LDL ratio (p<0.004); whereas the other changes were not significant (data not shown).

**Table 3. Selected blood chemistry values before and 8 weeks after Healthy Curb®.**

<i>Measurement</i>	<i>Week 0</i>	<i>Week 8</i>
Glucose	104.8 ± 8.8 mg/dl	103.4 ± 5.5 mg/dl
Cholesterol	209.6 ± 5.7 mg/dl	200.7 ± 5.4 mg/dl
Triglycerides	142.6 ± 13.6 mg/dl	129.2 ± 12.6 mg/dl
HDL	56.9 ± 2.8 mg/dl	58.0 ± 2.4 mg/dl
LDL (Calc)	124.2 ± 4.8 mg/dl	116.8 ± 4.3 mg/dl
VLDL (Calc)	28.5 ± 2.7 mg/dl	25.8 ± 2.5 mg/dl
Cholesterol/HDL Ratio	3.94 ± 0.25	3.7 ± 0.20
HDL/LDL Ratio	0.458 ± 0.003	0.500 ± 0.002

## **DISCUSSION:**

The test supplement used in this study, Healthy Curb®, is a combination of NT Factor® and alpha-amylase inhibitor extract. The latter extract has been shown to be effective in previous weight loss studies [14-17]. The use of alpha-amylase inhibitors has been touted for use in the treatment of diabetes, because it lowers blood sugar concentrations [27, 28]. Products containing alpha-amylase

inhibitors from *Phaseolus vulgaris* have been shown to control weight by slowing and preventing the absorption of carbohydrates through inhibition of enzymes responsible for their digestion [14-17, 27-29]. With the addition of NT Factor® for appetite control and reduction of fatigue, Healthy Curb® has the added benefit of helping overweight and obese persons from over-eating and reducing their physical activity due to fatigue.

Healthy Curb® significantly improved the overall fatigue scores of participants of this study as measured by the PFS instrument. There were improvements in all subcategories of fatigue. For example, there was a 26.8% perceived improvement ( $p < 0.004$ ) in cognition and ability to concentrate, remember and think clearly. These results were consistent with several other clinical studies where NT Factor® was used to control fatigue and improve mitochondrial function [13, 18, 21, 25, 30]. In these studies patients with severe fatigue, chronic fatigue syndrome or fibromyalgia syndrome, NT Factor® significantly reduced fatigue [30] and significantly improved mitochondrial function to a level that was similar to that found in young, healthy adults [31].

NT Factor® in Healthy Curb® also helped in appetite control along with the alpha-amylase inhibitor [27, 29]. In the present study there was a 44.5% reduction in appetite and reductions in sugar cravings. Blum and his associates [32] have found that a predisposition to glucose craving and obesity is due to inadequate dopaminergic activity in the reward center of the brain. This defect drives individuals to engage in activities of behavioral excess, which, in turn, enhance brain dopamine function. Consumption of large quantities of alcohol or carbohydrates (carbohydrate binging) stimulates production of dopamine within the brain. This has led to the term reward deficiency syndrome (RDS), which may be used to explain certain biologic influences on behavior [33]. In the case of dopamine receptors, which have been related to obesity, body mass index, overeating, carbohydrate binging and energy expenditure [34], it would be interesting to see if NT Factor® has any effect on this receptor.

As expected for a product containing two safe components, NT Factor® and alpha-amylase inhibitor, Healthy Curb® was extremely well tolerated and did not cause any adverse effects during the trial. Participants experienced gradual and consistent weight loss along with significant reductions in waist and hip measurements along with reduced food cravings without changing their eating and exercise routines. They also experienced improvements in blood lipid profiles. Thus Healthy Curb® has been shown to be a safe and effective weight loss supplement that has additional health benefits.

### **Abbreviations Used**

BMI, body mass index; BMR, basal metabolic rate; HDL, high density lipoprotein; LDL, low density lipoprotein; PFS, Piper Fatigue Scale;

### **Competing Interests**

The authors have no financial interests or conflicts of interest.

### **Authors' Contributions**

All authors contributed to this study.

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## References

1. Garaulet M, Ordovas JM, Madrid JA. The chronobiology, etiology and pathophysiology of obesity. *Int J Obesity (London)* 2010; 34: 1667-1683.
2. Farooqi IS. Genetic, molecular and physical insights into human obesity. *Eur J Clin Invest* 2011; 41: 451-455.
3. Ha TS, Tajar A, Lean ME. Obesity and weight management in the elderly. *Br Med Bull* 2011; 97: 169-196.
4. Buffenstein R, Karklin A, Driver HS. Beneficial physiological and performance responses to a month of restricted energy intake in healthy overweight women. *Physiol Behav* 2000; 68: 439-444.
5. Kroenke K, Wood DR, Mangelsdorff AD, Meier NJ, Powell JB. Chronic fatigue in primary care. Prevalence, patient characteristics, and outcome. *JAMA* 1988; 260: 929-934.
6. Morrison JD. Fatigue as a presenting complaint in family practice. *J Family Pract* 1980; 10: 795-801.
7. Resnick HE, Carter EA, Alola M, Phillips B. Cross-sectional relationship of reported fatigue to obesity, diet, and physical activity: results from the third national health and nutrition examination survey. *J Clin Sleep Med* 2006; 2(2): 163-169.
8. Mann T, Tomiyama AJ, Westling E, Lew AM, Samuels B, Chatman J. Medicare's search for effective obesity treatments: diets are not the answer. *Am Psychol* 2007; 62: 220-233.
9. Vetter ML, Faulconbridge LF, Webb VL, Wadden TA. Behavioral and pharmacologic therapies for obesity. *Nature Rev Endocrinol* 2010; 6(10): 578-588.
10. Hensrud DD. Pharmacotherapy for obesity. *Med Clin North Am* 2000; 84: 463-476.
11. Yun JW. Possible anti-obesity therapeutics from nature. *Phytochem* 2010; 71: 1625-1641.
12. Han LK, Kimura Y, Okuda H. Anti-obesity effects of natural products. *Stud Nat Prod Chem* 2005; 30: 79-110.
13. Nicolson GL, Settineri R. 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. *Funct Foods Health Dis* 2011; 4: 135-160.
14. Layer P, Zinsmeister AR, de Magno EP. Effects of decreasing intraluninal amylase activity on starch digestion and postprandial gastrointestinal function in humans. *Gastroenterol* 1986; 91: 41-48.
15. Layer P, Rizza RA, Zinsmeister AR, et al. Effect of a purified amylase inhibitor on carbohydrate tolerance in normal subjects and patients with diabetes mellitus. *Mayo Clin Proc* 1986; 61: 442-447.

16. Udani J, Hardy M, Madsen DC. Blocking carbohydrate absorption and weight loss: A clinical trial using phase 2 brand proprietary fractionated white bean extract. *Altern Med Rev* 2004; 9(1): 63-69.
17. Celleno L, Tolaini MV, D'Amore A, Perricone NV, Preuss HG. A dietary supplement containing standardized *Phaseolus vulgaris* extract influences body composition of overweight men and women. *Int J Med Sci* 2007; 4(1): 45-52.
18. Nicolson GL. Metabolic syndrome and mitochondrial function: molecular replacement and antioxidant supplements to prevent membrane oxidation and restore mitochondrial function. *J Cell Biochem* 2007; 100: 1352-1369.
19. Heckman MA, Weil J, Gonzalez de Mejia E. Caffeine (1,3,7-trimethylxanthine) in foods: a comprehensive review on consumption, functionality, safety and regulatory matters. *J Food Sci* 2010; 75: R77-R87.
20. Wang J, Li S, Fan Y, Chen Y, Liu D, Cheng H, Zhou Y. Anti-fatigue activity of the water-soluble polysaccharides isolated from Panax ginseng C. A. Meyer. *J Ethnopharmacol* 2010; 30: 421-423.
21. Ellithorpe RR, Settineri R, Nicolson GL. Pilot study: reduction of fatigue by use of a dietary supplement containing glycerophospholipids. *J Am Nutraceut Assoc.* 2003; 6(1): 23-28.
22. Piper BF, Dribble SL, Dodd MJ. The revised Piper Fatigue Scale: psychometric evaluation in women with breast cancer. *Oncol Nursing Forum* 1998; 25: 667-684.
23. Piper BF, Linsey AM, Dodd MJ. Fatigue mechanism in cancer. *Oncol Nursing Forum* 1987; 14: 17-23.
24. Arumugam V, Lee JS, Nowak JK, Pohle RJ, Nyrop JE, Leddy JJ, Pelkman CL. A high glycemic meal pattern elicited increased subjective appetite sensations in overweight and obese women. *Appetite* 2008; 50: 215-222.
25. Nicolson GL, Ellithorpe RR, Ayson-Mitchell C, Jacques B, Settineri R. Lipid Replacement Therapy with a glycerophospholipid-antioxidant-vitamin formulation significantly reduces fatigue within one week. *J Am Nutraceutical Assoc* 2010; 13(1): 11-15.
26. MacKay NJ. Scaling of human body mass with height: the Body Mass Index revisited. *J Biomechanics* 2010; 43: 764-766.
27. Tundis R, Loizzo MR, Menichini F. Natural products as alpha-amylase and alpha-glucosidase inhibitors and their hypoglycaemic potential in the treatment of diabetes: an update. *Mini Rev Med Chem* 2010; 10(4): 315-331.
28. Barrett ML, Udani JK. A proprietary alpha-amylase inhibitor from white bean (*Phaseolus vulgaris*): a review of clinical studies on weight loss and glycemic control. *Nutr J* 2011; 10: 24.
29. Carai MA, Fantini N, Loi B, Colombo G, Riva A, Morazzoni P. Potential efficacy of preparations derived from *Phaseolus vulgaris* in the control of appetite, energy intake and carbohydrate metabolism. *Diabetes Metab Syndr Obes* 2009; 2: 145-153.
30. Nicolson, G.L. and Ellithorpe, R. Lipid replacement and antioxidant nutritional therapy for restoring mitochondrial function and reducing fatigue in chronic fatigue syndrome and other fatiguing illnesses. *J Chronic Fatigue Syndr.* 2006; 13(1): 57-68.

31. Agadjanyan M, Vasilevko V, Ghochikyan A, Berns P, Kesslak P, Settineri R, Nicolson GL. Nutritional supplement (NTFactor) restores mitochondrial function and reduces moderately severe fatigue in aged subjects. *J Chronic Fatigue Syndr* 2003; 11(3): 23-26.
32. Blum K, Chen TJ, Meshkin B, Downs BW, Gordon CA, Blum S, Mengucci JF, Braverman ER, Arcuri V, Varshavskiy M, Deutsch R, Martinez-Pons M. Reward deficiency syndrome in obesity: a preliminary cross-sectional trial with a Genotrim variant. *Adv Ther* 2006; 23(6): 1040-1051.
33. Blum K, Liu Y, Shriner R, Gold MS. Reward circuitry dopaminergic activation regulates food and drug craving behavior. *Curr Pharm Des* 2011; 17(12): 1158-1167.
34. Chen AL, Blum K, Chen TJ, Giordano J, Downs BW, Han D, Barh D, Braverman ER. Correlation of the Taq1 dopamine D2 receptor gene and percent body fat in obese and screened control subjects: a preliminary report. *Food Funct* 2011; Nov. 3, 2011 [Epub ahead of print].