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Impact of Mushroom Consumption on Diabetic Type 2 Patients

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Abstract- The complicated disease known as diabetes mellitus is caused by the body producing insufficient amounts of insulin to regulate blood glucose levels. This illness poses a global health risk and calls for inexpensive, non-adverse medication. Many synthetic hypoglycemia diabetes medicines are ineffective due to side effects. This has caused studies to focus more on medicinal plants and herbs, which are thought to be relatively harmless. There is a kind of phytotherapy that includes edible mushrooms that may be used to treat diabetes. They are abundant in naturally occurring substances such fibers, polysaccharides, phenolics, and alkaloids and have long been recognized for their ability to have antihyperlipidemic, antioxidant, and antidiabetic properties. Dietary supplements and functional foods derived from mushrooms can help treat pre-existing problems and postpone the start of potentially fatal diseases. This is confined to the suppression of intestinal glucosidase and the breakdown of composite polysaccharides by pancreatic amylase, which helps prevent and effectively cure type 2 diabetes. Additionally, the carbohydrates included in mushrooms function as prebiotics and alter the makeup of gut bacteria, which can lower insulin resistance. This paper explores the phathophysiology and complication of diabetes and provides details on the potential antidiabetic properties of several mushroom species. Nevertheless, more investigation is required to completely comprehend the therapeutic applications of mushrooms. Pre-clinical and clinical research, tests for enzyme inhibition, human trials, pilot studies, prospective and retrospective studies, and human trials should all be included in this research.

Keywords: mushroom consumption, diabetic type 2 patients, patients

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INTRODUCTION

Hyperglycemia, or unusually high blood glucose levels while fasting and after meals, is a hallmark of diabetes mellitus, a complex set of illnesses with several etiologies and a major global health issue. Despite significant efforts to treat the condition, diabetes prevalence is rising along with a sharp rise in morbidity and death from the complications that arise from the disease (Harding et al. 2019). The International Diabetes Federation estimates that there are currently 500 million diabetics in the world. 2019 saw a sharp rise in this number, according to IDF predictions, reaching 578 million by 2030 and 700 million by 2045. This suggests that one of the health problems that is growing at the fastest rate in the world right now is diabetes. Schmeltz and Metzger (2006) have proposed a new classification scheme for diabetes that is based on pathophysiology and etiology rather than age at onset or kind of treatment. Type 1, type 2, and gestational are the three basic forms of diabetes mellitus. Deficits in insulin secretion and/or resistance to insulin action cause anomalies in the metabolism of carbohydrates, lipids, protein and fats in a number of tissues, including muscle, liver, and adipose tissue.

Uncontrolled diabetes is frequently accompanied with hyperglycemia, which over time causes major harm, malfunction, and failure of many organs, including the brain, kidneys, liver, eyes, nerves, and blood vessels. This can result in long-term consequences of diabetes (Harding et al. 2019). The mainstays of diabetes treatment include a variety of chemical and biological hypoglycemic drugs, such as insulin, tolbutamide, phenformin, troglitazone, rosigitazone, and repaglinide. Although these agents are effective in reducing hyperglycemia, they come with negative side effects and don't substantially change the course of diabetic complications (Lia et al. 2004).

Historically utilized as treatments for diabetes, mushrooms offer a promising area for the development of novel therapies to manage diabetes and its consequences. Certain mushrooms have been shown to regulate blood glucose levels in clinical and/or experimental settings and to alter the progression of diabetic complications while posing no adverse effects (Lo and Wasser, 2011; Jovanovic et al. 2017). Many bioactive components, including polysaccharides, fiber, ergosterols, flavonoids, lectins, terpenoids, and proteins, are abundant in mushrooms (Lu et al. 2020). Together with minerals, vitamins, and amino acids, they are also abundant in macro and micronutrients. Furthermore, they contain chemicals that have therapeutic effects and are biologically significant, such as beta-glucans (Sari et al. 2017; Guo et al. 2019). Terpenoids, peptides, and phenols are a few of the well-known components of mushrooms that are known to have anti-cancer properties. Antioxidants found in mushrooms are crucial because they fight reactive oxygen species (ROS), which is a major cause of diabetes, inflammation, cancer, and heart disease in human cells.

Due to their high dietary fiber content and low calorie and fat content, mushrooms are regarded as important health foods (Du et al. 2018). Long utilized as a diabetic treatment, mushrooms today provide a favorable environment for the study and creation of cutting-edge treatments to control diabetes and its aftereffects (Singh et al., 2022). Numerous scientists have worked to investigate the function of secondary metabolites from the fruiting body or mycelia of different edible mushrooms that are responsible for the anti-hyperglycemic action. Examples are *Agaricus blazei, Antrodia camphorate, Coprinus comatus, Cordyceps militaris, C. sinensis, Coriolus versicolor, Ganoderma atrum, G. leucocontextum, G. lucidum, Grifola frondosa, Hericium erinaceus, Inonotus obliquus, Lentinus edodes, L. strigosus, Morchella conica, Phellinus baumii, P. linteus, Pleurotus abalonus, P. citrinopileatus, P. cystidiosus, P. florida, P. pulmonarius, P. sajor-caju, P. tuber-regium, Poria cocos, Trametes pubescens, Tremella fuciformis (*Arunachalam et al. 2022).

TYPES OF DIABETES

High blood glucose levels are a hallmark of a group of chronic metabolic diseases collectively referred to as diabetes mellitus. These levels are caused by the body's incapability to manufacture insulin or its resistance to the action of insulin. (ADA, 2010). There are four clinically separate categories into which these disorders might be categorized:

1. Type 1, which is described by a total be short of of insulin production and is caused by autoimmune beta-cell destruction in the pancreas;

2. Type 2, which arises when the body develops an abnormally high resistance to the action of insulin and is unable to construct sufficient insulin to conquer the resistance;

3. A type of glucose intolerance known as gestational diabetes, which some pregnant women have; and

4. A collection of further forms of diabetes brought on by certain genetic variations in the function of beta cells or the action of insulin, pancreatic disorders, medications, or chemicals (ADA, 2010).

Type 1 diabetes affects 5–10% of people with diabetes. Its risk factors include autoimmune, genetic, and environmental factors. As of right now, there is no known way to reverse type 1 diabetes. Type 2 diabetes affects 90–95% of people with diabetes who receive a diagnosis. Insulin resistance is typically the first sign of this kind of diabetes. When the body cannot make adequate insulin to treat the resistance, the pancreas may finally stop producing it altogether or lower it. Gestational diabetes is more common in women from minority groups, obese women, women with a family history of the disease, and women who have already had gestational diabetes during pregnancy. Women with gestational diabetes need to follow stringent standards for glucose control and therapy in order to prevent delivery difficulties for the developing newborn. Women who had gestational diabetes have a 20% to 50% likelihood of developing type 2 diabetes later in life (CDC, 2005).

Elevated blood glucose levels in a person who does not fit the diagnostic criteria for diabetes is known as prediabetes, a disease that comes before diabetes. Impaired glucose tolerance, impaired fasting glucose, or both can be present in people with prediabetes.

PATHOPHYSIOLOGY OF DIABETES

Patients with diabetes may experience hyperglycemia. The etiology of diabetes mellitus may not be entirely clear-cut because the disorder might sometimes have numerous contributing factors. Hyperglycemia can harm pancreatic beta-cell activity and insulin secretion even on its own. Hyperglycemia thus starts an unending cycle that hinders metabolic activity. In this context, blood glucose levels above 180 mg/dL are commonly considered hyperglycemic; however, an exact cutoff value remains uncertain due to the multitude of mechanisms involved. Patients experience osmotic diuresis as a result of the nephron's glucose transporters becoming saturated due to elevated blood glucose levels. Polyuria and polydipsia symptoms are likely to occur when serum glucose levels are higher than 250 mg/dL, albeit the exact impact varies.

Insulin resistance is brought on by proinflammatory cytokines and excess fatty acids, which accelerate the breakdown of fat and hinder the transfer of glucose. The body inadvertently increases glucagon levels in response to inadequate insulin synthesis or responsiveness, exacerbating hyperglycemia. Type 2 diabetes includes insulin resistance, but the condition's full effects arise when a patient's insulin output is insufficient to counteract their insulin resistance.

Proteins and lipids are glycated nonenzymatically by chronic hyperglycemia. The glycation hemoglobin (HbA1c) test can be used to determine how much of this is present. Damage to small blood vessels in the kidney, retina, and peripheral nerves is caused by glucose. Increased glucose levels speed up the procedure. The traditional diabetic problems of nephropathy, neuropathy, and diabetic retinopathy, as well as the avoidable consequences of amputation, dialysis, and blindness, are brought on by this damage (Unger and Orci, 2010).

DIABETES MELLITUS AND INSULIN RESISTANCE PREVENTIVE MECHANISM BY EDIBLE MUSHROOM

The presence of several secondary metabolites, including polysaccharides, lactones, lectins, terpenoids, alkaloids, antibiotics, and metal-chelating agents, gives mushrooms their therapeutic properties (Aramabašic Jovanovic et al. 2021). The following is the mechanism of insulin resistance utilizing mushrooms.

1. Polysaccharide affect by lowering blood glucose level-

Biopolymers known as polysaccharides are widely present and consist of monosaccharides or simple sugars joined by glycosidic bonding. Prior research indicates that mushrooms are an excellent source of ß-D-glucans, or ß-glucan, a kind of dietary fiber with promise anti-type 2 diabetes effects (Dubey et al. 2019). Glucose transporter 4 (GLUT4), glycogen synthase (GS), and glycogen synthase kinase (GSK-3 ß) gene expression in the liver and muscle are all regulated by extracts from the following mushrooms.: *Pleurotus species* (Asrafuzzaman et al. 2018), *Boletu* (Xiao et al. 2019), *Grifola frondosa* (Kou et al. 2019), *Agaricus bisporus* (Ekowati et al. 2018) and *Hericium erinaceus* (Zhang et al. 2017). These extracts regulate the synthesis of glycogen and lower blood glucose levels.

As a result, GSK-3 ß was found to be a GS-regulated negative regulator mediated by insulin (Lin et al. 2018). Additional methods that polysaccharides reduce insulin resistance include decreasing the activity of α-amylase and α-glucosidase, as well as supporting the PI3K/AKT pathways, which are directly related to glucose homeostasis (Aramabašic Jovanovic et al. 2021).

The following are other ways that polysaccharides lower blood glucose levels

1.1 Inhibition of Glucose Absorption

Mushrooms slow down digestion rates and delay the absorption of glucose due to their water-soluble dietary fiber content, which causes a postprandial glucose spike (Zhang et al. 2018). Numerous studies have demonstrated the significant blood glucose-lowering effects of mushrooms, particularly Pleurotus spp. (Asrafuzzaman et al. 2018), Grifola frondosa (Kou et al. 2019), Agaricus bisporus (Ekowati et al. 2018), Hericium erinaceus (Zhang et al. 2017) and Ganoderma lucidum (Huang et al. 2021). These benefits stem from the delayed absorption of glucose, which improves hyperglycemia.

1.2 Maintain Pancreatic ß Cells Activity

ß-D-glucan, a polysaccharide found in mushrooms, is a powerful immune modulator that inhibits oxidative damage and inhibits the commencement of pro-inflammatory cytokines by decreasing NF-kB activity. Bioactive substances found in mushrooms, particularly polysaccharides, inhibit glucotoxicity and stop pancreatic ß-cell death (Dubey et al. 2019). Further research revealed that ß-cell proliferation is sustained by the considerable impact of mushroom extracts from Pleurotus spp., Boletus, Agaricus bisporus, and Hericium erinaceus (Zhang et al. 2017).

2. Blood Glucose-Reducing Effect of Terpenoids

Blood glucose levels are raised when oligosaccharides are hydrolyzed to monosaccharides by enzymes like α-glucosidase and α-amylase (Panigrahy et al. 2021). Terpenoids (monoterpenes, diterpenes, sesquiterpenes, and triterpenes) from *Pleurotus spp*. (Asrafuzzaman et al. 2018), *Laetiporus sulphurous* (Kolundzic et al. 2016), *Tremella fuciformis* (Ma et al. 2021) and *Ganoderma lucidum* (Patel et al. 2021) are thought to possess an α-glucosidase inhibitory activity that hinders the production of monosaccharide molecules and facilitates the formation of glycogen in the liver and muscle.

3. Vitamin D Released from Mushrooms in Blood Glucose Regulations

Unlike plants, mushrooms belong to the fungal kingdom and have high levels of ergosterol in their cell walls. When exposed to sunlight, ergosterol in the mushroom cell wall is transformed into pre-vitamin D2, which is subsequently thermally isomerized to ergocalciferol, or vitamin D2 (Cardwell et el. 2018). In order to maintain blood sugar regulation, it requires vitamin D, namely 1, 25-dihydroxyvitamin D, or 1, 5(OH) 2D. By acting directly on β-cells and indirectly on other immune cells such as dendritic cells, inflammatory macrophages, and various T cell types, it protects β-cells against deleterious immunological responses (Sung et al. 2012).

The bioavailability of vitamin D in the management of diabetes remains a source of uncertainty for scientists, despite a wealth of evidence (Al-Shoumer and Al-Essa, 2015). On the other hand, recent data from a randomized placebo-controlled study by Urbain et al. (2011) shows that eating button mushrooms treated with UV-B can boost vitamin D2 bioavailability in humans, and that this effect is statistically equivalent to vitamin D2 supplementation (Urbain et al. 2011).

COMPOSITION OF MUSHROOMS

Apart from bioactive polysaccharides and essential amino acids, mushrooms also include minerals like iron, zinc, calcium, potassium, and magnesium. An intriguing study found that dry mushrooms have a protein level of 228–249 g/kg dry matter (DM). (Bauer Petrovska, 2001). Carbohydrates, which make up around half of the DM in mushrooms, are another significant component of the fungus. When combined with other polysaccharides, carbohydrates and their immune-stimulating β glucans contribute significantly to the therapeutic qualities of mushrooms (Batbayar et al. 2012). Total lipids, or crude fat, have lower levels than protein and carbohydrates, often ranging from 20 to 30 g/kg DM. A variety of elements are present in mushrooms, with potassium being the most prevalent.

Many trace elements have compositions that differ significantly between species. Ascorbic acid typically contains 150–300 mg/kg DM. The B-group vitamin contents of four dried common farmed species were assessed: niacin (63.8–83.7 mg/kg), pyridoxine (1.4–5.6 mg/kg), thiamine (1.7–6.3 mg/kg), and riboflavin (2.6–9.0 mg/kg). The average ergosterol concentration of 35 different varieties of mushrooms was 1.98 mg/g, the average vitamin D2 level was 16.88 µg/g, and the average vitamin B2 value was 12.68 µg/g. Moreover, mushrooms' vitamin D2 content rose in response to UV-C (ultraviolet C) light (Huan et al. 2016). There is general agreement that the main active ingredient in mushrooms is phenolics, namely phenolic acids.

Benzoic acid hydroxy derivatives and trans-cinnamic acid are the two main categories of phenolic acids. Protocatechuic, gentisic, p-hydroxybenzoic, gallic, vanillic, and syringic acids are the members of the former category that are typically found in mushrooms (Robbins et al. 2003). According to a fascinating study on edible mushrooms that are widely consumed in China, mushrooms have the strongest metal chelating potential and significant antioxidant activity because of their phenolic makeup, including gallic acid (Islam et al. 2016).

KEY BIOACTIVE SUBSTANCES IN MUSHROOMS FOR DIABETES TREATMENT

Fruiting bodies are produced by filamentous fungi, such as mushrooms. They are a great source of nutrients, particularly carbs and protein. They are abundant in phosphorus, magnesium, selenium, copper, and potassium, among other minerals, vitamins, and vital amino acids that the body needs to function correctly (Valverde et al., 2015). Because of its antibacterial, antiviral, antioxidant, antidiabetic, anticancerous, and hypocholesterolemic qualities—as well as their ability to lower the risk of certain diseases—mushrooms have long been regarded as an essential component of the human diet (Passari and Sanchez, 2020). Although there are many different kinds of mushrooms in the wild, only a few number are used and grown for food. Due to their minimal resource and area requirements and worldwide cultivability, mushrooms are regarded as one of the delectable foods that are easy to grow. Globally, the most widely grown edible mushrooms are *Flammulina velutipes* (enoki mushroom), *Pleurotus spp*. (especially oyster mushroom), *Lentinus edodes* (shiitake mushroom), and *Agaricus bisporus* (common mushroom) (Valverde et al., 2015; Feenay et al. 2014).

Since diabetes is characterized by increased blood glucose levels, treating diabetic patients requires adhering to a nutritious diet that lowers blood glucose levels. Mushrooms have different looks and tastes, but they all have similar nutritional profiles: high levels of selenium and several B vitamins, low levels of sugar and fat. They are low in calories and have a low glycemic index, making them an excellent dietary choice for people with diabetes.

Mushrooms have medicinal properties due to their abundance of secondary metabolites, which include polysaccharides, lectins, lactones, terpenoids, alkaloids, antibiotics, and metal-chelating agents (Rahi and Malik, 2016). These bioactive secondary metabolites have a lot of potential for use as medicinal agents. Historically, field-cultivated mushrooms were the primary source of the bioactive components. With very little control over the quality of the last product and the productivity of preferred metabolites, this construction system was and remains a labor- and time-intensive operation (Zhong, 2004).

Although a mushroom can be utilized to treat medical conditions in any section of its body, mycelia have significantly more bioactivity than spores and fruiting bodies. Thus, the efficient large-scale production of mycelia biomass and value-added secondary metabolites in a condensed area, faster processing times, and lower contamination can be achieved through the submerged culture of mushroom mycelia (Zhong et al. 2009). Bioactive metabolites are affected by a variety of culture conditions, including temperature, pH, oxygen level, incubation time, and more. They are also influenced by the medium's composition, which includes different salts, carbon and nitrogen sources, special additives like vitamins and vegetative oils, and modes and methods of fermentation, such as static and agitated cultures (Mahapatra and Banerjee, 2013).

Accelerating mycelia growth and increasing the generation of secondary metabolites, particularly polysaccharides and triterpenoids, which are the majority active components of mushrooms, are the main goals of optimizing culturing conditions (Wagner et al. 2004; Zhang and Zhong, 2010). By addressing the major variables impacting the fermentation process and the purification systems, this technology may create a range of secondary metabolites with great efficiency, which could find practical applications. An examination of published studies on the use of isolated compounds and extracts obtained from several mushroom species with an anti-hyperglycemic action revealed that two classes of chemicals—polysaccharides and terpenoids—are the most significant.

MUSHROOM AS A FUNCTIONAL FOOD FOR DIABETIC PATIENTS

Mushrooms are fruiting bodies of filamentous fungi that are high in nutrients and high in protein and carbohydrates. Minerals including phosphorus, copper, magnesium, selenium and potassium, as well as critical amino acids that the body requires for correct operation, are also rich in them, in addition to vitamins B and D (Han et al. 2016). Mushrooms have long been a mainstay of human diets because of their numerous health benefits, as well as their antibacterial, antioxidant, antiviral, anticancer, and hypocholesterolemic qualities. (Passari and Sánchez, 2020). Although there are many different kinds of mushrooms in nature, only a few number are used and farmed for food. Given that elevated blood glucose levels are indicative of diabetes, individuals with diabetes need to follow a nutritious diet that supports blood glucose regulation. All mushrooms have comparable nutritional profiles, with low levels of sugar and fat and elevated levels of minerals like selenium and other B vitamins, despite their variances in appearance and flavor. They have a low calorie and glycemic index, making them an excellent nutritional choice for those with diabetes. Mushrooms has therapeutic qualities due to their diverse array of secondary metabolites, which include polysaccharides, alkaloids, lectins, lactones, terpenoids, and metal-chelating agents (Rahi and Malik, 2016). These bioactive substances, sometimes referred to as secondary metabolites, hold great medical potential.

Edible mushrooms are regarded as low-calorie meals for diabetics since they are elevated in protein, minerals, and vitamins and low in fat, cholesterol, and carbohydrates (Cui et al. 2009)). Kaur et al. and Chaturvedi et al. have described mushrooms as the best natural pharmaceutical sources with anti-diabetic characteristics (Kaur et al. 2015; Chaturvedi et al., 2019). These are acknowledged functional foods that include significant amounts of bioactive substances like proteins, fats, and polysaccharides, as well as highly active metabolites like phenolic components, lectins, sterols, alkaloids, and terpenoids.

CONCLUSION

With a notable increase in morbidity and mortality each year, diabetes is a major global health concern. Commercial hypoglycemic medications perform well to manage hyperglycemia, but they come with dangerous side effects, are expensive, and can lead to serious problems like hypoglycemia, insulin resistance, severe cardiovascular risks, and cancer-related hazards. Thus, there is hope for the development of innovative medicines through the hunt for strong antidiabetic chemicals originating from plants. Edible and medicinal mushrooms have a substantial therapeutic potential in the control of diabetes, as proved by various experimental studies as well as traditional medicine. Medicinal mushrooms have been utilized for many years due to their positive health effects and now offer a new avenue for the development of innovative treatments. Isolating and identifying bioactive substances from various mushroom species that may have anti-diabetic properties is crucial, though. In order to isolate the active biomolecules from new medicinal and edible mushrooms with anti-diabetic properties, more research and future studies are required.

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