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# Mushrooms as a functional food mediator in Preventing and ameliorating diabetes

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Submission date: March 23, 2011; Acceptance date: April 23, 2011; Publication date: April 25, 2011

**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

## Introduction

As of 2000 at least 171 million people worldwide suffer from diabetes, or 2.8% of the population [1]. Diabetes is a major health problem predisposing to markedly increased cardiovascular mortality and serious morbidity and mortality related to development of nephropathy, neuropathy and retinopathy [2]. Although chemical and biochemical hypoglycemic agents, e.g., insulin,

tolbutamide, phenformin, troglitazone, rosigitazone and repaglinide, are the mainstay of treatment of diabetes and are effective in controlling hyperglycemia, they have harmful side-effects and fail to significantly alter the course of diabetic complications [3].

Some mushrooms appear to be effective for both the control of blood glucose and the modification of the course of diabetic complications without side-effects. This review particularly explores the promising mushrooms that have demonstrated clinical or/and experimental anti-diabetic properties by preventing or lowering down the development of diabetes mellitus. But still scientific or clinical studies are not sufficient enough to show the hypoglycemic effects of mushrooms to be use as 'official' drugs or nutraceuticals. Therefore, we suggest a closer attention be paid to the mushrooms that have preventive and curative functions of diabetes mellitus and its complications.

## Diabetes mellitus (DM)

There are two main types of Diabetes mellitus (DM); type I diabetes and type II diabetes. Type I diabetes occurs as a result of deficiency of insulin due to destructive lesions of pancreatic β-cells, and usually progresses to the stage of absolute insulin deficiency [4]. Typically, type I diabetes occurs in young subjects with acute onset, but may occur at any age, sometimes with slow progression [5]. Type I diabetes may be further divided into subtypes according to the mode of onset (i.e. acute or slowly-progressive), HLA antigens, or epitopes of autoantigens [5, 6].

Most patients previously called non insulin-dependent diabetes mellitus (NIDDM) belong to Type II diabetes category. In this type, the mass of pancreatic β cells and their function are preserved to some extent, and insulin injection is seldom needed to sustain life. Ketoacidosis may occur in the presence of severe infection or other stress. Both decreased insulin secretion and decreased insulin sensitivity (insulin resistance) are involved in its pathogenesis. Insulin resistance may not always be present. The relative role of these two factors varies between patients. With regard to insulin secretion, the acute insulin response to a glucose load is characteristically defective. The majority of patients are obese or have been obese in the past. The prevalence of type II DM among adults varies from less than 5% to over 40% depending on the population in question [2]. With the increase of obesity, sedentariness and dietary habits in both developed and developing countries, the prevalence of type II DM is growing at an exponential rate [2, 7]. Typically, type II DM develops after middle age, but may occur in younger people. Screening by urine analysis of large numbers of school children has revealed that type II diabetes has been steadily increasing since the 1970s [8, 9].

## Mushrooms as a functional food

Chang *et al.* defined the mushrooms as "a macro fungus with distinctive fruiting bodies that could be hypogeous or epigeous, large enough to be seen by naked eyes and to be picked by hands [10]. From taxonomic point of view, basidiomycetes and some species of ascomycetes mainly belong to category of mushrooms. Mushrooms constitute 22,000 known species. They

are widely available on earth and about 10% of them are explored. Among the unexplored and unexamined mushrooms, if the proportion of useful mushroom is 5%, it suggests that 7000 undiscovered species would possibly provide benefit to mankind [11].

Numerous species of mushrooms exist in nature; however, only a few are used as edibles. Many Asian countries use traditionally wild edible mushrooms as delicious and nutritional foods and medicine [12]. Wild edible mushrooms are appreciated not only for their texture and flavor but also for the chemical and nutritional characteristics [13, 14]. Edible mushrooms have higher protein contents and minerals and contain less fat but are rich in B vitamins, vitamin D, vitamin K and sometimes vitamins A and C [15-18]. Mushrooms are not only sources of nutrients but also have been reported as therapeutic foods, useful in preventing diseases such as hypertension, diabetes, hypercholesterolemia and cancer [19, 20]. These functional characteristics are mainly due to the presence of dietary fiber and in particular chitin and beta glucans [16]. Studies have also shown that certain mushrooms species have antitumor, antiviral, antithrombotic and immunomodulating properties. [21]. Research has shown that some mushrooms may have potential to lower elevated blood sugar levels. But the explanation for this effect is limited, with the exception of some mushrooms. Therefore it is useful to carry out more research on mushrooms with a view to identify active principles in them for the treatment of diabetes mellitus and its complications.

## Medicinal mushrooms and diabetes

### *Tremella fuciformis* (berk)

*Tremella fuciformis* has been given the common names snow fungus or silver ear fungus. In Chinese cuisine, *Tremella fuciformis* is traditionally used in sweet dishes. Despite its tasteless nature, *T. fuciformis* is valued for its gelatinous texture as well as its supposed medicinal benefits [22]. Glucuronoxylomannan (AC) from the fruiting bodies of *T. fuciformis* exhibited a significant dose-dependent hypoglycemic activity in normal mice and also showed a significant activity in streptozotocin-induced diabetic mice, by intraperitoneal administration [23]. The anti-diabetic activities of the exopolysaccharides (EPS) produced by submerged mycelial culture of *T. fuciformis* in ob/ob mice were investigated [24]. The results suggested that EPS exhibited considerable hypoglycemic effect and improved insulin sensitivity possibly through regulating PPAR-gamma-mediated lipid metabolism [24]. These results indicated that *Tremella fuciformis* has potential oral hypoglycemic effect as a functional food for the management of DM.

### *Wolfiporia extensa* (Peck) Ginns (formerly known as *Poria cocos* F.A. Wolf)

*Poria cocos*, a rotten pine-tree fungus is a wood decay fungus but has a terrestrial growth habit. It has long been used as traditional Chinese medicine and food [25-27]. *Poria cocos*, alone or in combination with other herbs is often used to treat diabetes as well as other disorders [28-30]. Mechanistic study on streptozocin (STZ) treated mice showed that the crude extract,

dehydrotumulosic acid, dehydrotrametenolic acid, and pachymic acid of *Poria cocos* exhibited different levels of insulin sensitizer activity [31]. The data suggested that the *Poria cocos* extract and its triterpenes reduce postprandial blood glucose levels in db/db mice via enhanced insulin sensitivity irrespective of PPAR-γ [31].

***Ganoderma lucidum* (Curtis) P.Karst**

*Ganoderma lucidum* has been use since the 4th century A.D. and is well known in China as the herb of longevity. *Ganoderma* is to be famous tonic and found an important place in Chinese medicine due to its beneficial effects to all viscera and nontoxic nature [32]. Research workers have found that *Ganoderma lucidum* polysaccharides (Gl-PS) dose-dependently lowered the serum glucose levels after administration in mice. *Ganoderma lucidum* polysaccharides (Gl-PS) possess the hypoglycemic effect on normal mice; one mechanism is through its insulin releasing activity due to a facilitation of Ca2+ inflow to the pancreatic beta cells [33].

***Ganoderma applanatum* (Pers.) Pat. and *Collybia confluens* (Pers.: Fr.) Kummer**

The hypoglycemic effects of *Ganoderma applanatum* exo-polymer (GAE) and *Collybia confluens* exo-polymer (CCE) produced by submerged mycelial cultures in streptozotocin (STZ)-induced diabetic rats were shown hypoglycemic effects. The results strongly demonstrated the potential of GAE and CCE in combating diabetes in experimental animals [34].

***Auricularia auricula-judae* (Bull.)**

*Auricularia auricula-judae*, known as the Jew's Ear, Jelly Ear is a species of edible Auriculariales mushroom found worldwide. Distinguished by its noticeably ear-like shape and brown coloration, it grows upon wood. It is popular in China, where the medicinal use of food is common; a soup containing *A. auricula-judae*, chicken, pak choi and ginger is used medicinally for dealing with colds and fevers by reducing the heat of the body [35]. The hypoglycemic effect of water-soluble polysaccharide (FA) from fruiting bodies of *A. auricula-judae* was investigated on genetically diabetic mice (KK-Ay). This study showed that FA had a hypoglycemic effect on KK-Ay mice, and the reduced food consumption was not a major factor which contributed to the hypoglycemic action of FA [36].

***Agaricus campestris* (L.)**

*Agaricus campestris* has fast maturing and short shelf-life [37]. *A. campestris* (mushroom) has been documented as a traditional treatment for diabetes. The administration of mushroom in the diet and drinking water countered the hyperglycaemia of streptozotocin-diabetic mice [38].

***Agaricus subrufescens* (Peck)**

*Agaricus subrufescens* is a choice edible, with a somewhat sweet taste and fragrance of almonds [39].In Japan, *A. subrufescens* is also the most popular complementary and alternative medicine

used by cancer patients [40]. *A. brasiliensis* fruit body is useful as a health promoting food. Performed studies on murine models and human volunteers to examine the immune-enhancing effects of the naturally outdoor-cultivated fruit body of *Agaricus brasiliensis* KA21 (i.e. *Agaricus blazei*) has shown antitumor, leukocyte-enhancing, hepatopathy-alleviating and endotoxin shock-alleviating effects in mice [41]. In the human study, percentage body fat, percentage visceral fat, blood cholesterol level and blood glucose level were decreased and natural killer cell activity was increased [41]. Beta-glucans and oligosaccharides (AO) of *Agaricus blazei* Murill showed anti-hyperglycemic, anti-hypertriglyceridemic, anti-hypercholesterolemic, and anti-arteriosclerotic activity indicating overall anti-diabetic activity in diabetic rats, AO had about twice the activity of beta-glucans with respect to anti-diabetic activity [42]. Further supplement of *Agaricus blazei* Murill extract has improved insulin resistance among subjects with type 2 DM. The increase in adiponectin concentration after taking *Agaricus blazei* Murill extract might be the mechanism that brings the beneficial effect [43].

***Inonotus obliquus* (L.)**

Chaga mushroom (*Inonotus obliquus*), a white rot fungus, belongs to the hymenochaetaceae family of Basidomycetes. Chaga mushroom grows on birch trees in colder northern climates [44]. Since the sixteenth century, Chaga has been used as a folk medicine in Russia and western Siberia [45]. Researches exposed that the dry matter of culture broth of *Inonotus obliquus* possesses significant anti-hyperglycemic, anti-lipid peroxidative and antioxidant effects in alloxan-induced diabetic mice [46].

***Hericium erinaceus*** (Bull.)

*Hericium erinaceus* is named for its shape, and is literally interpreted as "Monkey Head Mushroom" in China. Recent studies have determined that many types of mushroom (eg *Hericium* spp), may have important physiological functions in humans, including antioxidant activities, the regulation of blood lipid levels and reduction of blood glucose levels [47]. Researchers have found that the hypoglycemic effects of feeding the methanol extract of *H erinaceus* to streptozotocin-induced diabetic rats were significantly lower elevation rates of blood glucose levels [47].

***Agrocybe aegerita***

It is an important valuable source possessing varieties of bioactive secondary metabolites such as indole derivatives with free radical scavenging activity, cylindan with anticancer activity, and also agrocybenine with antifungal activity [48]. A glucan and a heteroglycan were isolated from a hot-water extract of the fruiting bodies of *Agrocybe cylindracea*. A glucan showed a remarkable hypoglycemic activity in both normal and streptozotocin-induced diabetic mice by intraperitoneal administration, and its activity was higher than that of heteroglycan [49].

***Coprinus comatus*** (O.F.Mull)

The young mushrooms of *Coprinus comatus*, before the gills start to turn black, are edible. It can sometimes be used in mushroom soup with parasol mushroom [50].This species is cultivated in China as food. When young it is an excellent edible mushroom provided that it is eaten soon after being collected. It can be used as a hypoglycemic food or medicine for hyperglycemic people [51].The hypoglycemic activity of fermented mushroom, *Coprinus comatus* tested on Alloxan and adrenalin-induced hyperglycemic mice. It confirmed that *Coprinus comatus* rich in vanadium has significant anti-hyperglycemic effect [51].

***Cordyceps sinensis***

*Cordyceps sinensis*, known in English commonly as caterpillar fungus is considered a medicinal mushroom in traditional Chinese medicine [52]. Crude polysaccharides of *Cordyceps sinensis* were tested in normal mice and streptozotocin-induced diabetic mice. It significantly lowered the glucose level by oral administration in mice [53]. A polysaccharide obtained from the cultural mycelium of *Cordyceps sinensis* showed potent hypoglycemic activity in genetic diabetic mice after intraperitoneal administration, and the plasma glucose level was quickly reduced in normal and streptozotocin-induced diabetic mice after intravenous administration [54].Further *Cordyceps*, a Chinese herbal medicine with fruiting body and carcass, has been proposed to have multiple medicinal activities. The diabetic rats had significantly lower weight gain and higher blood glucose response in oral glucose tolerance test than the control rats; and these changes were significantly reduced by administrating the fruiting body of *Cordyceps* and these improvements suggested that fruiting body of *Cordyceps* has a potential to be the functional food for diabetes[55]. Another research revealed that isolated polysaccharide from *Cordyceps sinensis*, named CSP-1 produced a significant drop in blood glucose level in both STZ-induced diabetic rats and alloxan-induced diabetic mice. It suggested that CSP-1 may stimulate pancreatic release of insulin and/or reduce insulin metabolism [56].

***Grifola frondosa*** **(Dicks.)**

*Grifola frondosa* is also very popular in Korea, China and Japan, where it is cultivated as maitake, the dancing mushroom. Controlled experiments have found many beneficial activities attributable to *Grifola frondosa* and/or its extracts. The reason Maitake lowers blood sugar is due to the fact that the mushroom naturally contains an alpha-glucosidase inhibitor. Alpha-glucosidase inhibitory activities were found in aqueous methanol extracts of the seeds of *Momordica charantia* and the fruit bodies of *Grifola frondosa* [57]. Researchers evaluated the anti-diabetic effect of an alpha-glucan (MT-alpha-glucan) from the fruit body of maitake mushrooms (*Grifola frondosa*) on KK-Ay mice. These data suggest that MT-alpha-glucan has an anti-diabetic effect on KK-Ay mice, which might be related to its effect on insulin receptors (i.e.,

increasing insulin sensitivity and ameliorating insulin resistance of peripheral target tissues) [58]. Further animal and human experiments also proven that anti-diabetic activity present in the fruit body of *Grifola frondosa* [59-63].

**Table 1**. Medicinal mushrooms and major effective compounds

| Plant name | Major effective compounds |
|---|---|
| *Tremella fuciformis* (berk) | Glucuronoxylomannan[23] |
| *Wolfiporia extensa* (Peck) | Dehydrotumulosic acid, Dehydrotrametenolic acid and Pachymic acid [31] |
| *Ganoderma lucidum* (Curtis) | Polysaccharides (Gl-PS) [33] |
| *Ganoderma applanatum* (Pers.) Pat. | Exo-polymer (GAE) [34] |
| *Collybia confluens* (Pers.: Fr.) | Exo-polymer (CCE) [34] |
| *Auricularia auricula-judae* (Bull.) | Polysaccharide (FA) [36] |
| *Agaricus subrufescens* (Peck) | Beta-glucans and Oligosaccharides (AO) [42] |
| *Coprinus comatus* (O.F.Mull) | Vanadium[51] |
| *Cordyceps sinensis* | Polysaccharide CSP-1 [56] |
| *Grifola frondosa* (Dicks.) | Alpha-glucan (MT-alpha-glucan) [59-63] |

## Conclusion

Mushrooms with immune-modulating polysaccharides are used as delicious food or as health-promoting food supplement (nutraceutical) or as drug in limited geographic regions. But scientific or clinical studies are not sufficient for use as 'official' drug/nutraceutical worldwide till now. These functional mushrooms might have a particularly high impact for prevention or curative of diabetes more than in other species. Therefore further research needs to identify their active compounds to develop drug/nutraceutical use in diabetes.

## Competing interests

No competing interests.

## Authors' Contributions

Authors contributed equally to this work.

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