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A comprehensive review of a novel approach to the anti-diabetic properties of edible mushrooms

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Abstract

Mushrooms, part of the "Fungi" family is well-known for their medical benefits and accessibility globally. Diabetes has become more commonplace worldwide in recent times, which has made the search for alternate treatment approaches necessary. Because of their possible anti-diabetic effects, edible mushrooms—a natural source of bioactive compounds—have drawn interest. This research assesses the possible anti-diabetic benefits of edible mushrooms, concentrating on their bioactive constituents and mechanisms that modulate insulin sensitivity and glucose metabolism, and emphasises their potential significance in diabetes prevention. The review concludes that EM can predict insulin resistance through active chemicals like polysaccharides and vitamin D, as well as preventative activities like β-glucosidase and β-amylase. The therapeutic benefits of many mushroom types have not been thoroughly researched, and the mechanism remains unclear. More study on edible medicinal mushrooms is needed to fully utilise their therapeutic promise in preventing noncommunicable diseases.

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Introduction

Mushrooms, whose come from the Latin and Greek terms "fungus" and "mykes," are deemed edible if they do not create health problems. They are classified into edible, inedible, and non-poisonous varieties (Adhikari *et al.,* 2014). For thousands of years, mushrooms have been utilised as food and medicine in Asian and South Asian countries such as China, Japan, India, and Taiwan (Asrafuzzaman *et al.,* 2018). Mushrooms are highly nutritious, with 34 billion kg produced and 4.7 kg per capita consumption in 2013 (Ali Sangi *et al.,* 2018). They are high in protein, vitamins, B vitamins, vitamin D, vitamin K, and, in rare cases, vitamins A and C (Bao *et al.,* 2013). They are also low in fat, high in dietary fibre, nutraceuticals and polysaccharides, all of which have beneficial health effects (Blumfield *et al.,* 2020). Diabetes mellitus (DM) is a category of non-communicable metabolic illnesses characterised by chronic hyperglycemia caused by insulin secretion or action deficiencies (Chakraborty *et al.,* 2016). Diabetes is characterised as type 1 (T1DM), type 2 (T2DM), or gestational diabetes mellitus. Diabetes currently affects 415 million people and is estimated to reach 642 million by 2040 (Kosiborod *et al.,* 2018). T1DM is associated with an autoimmune condition, whereas T2DM results in glucotoxicity and endoplasmic reticulum-induced stress (Diyabalanage *et al.,* 2008). Polydipsia, polyphagia, polyuria, and nocturia are common symptoms, and micro vascular and macro vascular abnormalities might occur as consequences. Insulin resistance is a key cause of diabetic complications (Duvnjak *et al.,* 2009).

This review investigates the function of edible mushrooms in diabetes mellitus treatment by looking at bioactive components, insulin resistance patho-physiology, and prevention strategies (He *et al.,* 2017). Data from 50 scholarly publications were collected to identify 10 common edible mushroom types (He *et al.,* 2017; Hoa *et al.,* 2015). The review also looked at various species and hypoglycemic drugs, analysing both in vivo and in vitro data. The data is shown in Fig. 1

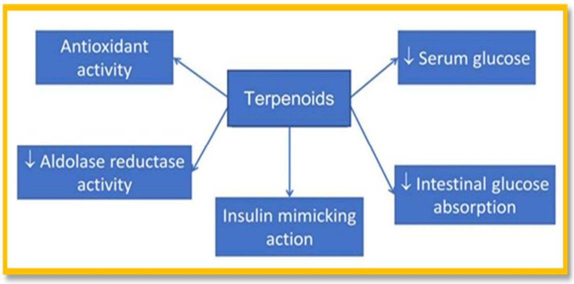

Fig. 1. Benefits of terpenoids (mono-, di-, sesquiterpene, and triterpene) found in mushrooms

Diabetes mellitus and insulin resistance

Diabetes Mellitus (T2DM) is a developing global problem, and obesity plays an important part in its development (Hu *et al.,* 2019). Insulin resistance (IR) is also rising in T1DM. T2DM affects insulin production by 50% and insulin sensitivity in peripheral tissues by up to 70%. Insulin operates by phosphorylating PI3K and Akt, which activates glucose transporter 4 (Karun *et al.,* 2018). Insulin sensitivity is a condition in which normal plasma insulin levels fail to control blood glucose levels (Kleftaki *et al.,* 2022). IR is linked to a variety of disorders, including cardiovascular disease, nonalcoholic fatty liver disease and cancer (Kosiborod *et al.,* 2022). Diabetes is a chronic metabolic condition characterised by high blood glucose levels as a result of impaired insulin secretion and action (Liang *et al.,* 2016). Insulin resistance, a defining feature of type 2 diabetes, is caused by a combination of genetic and environmental factors (Lin *et al.,* 2019). It is characterised by dysregulation of adipokines, cytokines, and lipid metabolism, which results in inflammation and lipid buildup (Lin *et al.,* 2019). Diagnosing insulin resistance is critical for early intervention and prevention (Ma *et al.,* 2018). Lifestyle changes and pharmaceutical therapies can help increase insulin sensitivity and glycemic management (Masaphy *et al.,* 2010).

Eating edible mushrooms can help prevent diabetes and insulin resistance

Diabetes mellitus and insulin resistance offer substantial health risks, necessitating the development of preventative methods, such as dietary interventions (Misra *et al.,* 2014). Edible mushrooms, which contain bioactive chemicals, have the ability to prevent certain diseases via a variety of ways (Montoya *et al.,* 2021). These include antioxidant, anti-inflammatory, and insulin-sensitizing qualities that reduce oxidative stress and inflammation, increase insulin sensitivity and glucose metabolism, and control critical signalling pathways involved in glucose and lipid metabolism (Montoya *et al.,* 2021; Ndisang *et al.,* 2015). Mushrooms also improve insulin secretion and pancreatic function. However, further study is needed to ensure that mushroom-derived medicines are as effective and safe as possible (Ndisang *et al.,* 2017).

Polysaccharide lowers blood glucose levels

Polysaccharides are biopolymers composed of simple sugars or monosaccharides connected by glycosidic bonds (Patel *et al.,* 2021). Mushroom extracts high in ß-D-glucans have showed potential health advantages against type 2 diabetes (Rahman *et al.,* 2021). These extracts control glycogen synthesis and blood glucose levels via modulating gene expression in the liver and muscle, avoiding insulin resistance by inhibiting acylase and glucosidase activity, and enabling the PI3K/AKT pathways (Senthilarasu, 2015).

Reduction in the absorption of glucose

Mushrooms slow down digestion rates and delay the absorption of glucose due to their water-soluble dietary fibre content, which causes a postprandial glucose spike (Slusarczyk *et al.,* 2021). Numerous studies have demonstrated the significant blood glucose-lowering effects of mushrooms, particularly *Pleurotus* spp., *Grifola frondosa* , *Agaricus bisporus*, *Hericium erinaceus* and *Ganoderma lucidum* (Song *et al.,* 2020). This is because they delay the absorption of glucose, which improves hyperglycaemic conditions (Thu *et al.,* 2020).

Sustains the activity of pancreatic β Cells

The polysaccharides found in mushrooms, called ß-D-glucan, have strong immune modulating properties (Tiane *et al.,* 2014). They also inhibit oxidative damage and inhibit the activation of pro-inflammatory cytokines by decreasing NF-kB activity (Ukwuru *et al.,* 2018). Glucotoxicity is inhibited and pancreatic ß-cell death is prevented by bioactive components from mushrooms, particularly polysaccharides (Vitak *et al.,* 2017). Additionally, research has demonstrated that ß-cell proliferation is maintained and ß-cell functionality is significantly impacted by mushroom extracts from *Pleurotus* spp., *Boletus*, *Agaricus bisporus*, and *Hericium erinaceus* (Wu *et al.,* 2018).

Terpenoids' hypoglycemic effect on blood

Blood glucose levels are raised by enzymes like -glucosidase and α--amylase, which hydrolyze oligosaccharides to monosaccharides (Ukwuru *et al.,* 2018; Montoya *et al.,* 2021). Terpenoids (monoterpenes, diterpenes, sesquiterpenes, and triterpenes) from Plagiophorus spp. Laetiporus sulphurous, Tremella fuciformis , Ganoderma lucidum and Pholiota microspore are thought to possess a β-glucosidase inhibitory activity that hinders the formation of monosaccharide molecules and promotes the formation of glycogen in the liver and muscle (Vitak *et al.,* 2017).

Vitamin D's function in blood glucose regulations

Unlike plants, mushrooms belong to the fungus kingdom and have high ergosterol content in their cell walls (Wu *et al.,* 2021). Ergosterol in the mushroom cell wall is converted to pre-vitamin D2 and then thermally isomerized to ergocalciferol, or vitamin D2, when exposed to sunlight (Ndisang *et al.,* 2017; Patel *et al.,* 2021). The hydroxy vitamin D, also known as 1, 25-dihydroxy vitamin D, is crucial for maintaining glucose homeostasis (Xiao *et al.,* 2021). By acting directly on ß-cells and indirectly on other immune cells such as dendritic cells, inflammatory macrophages, and other T cells, it also shields ß-cells from damaging immunological assaults (Ma *et al.,* 2018; Patel *et al.,* 2021). By controlling the intracellular calcium concentration, vitamin D sustains insulin production through molecular processes (Hu *et al.,* 2019; Liang *et al.,* 2016). Vitamin D promotes PLC production, PKA activation, and Ca+ absorption with the aid of calbindin. Consequently, the vitamin mediates the genomic mode of action of vitamin D. D receptor (VDR)

(Karun *et al.,* 2018; Kosiborod *et al.,* 2022). Vitamin D's active form, 1,25 (OH)2 D3, attaches itself to VDR and joins forces with the retinoid receptors (RXR) to form a heterodimer (Duvnjak *et al.,* 2009; Kosiborod *et al.,* 2018). The 1,25 (OH)2 D3-VDR-RXR complex is moved into the nucleus and bound to vitamin D-responsive elements (VDRE), allowing for the prevention of insulin resistance and the facilitation of epigenetic modifications (36). Briefly put, vitamin D functions in a variety of ways, including immune regulation, proliferation prevention, inherited gene polymorphism, anti-inflammatory (reducing the effects of pro-inflammatory cytokines, TNF-, IL-8b, and IL-6), and, finally, regulating adipokine production to prevent insulin resistance (through IRS, AKT, PPARy, and VDRE gene regulations) (Asrafuzzaman *et al.,* 2018; Duvnjak *et al.,* 2009) (Fig. 2).

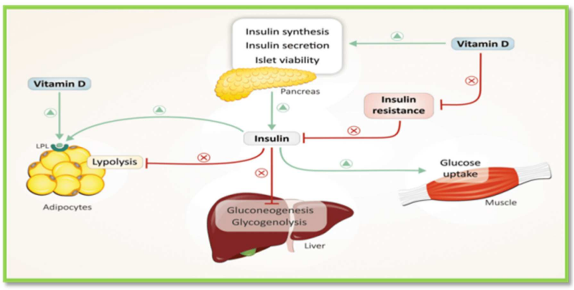

Fig. 2. Proposal-mechanisms-underlying-the-beneficial-effects-of-vitamin-D-for-glucose
Source: https://www.researchgate.net

According to the facts at hand, there is still disagreement among scientists on the bioavailability of vitamin D in the treatment of diabetes (Xiao *et al,* .2021). But button mushrooms treated with UV-B can increase vitamin D2 bioavailability among human participants, and the significant value does not change when vitamin D2 supplements are taken, according to recent findings using data from randomised placebo trials (Ma *et al.,* 2018). According to many researches has shown the beneficial effects of vitamin D supplementation (2000IU and 30,000IU) on type 2 diabetes (T2DM), albeit more studies are needed (Xiao *et al.,* 2019). Because of this, it is still unclear how precisely vitamin D works and how much of it is needed to cure diabetes mellitus (Xiao *et al.,* 2019).

Conclusion

The review looks at the potential medical benefits and diabetes preventive strategies of ten edible mushrooms. Thirteen of the varieties—mainly because of their polysaccharide and vitamin D content—have anti-diabetic qualities. Of the species that have been investigated the most, *Pleurotus*, *Grimola*, and *Ganoderma* are the only 11 that have demonstrated anti-diabetic capabilities. Further investigation is required to examine the possible medicinal uses of mushrooms, including the connection between vitamin D deficiency and insulin resistance.

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