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ANTIDIABETIC POTENTIAL OF MUSHROOMS

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ABSTRACT

Diabetes mellitus is a common endocrine disorder that affects more than 180 million people worldwide and this number is expected to rise to 366 million by the year 2030. Though different types of oral hypoglycemic agents are available along with insulin for the management of diabetes mellitus, they are associated with undesirable side effects. Therefore, there is an increasing demand of safer anti-diabetics especially from natural sources. Mushrooms are exemplary sources of natural medicines with antidiabetic potential. They serve as an ideal choice for diabetic patients owing to their high content of fiber and protein along with low fat content. Mushrooms are regarded as functional foods and are also important sources of bioactive compounds which include high molecular weight compounds such as polysaccharides, proteins and lipids as well as a number of low molecular weight metabolites such as lectins, lactones, terpenoids, alkaloids, sterols and phenolic substances which are responsible for the therapeutic activity. The present review describes the anti-diabetic role of mushrooms in experimental and/or clinical studies. Published literature demonstrates that mushrooms have immense potential and may be developed as effective and safe anti-diabetic therapy.

Key words: Diabetes mellitus; Anti-diabetic agents; Medicinal mushrooms.

INTRODUCTION

Mushrooms are an assemblage of fleshy macroscopic fungi [1, 2]. They possess a distinctive fruiting body that could be hypogeous or epigeous, large enough to be seen by naked eyes and to be picked by hands [3]. Mushrooms have been treasured all through the globe as food and medicine for thousands of years. In countries, such as China, India, Japan and Korea, medicinal mushrooms have a long history of use in traditional folk medicine for treatment of various diseases [4, 5]. Medicinal mushrooms are used as both nutritional and therapeutic foods. They are useful in prevention of diseases such as hypertension, diabetes, hypercholesterolemia and cancer. Studies have shown that mushroom species exhibit antitumor, antiviral, antithrombotic, antioxidant and immunomodulatory properties [6].

Edible mushrooms are ideal low calorie foods for diabetic patients since they contain very low amounts of fats and cholesterol, low levels of carbohydrates, high content of proteins, vitamins and minerals [4, 7]. The therapeutic activity of medicinal mushrooms is due to the presence of bioactive components, which include mainly high molecular weight compounds such as Polysaccharides, proteins and lipids as well as a number of low molecular weight metabolites such as lectins, lactones, terpenoids, alkaloids, sterols and phenolic substances [8, 9].

Mushrooms also contain important micronutrients (vitamins) and non nutrients (phenolics), that contribute to antioxidant property which can be valuable as a dietary supplement in favor of the patients suffering from a majority of disease conditions like Alzheimer's disease, atherosclerosis, cancer, diabetes mellitus, hypertension, inflammatory conditions, ischaemia, obesity, Parkinsonism and so on [10-14]. Many studies have focused on their immunomodulatory and anti-tumor effects because of the presence of various biologically active metabolites (β-D-glucans, immunomodulatory proteins, secondary metabolites) with well-known immune enhancing capabilities [15-22].

Role of mushrooms as antidiabetic agents

Diabetes mellitus is a metabolic disorder which can be controlled or prevented with lifestyle adaptations including exercise and appropriate diet [4]. Indeed healthy

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foods rich in various medicinal properties provide a means to good health [23-24]. Edible and medicinal mushrooms are functional foods and thus a good solution to controlling diabetes and a potent source of biologically active compounds with anti-diabetic effects. Many mushroom species appear to be effective for both the control of blood glucose levels and the modification of the course of diabetic complications. Medicinal mushrooms such as *Agaricus bisporus, A. subrufescens, Cordyceps sinensis, Coprinus comatus, Ganoderma lucidum, Inonotus obliquus, Phellinus linteus, Pleurotus* spp, *Poria cocos* and *Sparassis crispa* have been reported to have hypoglycemic effects (reduction of blood glucose levels) and anti-hyperglycemic effects [4]. Mushrooms are known to contain compounds which help in proper functioning of the liver [25], pancreas and other endocrinal glands, thereby promoting formation of insulin and related hormones which ensure healthy metabolic functioning [26-28]. Polysaccharides, such as beta glucans contained in mushrooms have the ability to restore the function of pancreatic tissues by causing increased insulin output by β – cells, which leads to lowering of blood glucose levels. It has also been shown to improve the sensitivity of peripheral tissues to insulin. Consumption of mushrooms markedly decreases the lipid levels including total cholesterol, total triglyceride, and low-density lipoproteins; and increases the level of high-density lipoproteins [5].

Summary of studies demonstrating the anti-diabetic effects of several medicinal mushroom in experimental models as well as in clinical studies are shown in table 1 and 2 respectively.

Table1. Medicinal mushrooms used for management of DM in experimental models

S.no.	Biological source	Extract/ Fraction/ Isolate	Dose	Experimental Models	Observations	References
1.	*Agaricus bisporus* (J.E. Lange) Imbach (Agaricaceae) White button mushroom	Dehydrated fruiting body extracts	400 mg/kg, p.o.	STZ induced diabetic rats	Serum glucose levels decreased by 29.68 % and insulin levels increased to 78.5 %	[29]
		Powdered fruiting bodies	200 mg/kg for 3 weeks, p.o.	STZ-induced diabetic male Sprague-Dawley rats	Significantly reduced plasma glucose, total cholesterol, low-density lipoprotein (LDL), levels	[30]
2.	*Agaricus campestris* L. (Agaricaceae) Field mushroom, Meadow mushroom	Aqueous extract of fruiting body	1mg/ml, p.o.	STZ induced diabetic mice	Stimulation of 2-deoxyglucose transport, glucose oxidation, and the incorporat-ion of glucose into glycogen in the abdominal muscle of mice	[31]
		Aqueous extract of fruiting body	0.25–1.0 mg/ml, p.o.	Alloxan induced diabetic mice	Stepwise 3.5 to 4.6 fold stimulation of insulin secretion from the pancreatic β-cell line	[31]
3.	*Agaricus subrufescens* Peck. (Agaricaceae) Almond mushroom	β-glucans and enzymatic-ally produced oligo-sacchari-des	-	Diabetic rats	Anti-hyperglycemic; anti-hypertrigly-ceridemic, anti-hypercholes-terolemic, and anti-arteriosclerotic activity	[32]

		Hot water extract of the submerged-culture broth (ethyl acetate fraction)	200 and 400 mg/ kg, p.o.	Diabetic male Sprague-Dawley rats	Reduced blood glucose level and elevated plasma insulin and glucose transport-4 proteins	[33]
		Powdered fruiting bodies	1g/kg for 2 months, p.o.	STZ-induced diabetic rats	Significant suppression of increased fasting plasma glucose; increased Serum insulin levels	[34]
4.	*Agrocybe cylindracea* (DC.) Maire (Strophariaceae) Chestnut Mushroom, Poplar mushroom	A glucan (AG-HN1) and a heteroglycan (AG-HN2) isolated from hot-water extract of the fruiting bodies	I.p.	Normal and STZ-induced diabetic mice	AG-HN1 showed a remarkable hypoglycemic activity in both normal and STZ-induced diabetic mice, higher than that of AG-HN2	[35]
5.	*Astraeus hygrometricus* (Pers.) Morgan (Diplocystaceae) False earthstar	Ethanolic extract of fruiting bodies	250,500, 1000 mg/kg, p.o.	Alloxan induced diabetic mice	Reduced levels of blood glucose; better tolerance to glucose	[36]
6.	*Auricularia auricula-judae* (Bull.) J. Schrot. (Auriculariaceae) Jew's Ear, Jelly Ear mushroom	Water-soluble poly-saccharide from fruiting bodies	30 g/kg; in diet	Genetically diabetic KK-Ay mice	Significant effect in lowering plasma glucose, insulin, urinary glucose, and food intake; increased tolerance to intraperitoneal glucose loading and the hepatic glycogen content	[37]
		Hot water extract from fruiting bodies	Diet containing 5% extract	Genetically diabetic (type 2) KK-Ay	Reduced postprandial hyperglycemia	[38]
		Dried mycelia powder	0.5 and 1.0g/kg, p.o.	Genetically diabetic mice	Significant reduction of plasma glucose, total cholesterol and triglyceride levels	[39]
7.	*Coprinus comatus* (O.F. Mull.) Pers.(Coprinaceae) Shaggy ink cap	Powdered dried fruiting bodies	Diet with 33.3% w/w powder	Normal mice	Reduced Plasma glucose; improved intraperitoneal glucose tolerance	[40]
		Fermented mushroom rich in vanadium	i.g. route	Normal, Alloxan and adrenalin induced hyperglyc-emic mice	Decreased blood glucose levels; improved sugar tolerance of normal mice	[41]
		4,5- Dihydroxy-2-methoxybenzaldehyde (comatin) isolated from fermentation broth	80 mg/kg, p.o.	Normal and alloxan induced diabetic rats	Inhibition of the non-enzymatic glycosylation (NEG) reaction; decreased concentrations of fructosamine,triglycerides and total cholesterol. Maintained levels of blood glucose and improved glucose tolerance	[42]

8.	*Cordyceps militaris* (L.) Link (Clavicipitaceae) Caterpillar Killer	Exo-polymers produced from submerged mycelia cultures	50mg/kg for 7 days, p.o.	STZ- induced diabetic rats	Significantly decreased levels of plasma glucose, total cholesterol, triglyceride and plasma glutamate-pyruvate transaminase (GPT)	[43]
		Aqueous fruiting body extract	0.5 g/kg in diet	Type 2 diabetic rats	Amelioration of insulin resistance and improved insulin secretion	[44]
		Aqueous fruiting body extract	10 g/kg in diet	Rats (90% of pancreas removed)	Significant reduction of fasting serum glucose levels, increased body glucose disposal rates and glucose utilization in skeletal muscles	[45]
9.	*Cordyceps sinensis* (Berk.) Sacc. (Clavicipitaceae) Caterpillar fungus	Polysaccharide fraction CSP-1, isolated from cultured mycelia	200 and 400mg/kg/ day for 7 days, p.o.	Normal; alloxan and STZ-induced diabetic rats	Significant drop in blood glucose levels and increased serum insulin levels, stimulation of pancreatic release of insulin and/or reduced insulin metabolism	[46, 47]
10.	*Cordyceps. takaomontana* [anamorph: Paecilomyces tenuipes (Peck) Samson] (Clavicipitaceae)	Aqueous extract of fruiting bodies	0.5 g/kg, in diet for 8 weeks	90% pancrea-tectomized male Sprague Dawley rats	Improvement of insulin Resistance and insulin secretion	[48]
		Fruiting body extract containing 4- β-acetoxyscirpe-ndiol (ASD)	-	-	Decreased blood sugar in the circulatory system as specific inhibitors of Na+/ glucose transporter-1 (SGLT-1)	[49, 50]
11	*Fomitopsis pinicola* (Sw.) P. Karst. (Fomitopsidaceae) Red Banded Polypore	Water extract (WE) and an alkali extract (AE) from the fruit body	Dietary supplementati on	STZ- induced diabetic rats.	AE showed the highest antidiabetic effect. These results indicate that constituents of *F. pinicola* may regulate hyperglycemia via either increased insulin secretion during recovery or the prevention of STZ-induced pancreatic damage.	[51]
12.	*Ganoderma applanatum* (Pers.) Pat. (Ganodermataceae) Artist's Bracket	*Ganoderma applanatum* exo-polymer (GAE), produced by submerged mycelial cultures	100 mg/kg, p.o. for 3 weeks	STZ-induced diabetic rats	Reduced plasma glucose; plasma total cholesterol and triglyceride levels	[52]
13.	*Ganoderma lucidum* (Curtis) P.Karst	Aqueous extract of fruiting bodies	500 and 1000 mg/kg, p.o.	Alloxan induced and normal Wistar rats	Significant hypoglycemic and antihyper-glycemic effects	[53]

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	(Ganodermataceae) Reishi or Lingzhi mushroom	Aqueous extract of fruiting bodies (Ethylacetate and n-Butanol fractions)	50 mg/kg i.p. daily for two weeks	Alloxan-induced wistar rats	Significant reduction of fasting blood glucose	[54]
		Aqueous extract of fruiting bodies	100 and 200 mg/kg, by gavage once daily for four weeks	Normal and STZ-induced hyper-glycemic rats.	Decreased serum glucose levels; increased serum insulin levels; improved serum lipid profile in both normal and diabetic animals	[55]
		Ganoderma lucidum polysacchari-des (Gl-PS)	50 mg/kg and 150 mg/kg, p.o.	STZ induced diabetic mice	Significant increase in body weights and serum insulin levels; decreased fasting blood glucose levels	[56]
		Proteoglycan extract, FYGL (Fudan-Yueyang-G. lucidum), from the fruiting bodies	40 and 120 mg/kg, p.o.	STZ induced type 2 diabetic rats	Decrease in fasting plasma glucose and increase in insulin concentration; decreased levels of free fatty acid, triglyceride, total cholesterol and low density lipoprotein cholesterol as well as increased level of high density lipoprotein cholesterol	[9]
14.	*Grifola frondosa* (Dicks.) Gray (Fomitopsidaceae) Hen of the woods, Maitake	Powdered fruiting body	1g/day, p.o.	Genetically diabetic mouse (KK-Ay)	Reduced levels of blood glucose, insulin and triglycerides	[57]
		Ether-ethanol soluble (ES) and hot water-soluble (WS) fractions from fruiting body	ES-fraction or WS-50% ethanol float (X) fraction, p.o.	Genetically diabetic mouse (KK-Ay)	Blood glucose lowering activity not only in the ES-fraction consisting of lipid but also in the X-fraction of peptidoglycan	[57]
		Powdered fruiting bodies	20% maitake solid feed	Type 2 diabetic Female KK-Ay mice	Inhibition of increase in blood glucose levels	[58]
		MT-α-glucan, from the fruiting bodies	150-450 mg/kg	Type 2 diabetic KK-Ay mice.	Antidiabetic activity, related to its effect on insulin receptors (i.e., increasing insulin sensitivity and ameliorating insulin resistance of peripheral target tissues	[59]
		Fermented *G. frondosa* rich in vanadium (GFRV)	i.g. route	Alloxan- and adrenalin-induced hyperglycemic mice	Significant decrease in blood glucose levels	[60]

15.	*Hericium erinaceus* (Bull.) Pers. (Ericaceae) Lion's Mane Mushroom, Hedgehog Mushroom	Methanol extract of fruiting bodies	100 mg/kg, in diet	STZ-induced diabetic rats	Decreased blood sugar levels and lipid levels	[61]
16.	*Inonotus obliquus* (Ach. ex Pers.) Pilat (Hymenochaetace-ae) Chaga mushroom	Protein-containing polysacchari-des, extracted from sclerotia and mycelia	-	-	Hypo-glycemic effect	[62]
		Fruiting body extract	Chaga 1 (dose of 0.09 mg/kg), Chaga 5 (5 times of Chaga 1), and Chaga 10 (10 times of Chaga 1) for 6 weeks, p.o.	Genetically obese mice	Fasting blood glucose level was significantly lower in the Chaga 5 group; glucose-6-phosphatase activity in liver was significantly the lowest in Chaga 10 group	[63]
		Dried matter of culture broth	500 and 1000 mg/kg, in diet	Alloxan induced diabetic mice	Significant antihyper-glycemic; antilipid-peroxidative and antioxidant effects	[64]
		Ethyl acetate fraction	-	Alloxan-induced diabetic mice	Significant antihyper-glycaemic and antilipidperoxidative effects	[65]
17.	*Laetiporus sulphureus* var. *miniatus* (Jungh.) Imazeki (Fomitopsidaceae) Sulphur polypore	Crude extracellular polysaccharides (EPS), produced from submerged mycelial culture	200 mg/kg for 14 days, p.o.	STZ-induced diabetic rats	Decreased plasma glucose levels, increased insulin antigenesity via proliferation or regeneration of diabetic islet β-cells	[66]
18.	*Lentinula edodes* (Berk.) Pegler (Marasmiaceae) Shiitake	Exopolymers produced from submerged mycelia cultures	50 mg/kg for 7 days, p.o.	STZ-induced diabetic rats	Significant reduction in plasma glucose, total cholesterol and triglyceride levels	[43]
		Exopolymer produced from submerged mycelia cultures	200 mg/kg, p.o.	STZ-induced diabetic rats	Reduced plasma glucose, total cholesterol and triglyceride levels; increased plasma insulin levels	[67]
19.	*Lentinus strigosus* Fr. (Polyporaceae) Ruddy panus	Exopolysacch-arides (EPS) from submerged mycelial culture	150 mg/kg for 7 days, p.o.	STZ-induced diabetic rats	Decreased plasma glucose level; induces regeneration of pancreatic islets and remediates destruction of micro-vascular pancreatic islets	[68]

20.	*Phellinus badius* (Cooke) G. Cunn (Hymenochaetace-ae)	Aqueous extract of fruit body and mycelial biomass	Aqueous extracts of basidio-carp, and mycelial biomass at the doses of 800 mg/kg and 1000 mg/kg respecti-vely	Alloxan-induced diabetic rats.	Significant reduction in blood glucose, plasma triglyceride and cholesterol levels; marked reduction in the level of aspartate amino-transferase (AST) and alanine amino-transferase (ALT).	[69]
21.	*Phellinus baumii* Pilat (Hymenochaetace-ae)	Crude exopolysaccharid es from submerged mycelial cultures	200 mg/kg, p.o.	STZ-induced diabetic rats	Hypoglycemic effect with substantially reduced plasma glucose levels	[70]
		Exopolysacch-arides (EPS) produced by submerged mycelial culture	200 mg/kg for 52 days, p.o.	ob/ob mice	Reduced plasma glucose levels, increased glucose disposal, reduced blood triglyceride levels	[71]
22.	*Phellinus linteus* (Berk. & M.A. Curtis) Teng, Zhong Guo De Zhen Jun (Hymenochaetacea e)Meshimakobu, Song-Gen, Sang-Hwang	Exo-polymers from submerged mycelia cultures	50 mg/kg for 7 days, p.o.	STZ-induced diabetic rats	Reduced plasma glucose, total cholesterol and plasma glutamate-pyruvate transaminase (GPT) levels	[43]
		Extracellular polysaccharides extracted from submerged mycelia cultures	100 mg/kg, p.o.	STZ-induced male Sprague–Dawley rats	Hypoglycemic effects with decreased plasma glucose, total cholesterol and triacyl-glycerol concentrat-ion	[72]
		Polysaccharide (PLP) isolated from *Phellinus linteus*	-	Non-obese diabetic (NOD) mice	Mean blood glucose levels were 110mg/dl in PLP-treated mice as compared to 499mg/dl in control NOD mice	[73]
23.	*Phellinus merrillii* (Murrill) Ryvarden (Hymenochaetace-ae)	EtOAc-soluble fractions of ethanol extract of fruiting bodies	-	Male Sprague-Dawley rats	Strong α-glucosidase and aldose reductase inhibitory activities	[74]
24.	*Phellinus ribis* (Schumach.) Quel (Hymenochaetace-ae)	Polychlorinat-ed compounds from methanolic extract of the fruiting body	-	-	Therapeutic effects through the enhanced PPAR-γ agonistic activity	[75, 76]
25.	*Phellinus rimosus* (Berk.) Pilat (Hymenochaetace-ae) Cracked cap polypore	Fruiting body extract	50 and 250 mg/kg for 10 days, p.o.	Alloxan-induced diabetic rats	Significant dose-dependent hypo-glycemic activity	[77]
26.	*Pleurotus abalonus* Y.H. Han, K.M. Chen & S. Cheng (Pleurotaceae) Abalone mushroom	Polysaccharide-peptide complex LB-1b from fruiting bodies	-	Drug-induced diabetic mice	High antioxidant activity with a significant hypoglycemic effect	[78]
27.	*Pleurotus*	Water-soluble	0.4 g/kg, in	STZ- induced	Reduced fasting blood	[79]

	citrinopileatus Singer (Pleurotaceae) Golden oyster mushroom	polysaccha-rides (WSPS), extracted from submerged fermented medium	diet	diabetic rats	glucose levels	
28.	*Pleurotus eryngii* (DC.) Quél. (Pleurotaceae) King trumpet mushroom, French horn mushroom, King oyster mushroom, King brown mushroom, Boletus of the steppes, Trumpet royale	Freeze-dried, powdered fruiting body	Diet containing 5% freeze dried mushroom	Male db/db mice	Reduced total cholesterol, triglyceride levels, and increased high density lipoprotein cholesterol levels with improved insulin sensitivity	[80]
29.	*Pleurotus ostreatus* (Jacq.) P. Kumm. (Pleurotaceae) Oyster mushroom	Powdered fruiting bodies	Diet containing 4 % mushroom	Type 2 diabetic rats	Significantly lower basal and postprandial glycaemia.	[81]
		Ethanol extract of fruiting bodies	250, 500 and 1000 mg/kg	Alloxan induced diabetic rats	Dose dependent decrease in blood glucose and cholesterol effects	[82]
		Ethanol extract of fruiting bodies	100 and 200 mg/kg for 30 days, p.o.	STZ - induced diabetic rats	Significant decrease of blood glucose levels, genetic alterations and sperm abnormalities	[83]
		Suspension of freeze-dried and powdered fruiting body	250, 500, 750, 1000, and 1250 mg/kg, p.o.	Normal and alloxan-induced diabetic Wistar rats	Significantly reduced levels of serum glucose. Hypo-glycemic effect comparable with metformin and glibenclamide	[84]
		Ethanol extract of fruiting bodies	380, 760 and 1140 mg/kg, i.p.	Alloxan-induced diabetic rats	Significant reduction in blood glucose levels	[85]
		Ethanol extract of fruiting bodies	-	Normal and alloxan-induced diabetic mice.	Significant decrease in serum glucose level; reduced serum cholesterol, triglyceride and LDL-cholesterol levels	[86]
30.	*Pleurotus pulmonarius* (Fr.) Quel (Pleurotaceae) Indian Oyster, Italian Oyster, Phoenix Mushroom, Lung Oyster	Aqueous extract of fruiting bodies	250, 500, and 1000 mg/kg, p.o.	Normal and Alloxan-induced diabetic mice	Antihyper-glycemic effect (increased glucose tolerance in both normal and diabetic mice)	[2]

31.	*Sparassis crispa* (Wulfen) Fr. (Sparassidaceae) Cauliflower fungus	β-glucan component	-	-	An effective promoter of wound healing in patients with diabetes. Increase in the migration of macrophages and fibroblasts, and directly increased synthesis of type I collagen	[87]
		Freeze dried fruiting body samples	Dietary supplementation	Diabetic KK-Ay mice	Increased plasma levels of adiponectine; decreased blood glucose levels, serum triglycerides and total cholesterol levels	[88]
32.	*Stropharia rugosoannulata* Farl. ex Murrill. (Strophariaceae) Wine cap, Burgundy mushroom King stropharia	Extracellular polysaccharide (EPS)	-	STZ- induced diabetic rats	Decrease in plasma concentrations of glucose,total cholesterol, and triacylglycerol; decreased aspartate amino-transferase activity	[89]
33.	*Trametes gibbosa* (Pers.) Fr. (Polyporaceae) Lumpy bracket	Extracellular polysaccharide (EPS)	-	STZ- induced diabetic mice	Decreased plasma glucose, total cholesterol and triacylglycerol concentrations	[90]
34.	*Tremella aurantia* Schwein. (Tremellaceae) Golden ear	Acidic polysaccharide (TAP) solution and TAP-H (degradation products of TAP) solution	TAP solution- 0.5 g/l; TAP-H solution- 1.5 g/l, p.o.; for 10 weeks	Genetically type 2 diabetic model (KK-Ay mice)	Reduced serum glucose levels, total cholesterol and triglyceride levels; Significant decrease in plasma lipoperoxide level	[91]
35.	*Tremella fuciformis* Berk. (Tremellaceae) Snow fungus, Silver ear fungus, White jelly mushroom	Glucuronoxylomannan (AC) from the fruiting bodies	Oral administrations of the AC solution	Normal and STZ- induced diabetic mice	Significant dose-dependent hypo-glycemic activity	[92]
		Exopolysaccharides (EPS) produced by submerged mycelial culture	(0.75 g/l) 200 mg/kg for 52 days, p.o.	ob/ob Mice	Hypoglycemic effects and improved insulin sensitivity possibly through regulating PPAR-γ mediated lipid metabolism	[93]
36.	*Tremella mesenterica* (Schaeff.) Retz. (Tremellaceae) Yellow brain mushroom, Golden jelly fungus, Yellow trembler, Witches' butter	Tremellastin, containing 40-45% acidic polysaccharide glucuronoxylomannan, obtained by alcoholic precipitation of culture broth after submerged cultivation	100 mg/kg and 500 mg/kg, p.o.	STZ-induced hyperglyc-emic mice	Statistically significant and dose-dependent reduction of intrinsic blood glucose levels as well as significantly decreased triglyceride levels	[94]
		Fruiting bodies	-	STZ-induced	Significant reduction in	[95]

		containing acidic heteropolysa-ccharide and several sugars including glucose		type 1 diabetic rats and nicotinamide and STZ-induced prediabetic impared glucose tolerant rats	elevated blood glucose levels	
37.	*Wolfiporia extensa* (Peck) Ginns (Polyporaceae) Pine-tree rotting mushroom	Crude extract containing dehydro-tumulosic acid, dehydro-trametenolic acid and pachymic acid	-	STZ-induced diabetic mice	Insulin sensitizer activity	[96, 97]

Table 2. Clinical studies carried out with mushrooms for management of DM.

S.no.	Biological source	Extract/ Fraction/ Isolate	Dose	Type of trial	Observations	References
1.	*Agaricus sylvaticus* Schaeff. (Agaricaceae) Sun Mushroom	Fruiting bodies	30mg/kg; Dietary supplementation	Random-ized, double-blind, placebo-controlled clinical trial on 56 patients with colorectal cancer	Significant reduction of fasting plasma glucose,total cholesterol, creatinine, aspartate aminotransf-erase,alanine aminotransf-erase, systolic blood pressure	[98, 99]
2.	*Grifola frondosa* (Dicks.) Gray (Fomitopsidaceae) Hen of the woods, Maitake	*Grifola frondosa* polysacchande caplets (MFCs) containing active SX-fraction..	-	5 patients with type 2 diabetes	Improved glycemic levels. One patient showed complete glycemic control with MFCs; whereas others showed over 30% decline in their serum glucose levels with MFCs in 2 to 4 weeks	[8]
3.	*Pleurotus ostreatus* (Jacq.) P. Kumm. (Pleurotaceae) Oyster mushroom	Powdered fruiting bodies	Dietary supplem-entation	120 patients with type 2 diabetes	Significant association between mushroom supplement-ation and gradual reduction in hyperglycemia in type 2 diabetic subjects	[100]

CONCLUSION

DM is a metabolic disorder of the endocrine system characterized by hyperglycemia and alterations in carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action or both. The ultimate consequences of diabetes are reduced life expectancy, significant morbidity due to specific diabetes related microvascular and macrovascular complications, along with diminished quality of life [56]. Insulin therapy fails as a curative agent for complications of diabetes and the conventional drug therapy is expensive and is associated with various side effects. Moreover, certain drugs are contraindicated in various medical conditions like renal/liver disease, congestive heart failure and pregnancy. Therefore the search for more effective and safer hypoglycemic agents has continued to be an important area of investigation due to which exploring the potential antidiabetic agents from natural sources have attracted a great deal of attention [101].Mushrooms are incredibly popular foods and have been valued as remedies for various diseases in numerous countries throughout the world. Medicinal mushrooms thereby provide a rich reservoir for the development of new therapeutic agents [1, 102-105]. This review highlights that biologically active metabolites and components derived from medicinal mushrooms have demonstrated beneficial effects on diabetes through the regulation of several pathophysiological pathways related to the onset of diabetes [32, 42, 106-107]. Some of the antihyperglycemic mechanisms of medicinal mushrooms have been investigated including β-cell improvement and insulin releasing activity, antioxidant defenses, carbohydrate metabolism pathways, α-glucosidase and aldose reductase inhibitory activities [108].

It may be concluded that mushrooms have immense potential and may be developed as effective and safe anti-diabetic therapy though detailed studies are still needed for the isolation and production of novel anti-diabetic compounds from mushrooms.

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