

## Review Article

# Diabetes ameliorating effect of mushrooms

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The growing impact of type 2 diabetes in the majority of the population requires the introduction of better and more secure treatments, but also requires the development of new prevention strategies to reduce the incidence and prevalence of the disease. Significantly, type 2 diabetes is an important preventable disease and can be prevented or delayed by lifestyle intervention. Edible and medicinal macro fungi, mushrooms have been reported having diabetes ameliorating effects. Current study reviews the potentiality of both edible and medicinal mushrooms in preventing and ameliorating the diabetic complications as well as the future aspects of mushrooms against this metabolic disorder.

**Key words:** Diabetes mellitus, hyperglycemia, metabolic disorder

## INTRODUCTION

Diabetes mellitus is a life-threatening chronic metabolic disease caused by lack of insulin and/or insulin dysfunction characterized by hyperglycemia. Over 220 million people worldwide suffer from diabetes and its complications, and this number is predicted to increase in future years. Diabetes is a chronic disease that occurs when the pancreas is no longer able to make insulin, or when the body cannot make good use of the insulin it produces. Insulin is a hormone made by the pancreas that acts like a key to let glucose from the food we eat pass from the blood stream into the cells in the body to produce energy. All carbohydrate foods are broken down into glucose in the blood. Insulin helps glucose get into the cells (American Diabetes Association, 2011). There are three main types of diabetes-type 1, type 2 and gestational. Type 1 diabetes can develop at any age, but occurs most frequently in children and adolescents (Kerner, et al. 2014). When one have type 1 diabetes, body produces very little or no insulin, which means that one need daily insulin injections to maintain blood glucose levels under control (Kerner, et al. 2014). Type 2 diabetes is more common in adults and accounts for around 90% of all diabetes cases. When one have type 2 diabetes, body does not make good use of the insulin that it produces. The cornerstone of type 2 diabetes treatment is healthy lifestyle, including increased physical activity and healthy diet. However, over time most people with type 2 diabetes will

require oral drugs and/or insulin to keep their blood glucose levels under control. Gestational Diabetes Mellitus (GDM) is a type of diabetes that consists of high blood glucose during pregnancy and is associated with complications to both mother and child (Khursheed, et al. 2019). GDM usually disappears after pregnancy but women affected and their children are at increased risk of developing type 2 diabetes later in life (Khursheed, et al. 2019). Diabetes dramatically increases risk of various cardiovascular problems, including coronary artery disease with chest pain (angina), heart attack, stroke, narrowing of the arteries (atherosclerosis) and high blood pressure, nerve damage (neuropathy) (Khursheed, et al. 2019).

## LITERATURE REVIEW

Diabetes mellitus is a life-threatening chronic metabolic disease caused by lack of insulin and/or insulin dysfunction characterized by hyperglycemia. Over 220 million people worldwide suffer from diabetes and its complications, and this number is predicted to increase in future year. The growing impact of type 2 diabetes in the majority of the population requires the introduction of better and more secure treatments, but also requires the development of new prevention strategies to reduce the incidence and prevalence of the disease. Significantly, type 2 diabetes is an important preventable disease and can be prevented or delayed by lifestyle intervention.

Many studies have been published on the efficacy of new preventive treatments for diabetes or its complications; however, there is still little information on its applicability. Medicinal mushrooms present an exciting opportunity for the development of new types of therapeutics and have been valued for their potential healing properties for centuries.

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Mushrooms have been valued as remedies for disease and as natural health foods for thousands of years, and they are incredibly popular foods in numerous countries throughout the world. Biologically active metabolites and components derived from medicinal mushrooms have been demonstrated to have controlling effects on diabetes through the regulation of several pathophysiological pathways related to the onset of diabetes. Some of the anti-hyperglycemic mechanisms of medicinal mushrooms have been investigated including  $\beta$ -cell improvement and insulin releasing activity, antioxidant defenses, carbohydrate metabolism pathways,  $\alpha$ -glucosidase and aldose reductase inhibitory activities.

### **Mushrooms as a functional food mediator in preventing and ameliorating diabetes**

Mushroom has ameliorating effects on diabetes (Dubey, et al. 2019). Beta-D glucan is a form of soluble dietary fiber that has been strongly linked to improving cholesterol and boosting heart health (Dubey, et al. 2019). It can also help our body regulate blood sugar, reducing the risk of type 2 diabetes (Lindequist, et al. 2020). Oyster (*Pleurotus*) and shiitake (*Lentinula*) mushrooms are believed to have the most effective beta glucans (Lindequist, et al. 2020). 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 (Lindequist, et al. 2020).

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. Wild edible mushrooms are appreciated not only for their texture and flavor but also for the chemical and nutritional characteristics. 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 (Rahman, et al. 2015).

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 (Yahaya, et al. 2014). These functional characteristics are mainly due to the presence of dietary fiber and in particular chitin and beta glucans (Yahaya, et al. 2014). Certain mushrooms species have antitumor, antiviral, antithrombotic and immunomodulating properties (Rahman, et al. 2015; Rahman, et al. 2017). 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 (Cho, et al. 2007). In Chinese cuisine, *T. fuciformis* is traditionally used in sweet dishes (Cho, et al. 2007). Despite its tasteless nature, *T. fuciformis* is valued for its gelatinous texture as well as its supposed medicinal benefits. 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 (Cho, et al. 2007). The anti-diabetic activities of the Exo-Polysaccharides

(EPS) produced by submerged mycelial culture of *T. fuciformis* in ob/ob mice were investigated (Wu, et al. 2015). The results suggested that EPS exhibited considerable hypoglycemic effect and improved insulin sensitivity possibly through regulating PPAR-gamma-mediated lipid metabolism (Wu, et al. 2015). These results indicated that *T. fuciformis* has potential oral hypoglycemic effect as a functional food for the management of DM (Cho, et al. 2007; Wu, et al. 2015).

*Wolfiporia extensa* (Peck) Ginns (formerly known as *Poriacocos*): *Poriacocos*, a rotten pine-tree fungus is a wood decay fungus but has a terrestrial growth habit (Kim, et al. 2019). It has long been used as traditional Chinese medicine and food. *Poriacocos*, alone or in combination with other herbs is often used to treat diabetes as well as other disorders (Kim, et al. 2019). Mechanistic study on Streptozotocin (STZ) treated mice showed that the crude extract, dehydrotumulosic acid, dehydrotrametenolic acid, and pachymic acid of *Poriacocos* exhibited different levels of insulin sensitizer activity (Kim, et al. 2019; Li, et al. 2019). The data suggested that the *Poriacocos* extract and its triterpenes reduce postprandial blood glucose levels in db/db mice via enhanced insulin sensitivity irrespective of PPAR- $\gamma$  (Kim, et al. 2019; Li, et al. 2019).

*Ganoderma lucidum* (Curtis): *Ganoderma lucidum* has been used 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 (Rahman, et al. 2017). Research workers have found that *G. lucidum* Polysaccharides (GL-PS) dose-dependently lowered the serum glucose levels after administration in mice. *G. lucidum* Polysaccharides (GL-PS) possess the hypoglycemic effect on normal mice; one mechanism is through its insulin releasing activity due to a facilitation of  $\text{Ca}^{2+}$  inflow to the pancreatic beta cells (Chen, et al. 2020).

*Ganoderma applanatum* (Pers.) Pat. and *Collybiaconfluens* (Pers.: Fr.): The hypoglycemic effects of *Ganodermaapplanatum*exo-polymer (GAE) and *Collybiaconfluens*exo-polymer (CCE) produced by submerged mycelial cultures in streptozotocin (STZ)-induced diabetic rats were shown hypoglycemic effects (Winska, et al. 2019). The results strongly demonstrated the potential of GAE and CCE in combating diabetes in experimental animals (Winska, et al. 2019).

*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, pakchoi and ginger is used medicinally for dealing with colds and fevers by reducing the heat of the body. The hypoglycemic effect of water-soluble polysaccharide from fruiting bodies of *A. auricula-judae* was investigated on genetically diabetic mice (KK-Ay) (Winska, et al. 2019; Yuan, et al. 1998). 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 soluble

polysaccharide from fruiting bodies of *A. auricula-judae* (Winska, et al. 2019; Yuan, et al. 1998).

***Agaricus campestris*:** *Agaricus campestris* has fast maturing and short shelf-life. *A. campestris* has been documented as a traditional treatment for diabetes. Its insulin-like and insulin releasing activities have been reported (Gray, et al. 1998). The administration of mushroom in the diet and drinking water countered the hyperglycaemia of streptozotocin-diabetic mice (Gray, et al. 1998).

***Agaricus subrufescens* (Peck):** *Agaricus subrufescens* is a choice edible, with a somewhat sweet taste and fragrance of almonds. In Japan, *A. subrufescens* is also the most popular complementary and alternative medicine used by cancer patients (Wisitrassameewong, et al. 2012). *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 *A. brasiliensis* KA21 (i.e. *Agaricus blazei*) has shown antitumor, leukocyte-enhancing, hepatopathy-alleviating and endotoxin shock-alleviating effects in mice (Yamanaka, et al. 2013). 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. 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 (Yamanaka, et al. 2013; Silva, et al. 2017; Yamamoto, et al. 2019). Further supplement of *A. blazei* Murill extract has improved insulin resistance among subjects with type 2 DM (Yamanaka, et al. 2013; Silva, et al. 2017; Yamamoto, et al. 2019). The increase in adiponectin concentration after taking *A. blazei* Murill extract might be the mechanism that brings the beneficial effect (Yamanaka, et al. 2013; Silva, et al. 2017; Yamamoto, et al. 2019).

***Inonotus obliquus*:** Chaga mushroom (*Inonotus obliquus*), a white rot fungus, belongs to the Hymenochaetaceae family of Basidiomycetes. Chaga mushroom grows on birch trees in colder northern climates. Since the sixteenth century, Chaga has been used as a folk medicine in Russia and western Siberia (Xu, et al. 2010; Bijl, et al. 2019). Researches exposed that the dry matter of culture broth of *I. obliquus* possesses significant anti-hyperglycemic, anti-lipid peroxidative and antioxidant effects in alloxan-induced diabetic mice (Xu, et al. 2010; Bijl, et al. 2019).

***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 (*Hericium spp*), may have important physiological functions in humans, including antioxidant activities, the regulation of blood lipid levels and reduction of blood glucose levels (Liang, et al. 2013; Zhang, et al. 2017). 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 (Liang, et al. 2013; Zhang, et al. 2017).

***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 (Zhang, et al. 2015). A glucan and a heteroglycan were isolated from a hot-water extract of the fruiting bodies of *A. cylindracea* (Zhang, et al. 2015). 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 (Zhang, et al. 2015).

***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. 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. The hypoglycemic activity of fermented mushroom, *C. comatus* tested on Alloxan and adrenalin-induced hyperglycemic mice (Gao, et al. 2021; Zhou, et al. 2015; Lv, et al. 2009). It confirmed that *C. comatus* rich in vanadium has significant anti-hyperglycemic effect (Gao, et al. 2021; Zhou, et al. 2015; Lv, et al. 2009).

***Cordyceps sinensis*:** *Cordyceps sinensis*, known in English commonly as caterpillar fungus is considered a medicinal mushroom in traditional Chinese medicine. Crude polysaccharides of *C. sinensis* were tested in normal mice and streptozotocin-induced diabetic mice. It significantly lowered the glucose level by oral administration in mice (Ashry, et al. 2012; Cao, et al. 2020). 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 (Ashry, et al. 2012; Cao, et al. 2020). 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 administering the fruiting body of Cordyceps and these improvements suggested that fruiting body of Cordyceps has a potential to be the functional food for diabetes (Luo, et al. 2015). Another research revealed that isolated polysaccharide from *C. sinensis*, named CSP-1 produced a significant drop in blood glucose level in both STZ-induced diabetic rats and alloxan-induced diabetic mice (Luo, et al. 2015). It suggested that CSP-1 may stimulate pancreatic release of insulin and/or reduce insulin metabolism.

***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 *G. 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 (Lindequist, et al. 2020; He, et al. 2020). Alpha-glucosidase inhibitory activities were found in aqueous methanol extracts of the seeds of *Momordica charantia* and the fruit bodies of *G. frondosa*. Researchers evaluated the anti-diabetic effect of an alpha-glucan (MT-alpha-glucan) from the fruit body of *G. frondosa* on KK-Ay mice (Guo, et al. 2019). 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 (increasing insulin sensitivity and ameliorating insulin resistance of peripheral target tissues). Further animal and human experiments also proven that anti-diabetic activity present in the fruit body of *G. frondosa* (Jiang, et al. 2020).

## DISCUSSION AND CONCLUSION

Many studies have been published on the efficacy of new preventive treatments for diabetes or its complications; however, there is still little information on its applicability. Medicinal mushrooms present an exciting opportunity for the development of new types of therapeutics and have been valued for their potential healing properties for centuries. Mushrooms have been valued as remedies for disease and as natural health foods for thousands of years, and they are incredibly popular foods in numerous countries through-out the world. Biologically active metabolites and components derived from medicinal mushrooms have been demonstrated to have controlling effects on diabetes through the regulation of several pathophysiological pathways related to the onset of diabetes. Some of the anti-hyperglycemic mechanisms of medicinal mushrooms have been investigated including  $\beta$ -cell improvement and insulin releasing activity, antioxidant defenses, carbohydrate metabolism pathways,  $\alpha$ -glucosidase and aldose reductase inhibitory activities. Thus, mushrooms could be a potential therapeutic agent against diabetes mellitus.

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