ANTIDIABETIC POTENTIAL OF MUSHROOMS

Amandip Kaur¹, Gurpaul Singh Dhingra², Richa Shri¹*

¹Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala-1470 02, Punjab, India.
²Department of Botany, Punjabi University, Patiala-1470 02, Punjab, India.

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
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.

### Table 1. Medicinal mushrooms used for management of DM in experimental models

<table>
<thead>
<tr>
<th>S.no</th>
<th>Biological source</th>
<th>Extract/Fraction/Isolate</th>
<th>Dose</th>
<th>Experimental Models</th>
<th>Observations</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td><em>Agaricus bisporus</em> (J.E. Lange) Imbach (Agaricaceae) White button mushroom</td>
<td>Dehydrated fruiting body extracts</td>
<td>400 mg/kg, p.o.</td>
<td>STZ induced diabetic rats</td>
<td>Serum glucose levels decreased by 29.68 % and insulin levels increased to 78.5 %</td>
<td>[29]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Powdered fruiting bodies</td>
<td>200 mg/kg for 3 weeks, p.o.</td>
<td>STZ-induced diabetic male Sprague-Dawley rats</td>
<td>Significantly reduced plasma glucose, total cholesterol, low-density lipoprotein (LDL), levels</td>
<td>[30]</td>
</tr>
<tr>
<td>2.</td>
<td><em>Agaricus campestris</em> L. (Agaricaceae) Field mushroom, Meadow mushroom</td>
<td>Aqueous extract of fruiting body</td>
<td>1mg/ml, p.o.</td>
<td>STZ induced diabetic mice</td>
<td>Stimulation of 2-deoxyglucose transport, glucose oxidation, and the incorporat-ion of glucose into glycogen in the abdominal muscle of mice</td>
<td>[31]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aqueous extract of fruiting body</td>
<td>0.25–1.0 mg/ml, p.o.</td>
<td>Alloxan induced diabetic mice</td>
<td>Stepwise 3.5 to 4.6 fold stimulation of insulin secretion from the pancreatic β-cell line</td>
<td>[31]</td>
</tr>
<tr>
<td><strong>4.</strong></td>
<td><em>Agrocybe cylindracea</em> (DC.) Maire (Strophariaceae) Chestnut Mushroom, Poplar mushroom</td>
<td>Hot water extract of the submerged-culture broth (ethyl acetate fraction)</td>
<td>200 and 400 mg/kg, p.o.</td>
<td>Diabetic male Sprague-Dawley rats</td>
<td>Reduced blood glucose level and elevated plasma insulin and glucose transport-4 proteins</td>
<td>[33]</td>
</tr>
<tr>
<td><strong>5.</strong></td>
<td><em>Astraeus hygrometricus</em> (Pers.) Morgan (Diplocystaceae) False earthstar</td>
<td>Powdered fruiting bodies</td>
<td>1g/kg for 2 months, p.o.</td>
<td>STZ-induced diabetic rats</td>
<td>Significant suppression of increased fasting plasma glucose; increased Serum insulin levels</td>
<td>[34]</td>
</tr>
<tr>
<td><strong>6.</strong></td>
<td><em>Auricularia auricula-judae</em> (Bull.) J. Schrot. (Auriculariaceae) Jew’s Ear, Jelly Ear mushroom</td>
<td>Ethanolic extract of fruiting bodies</td>
<td>250,500, 1000 mg/kg, p.o.</td>
<td>Alloxan induced diabetic mice</td>
<td>Significant effect in lowering plasma glucose, insulin, urinary glucose, and food intake; increased tolerance to intraperitoneal glucose loading and the hepatic glycogen content</td>
<td>[35]</td>
</tr>
<tr>
<td><strong>7.</strong></td>
<td><em>Coprinus comatus</em> (O.F. Mull.) Pers.(Coprinaceae) Shaggy ink cap</td>
<td>Water-soluble poly-saccharide from fruiting bodies</td>
<td>30 g/kg; in diet</td>
<td>Genetically diabetic KK-Ay mice</td>
<td>Significant effect in lowering plasma glucose, insulin, urinary glucose, and food intake; increased tolerance to intraperitoneal glucose loading and the hepatic glycogen content</td>
<td>[36]</td>
</tr>
<tr>
<td><strong>4.</strong></td>
<td><em>Agrocybe cylindracea</em> (DC.) Maire (Strophariaceae) Chestnut Mushroom, Poplar mushroom</td>
<td>A glucan (AG-HN1) and a heteroglycan (AG-HN2) isolated from hot-water extract of the fruiting bodies</td>
<td>I.p.</td>
<td>Normal and STZ-induced diabetic mice</td>
<td>AG-HN1 showed a remarkable hypoglycemic activity in both normal and STZ-induced diabetic mice, higher than that of AG-HN2</td>
<td>[37]</td>
</tr>
<tr>
<td><strong>5.</strong></td>
<td><em>Astraeus hygrometricus</em> (Pers.) Morgan (Diplocystaceae) False earthstar</td>
<td>Ethanolic extract of fruiting bodies</td>
<td>250,500, 1000 mg/kg, p.o.</td>
<td>Alloxan induced diabetic mice</td>
<td>Reduced levels of blood glucose; better tolerance to glucose</td>
<td>[38]</td>
</tr>
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<td><strong>6.</strong></td>
<td><em>Auricularia auricula-judae</em> (Bull.) J. Schrot. (Auriculariaceae) Jew’s Ear, Jelly Ear mushroom</td>
<td>Water-soluble poly-saccharide from fruiting bodies</td>
<td>30 g/kg; in diet</td>
<td>Genetically diabetic KK-Ay mice</td>
<td>Significant reduction of plasma glucose, total cholesterol and triglyceride levels</td>
<td>[39]</td>
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<tr>
<td><strong>7.</strong></td>
<td><em>Coprinus comatus</em> (O.F. Mull.) Pers.(Coprinaceae) Shaggy ink cap</td>
<td>Powdered dried fruiting bodies</td>
<td>Diet with 33.3% w/w powder</td>
<td>Normal mice</td>
<td>Reduced Plasma glucose; improved intraperitoneal glucose tolerance</td>
<td>[40]</td>
</tr>
<tr>
<td><strong>7.</strong></td>
<td><em>Coprinus comatus</em> (O.F. Mull.) Pers.(Coprinaceae) Shaggy ink cap</td>
<td>Fermented mushroom rich in vanadium</td>
<td>i.g. route</td>
<td>Normal, Alloxan and adrenalin induced hyperglycemic mice</td>
<td>Decreased blood glucose levels; improved sugar tolerance of normal mice</td>
<td>[41]</td>
</tr>
<tr>
<td><strong>7.</strong></td>
<td><em>Coprinus comatus</em> (O.F. Mull.) Pers.(Coprinaceae) Shaggy ink cap</td>
<td>4,5-Dihydroxy-2-methoxybenzaldehyde (comatin) isolated from fermentation broth</td>
<td>80 mg/kg, p.o.</td>
<td>Normal and alloxan induced diabetic rats</td>
<td>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</td>
<td>[42]</td>
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<tr>
<td>No.</td>
<td>Fungal Name</td>
<td>Extract/Preparation</td>
<td>Dose/Condition</td>
<td>Effects</td>
<td>Ref.</td>
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<td>8.</td>
<td><em>Cordyceps militaris</em> (L.) Link (Clavicipitaceae) Caterpillar Killer</td>
<td>Exo-polymers produced from submerged mycelia cultures</td>
<td>50mg/kg for 7 days, p.o.</td>
<td>STZ-induced diabetic rats</td>
<td>Significantly decreased levels of plasma glucose, total cholesterol, triglyceride and plasma glutamate-pyruvate transaminase (GPT)</td>
<td>[43]</td>
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<td></td>
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<td>Aqueous fruiting body extract</td>
<td>0.5 g/kg in diet</td>
<td>Type 2 diabetic rats</td>
<td>Amelioration of insulin resistance and improved insulin secretion</td>
<td>[44]</td>
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<td>Aqueous fruiting body extract</td>
<td>10 g/kg in diet</td>
<td>Rats (90% of pancreas removed)</td>
<td>Significant reduction of fasting serum glucose levels, increased body glucose disposal rates and glucose utilization in skeletal muscles</td>
<td>[45]</td>
</tr>
<tr>
<td>9.</td>
<td><em>Cordyceps sinensis</em> (Berk.) Sacc. (Clavicipitaceae) Caterpillar fungus</td>
<td>Polysaccharide fraction CSP-1, isolated from cultured mycelia</td>
<td>200 and 400mg/kg/day for 7 days, p.o.</td>
<td>Normal; alloxan and STZ-induced diabetic rats</td>
<td>Significant drop in blood glucose levels and increased serum insulin levels, stimulation of pancreatic release of insulin and/or reduced insulin metabolism</td>
<td>[46, 47]</td>
</tr>
<tr>
<td>10.</td>
<td><em>Cordyceps, takaomontana</em> [anamorph: Paecilomyces tenuipes (Peck) Samson] (Clavicipitaceae) Caterpillar fungus</td>
<td>Aqueous extract of fruiting bodies</td>
<td>0.5 g/kg, in diet for 8 weeks</td>
<td>90% pancreatetectomized male Sprague Dawley rats</td>
<td>Improvement of insulin Resistance and insulin secretion</td>
<td>[48]</td>
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<td></td>
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<td>Fruiting body extract containing 4-β-acetoxyscirpenol (ASD)</td>
<td>-</td>
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<td>Decreased blood sugar in the circulatory system as specific inhibitors of Na+/glucose transporter-1 (SGLT-1)</td>
<td>[49, 50]</td>
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<tr>
<td>11.</td>
<td><em>Fomitopsis pinicola</em> (Sw.) P. Karst, (Fomitopsidaceae) Red Banded Polypore</td>
<td>Water extract (WE) and an alkali extract (AE) from the fruit body</td>
<td>Dietary supplementati</td>
<td>STZ- induced diabetic rats</td>
<td>AE showed the highest antidiabetic effect. These results indicate that constituents of <em>F. pinicola</em> may regulate hyperglycemia via either increased insulin secretion during recovery or the prevention of STZ-induced pancreatic damage.</td>
<td>[51]</td>
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<tr>
<td>12.</td>
<td><em>Ganoderma applanatum</em> (Pers.) Pat. (Ganodermataceae) Artist's Bracket</td>
<td><em>Ganoderma applanatum</em> exo-polymer (GAE), produced by submerged mycelial cultures</td>
<td>100 mg/kg, p.o. for 3 weeks</td>
<td>STZ-induced diabetic rats</td>
<td>Reduced plasma glucose; plasma total cholesterol and triglyceride levels</td>
<td>[52]</td>
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<tr>
<td>13.</td>
<td><em>Ganoderma lucidum</em> (Curtis) P.Karst</td>
<td>Aqueous extract of fruiting bodies</td>
<td>500 and 1000 mg/kg, p.o.</td>
<td>Alloxan induced and normal Wistar rats</td>
<td>Significant hypoglycemic and antihyperglycemic effects</td>
<td>[53]</td>
</tr>
<tr>
<td>Mushroom (Family)</td>
<td>Extract/Preparation</td>
<td>Dose/Route</td>
<td>Model/Condition</td>
<td>Effect</td>
<td>Reference</td>
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<td>Reishi or Lingzhi mushroom (Ganodermataceae)</td>
<td>Aqueous extract of fruiting bodies (Ethylacetate and n-Butanol fractions)</td>
<td>50 mg/kg i.p. daily for two weeks</td>
<td>Alloxan-induced wistar rats</td>
<td>Significant reduction of fasting blood glucose</td>
<td>[54]</td>
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<td></td>
<td>Aqueous extract of fruiting bodies</td>
<td>100 and 200 mg/kg, by gavage once daily for four weeks</td>
<td>Normal and STZ-induced hyperglycemic rats.</td>
<td>Decreased serum glucose levels; increased serum insulin levels; improved serum lipid profile in both normal and diabetic animals</td>
<td>[55]</td>
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<td></td>
<td><strong>Ganoderma lucidum</strong> polysaccharides (Gl-PS)</td>
<td>50 mg/kg and 150 mg/kg, p.o.</td>
<td>STZ induced diabetic mice</td>
<td>Significant increase in body weights and serum insulin levels; decreased fasting blood glucose levels</td>
<td>[56]</td>
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<td></td>
<td>Proteoglycan extract, FYGL (Fudan-Yueyang-G. lucidum), from the fruiting bodies</td>
<td>40 and 120 mg/kg, p.o.</td>
<td>STZ induced type 2 diabetic rats</td>
<td>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</td>
<td>[9]</td>
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<td><strong>14. Grifola frondosa</strong> (Dicks.) Gray (Fomitopsidaceae) Hen of the woods, Maitake</td>
<td>Powdered fruiting body</td>
<td>1g/day, p.o.</td>
<td>Genetically diabetic mouse (KK-Ay)</td>
<td>Reduced levels of blood glucose, insulin and triglycerides</td>
<td>[57]</td>
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<td>Ether-ethanol soluble (ES) and hot water-soluble (WS) fractions from fruiting body</td>
<td>ES-fraction or WS-50% ethanol float (X) fraction, p.o.</td>
<td>Genetically diabetic mouse (KK-Ay)</td>
<td>Blood glucose lowering activity not only in the ES-fraction consisting of lipid but also in the X-fraction of peptidoglycan</td>
<td>[57]</td>
<td></td>
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<tr>
<td></td>
<td>Powdered fruiting bodies</td>
<td>20% maitake solid feed</td>
<td>Type 2 diabetic Female KK-Ay mice</td>
<td>Inhibition of increase in blood glucose levels</td>
<td>[58]</td>
<td></td>
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<td></td>
<td>MT-α-glucan, from the fruiting bodies</td>
<td>150-450 mg/kg</td>
<td>Type 2 diabetic KK-Ay mice.</td>
<td>Antidiabetic activity, related to its effect on insulin receptors (i.e., increasing insulin sensitivity and ameliorating insulin resistance of peripheral target tissues)</td>
<td>[59]</td>
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<td></td>
<td>Fermented <em>G. frondosa</em> rich in vanadium (GFRV)</td>
<td>i.g. route</td>
<td>Alloxan- and adrenaline-induced hyperglycemic mice</td>
<td>Significant decrease in blood glucose levels</td>
<td>[60]</td>
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<tr>
<td>No.</td>
<td><strong>Mushroom</strong></td>
<td><strong>Extract/Preparation</strong></td>
<td><strong>Dosage</strong></td>
<td><strong>Model</strong></td>
<td><strong>Efficacy</strong></td>
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<td>15.</td>
<td><em>Hericium erinaceus</em> (Bull.) Pers. (Ericaceae) Lion’s Mane Mushroom, Hedgehog Mushroom</td>
<td>Methanol extract of fruiting bodies</td>
<td>100 mg/kg, in diet</td>
<td>STZ-induced diabetic rats</td>
<td>Decreased blood sugar levels and lipid levels [61]</td>
<td></td>
</tr>
<tr>
<td>16.</td>
<td><em>Inonotus obliquus</em> (Ach. ex Pers.) Pilat (Hymenochaetaceae) Chaga mushroom</td>
<td>Protein-containing polysaccharides, extracted from sclerotia and mycelia</td>
<td>-</td>
<td>-</td>
<td>Hypoglycemic effect [62]</td>
<td></td>
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<td></td>
<td><strong>Fruiting body extract</strong></td>
<td>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.</td>
<td>Genetically obese mice</td>
<td>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]</td>
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<td></td>
<td><strong>Dried matter of culture broth</strong></td>
<td>500 and 1000 mg/kg, in diet</td>
<td>Alloxan induced diabetic mice</td>
<td>Significant antihyperglycemic; antilipidperoxidative and antioxidant effects [64]</td>
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<td></td>
<td><strong>Ethyl acetate fraction</strong></td>
<td>-</td>
<td>Alloxan-induced diabetic mice</td>
<td>Significant antihyperglycaemic and antilipidperoxidative effects [65]</td>
<td></td>
<td></td>
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<tr>
<td>17.</td>
<td><em>Laetiporus sulphureus</em> var. <em>miniatus</em> (Jungh.) Imazeki (Fomitopsidaceae) Sulphur polypore</td>
<td>Crude extracellular polysaccharides (EPS), produced from submerged mycelial culture</td>
<td>200 mg/kg for 14 days, p.o.</td>
<td>STZ-induced diabetic rats</td>
<td>Decreased plasma glucose levels, increased insulin antigenesity via proliferation or regeneration of diabetic islet β-cells [66]</td>
<td></td>
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<td>18.</td>
<td><em>Lentinula edodes</em> (Berk.) Pegler (Marasmiaceae) Shiitake</td>
<td>Exopolymers produced from submerged mycelia cultures</td>
<td>50 mg/kg for 7 days, p.o.</td>
<td>STZ-induced diabetic rats</td>
<td>Significant reduction in plasma glucose, total cholesterol and triglyceride levels [43]</td>
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<tr>
<td></td>
<td><strong>Exopolymer produced from submerged mycelia cultures</strong></td>
<td>200 mg/kg, p.o.</td>
<td>STZ-induced diabetic rats</td>
<td>Reduced plasma glucose, total cholesterol and triglyceride levels; increased plasma insulin levels [67]</td>
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<td>19.</td>
<td><em>Lentinus strigosus</em> Fr. (Polyporaceae) Ruddy panus</td>
<td>Exopolysaccharides (EPS) from submerged mycelial culture</td>
<td>150 mg/kg for 7 days, p.o.</td>
<td>STZ-induced diabetic rats</td>
<td>Decreased plasma glucose level; induces regeneration of pancreatic islets and remediates destruction of micro-vascular pancreatic islets [68]</td>
<td></td>
</tr>
<tr>
<td>20.</td>
<td><strong>Phellinus badius</strong> (Cooke) G. Cunn (Hymenochaetaeae)</td>
<td>Aqueous extract of fruit body and mycelial biomass</td>
<td>Aqueous extracts of basidio-carp, and mycelial biomass at the doses of 800 mg/kg and 1000 mg/kg respectively</td>
<td>Alloxan-induced diabetic rats.</td>
<td>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).</td>
<td>[69]</td>
</tr>
<tr>
<td>21.</td>
<td><strong>Phellinus baumii</strong> Pilat (Hymenochaetaeae)</td>
<td>Crude exopolysaccharides from submerged mycelial cultures</td>
<td>200 mg/kg, p.o.</td>
<td>STZ-induced diabetic rats</td>
<td>Hypoglycemic effect with substantially reduced plasma glucose levels</td>
<td>[70]</td>
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<td></td>
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<td>Exopolysaccharides (EPS) produced by submerged mycelial culture</td>
<td>200 mg/kg for 52 days, p.o.</td>
<td>ob/ob mice</td>
<td>Reduced plasma glucose levels, increased glucose disposal, reduced blood triglyceride levels</td>
<td>[71]</td>
</tr>
<tr>
<td>22.</td>
<td><strong>Phellinus linteus</strong> (Berk. &amp; M.A. Curtis) Teng, Zhong Guo De Zhen Jun (Hymenochaetaceae)Meshimakobu, Song-Gen, Sang-Hwang</td>
<td>Exo-polymers from submerged mycelia cultures</td>
<td>50 mg/kg for 7 days, p.o.</td>
<td>STZ-induced diabetic rats</td>
<td>Reduced plasma glucose, total cholesterol and plasma glutamate-pyruvate transaminase (GPT) levels</td>
<td>[43]</td>
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<tr>
<td></td>
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<td>Extracellular polysaccharides extracted from submerged mycelia cultures</td>
<td>100 mg/kg, p.o.</td>
<td>STZ-induced male Sprague–Dawley rats</td>
<td>Hypoglycemic effects with decreased plasma glucose, total cholesterol and triacyl-glycerol concentration</td>
<td>[72]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Polysaccharide (PLP) isolated from <em>Phellinus linteus</em></td>
<td>-</td>
<td>Non-obese diabetic (NOD) mice</td>
<td>Mean blood glucose levels were 110mg/dl in PLP-treated mice as compared to 499mg/dl in control NOD mice</td>
<td>[73]</td>
</tr>
<tr>
<td>23.</td>
<td><strong>Phellinus merrillii</strong> (Murrill) Ryvarden (Hymenochaetaeae)</td>
<td>EtOAc-soluble fractions of ethanol extract of fruiting bodies</td>
<td>-</td>
<td>Male Sprague–Dawley rats</td>
<td>Strong α-glucosidase and aldose reductase inhibitory activities</td>
<td>[74]</td>
</tr>
<tr>
<td>24.</td>
<td><strong>Phellinus ribis</strong> (Schumach.) Quel (Hymenochaetaeae)</td>
<td>Polychlorinated compounds from methanolic extract of the fruiting body</td>
<td>-</td>
<td>-</td>
<td>Therapeutic effects through the enhanced PPAR-γ agonistic activity</td>
<td>[75, 76]</td>
</tr>
<tr>
<td>25.</td>
<td><strong>Phellinus rimosus</strong> (Berk.) Pilat (Hymenochaetaeae) Cracked cap polypore</td>
<td>Fruiting body extract</td>
<td>50 and 250 mg/kg for 10 days, p.o.</td>
<td>Alloxan-induced diabetic rats</td>
<td>Significant dose-dependent hypo-glycemic activity</td>
<td>[77]</td>
</tr>
<tr>
<td>26.</td>
<td><strong>Pleurotus abalonus</strong> Y.H. Han, K.M. Chen &amp; S. Cheng (Pleurotaceae) Abalone mushroom</td>
<td>Polysaccharide-peptide complex LB-1b from fruiting bodies</td>
<td>-</td>
<td>Drug-induced diabetic mice</td>
<td>High antioxidant activity with a significant hypoglycemic effect</td>
<td>[78]</td>
</tr>
<tr>
<td>27.</td>
<td><strong>Pleurotus</strong> Water-soluble</td>
<td>0.4 g/kg, in</td>
<td>STZ-induced</td>
<td>Reduced fasting blood</td>
<td></td>
<td>[79]</td>
</tr>
<tr>
<td><strong>citrinopileatus</strong> Singer (Pleurotaceae) Golden oyster mushroom</td>
<td>polysaccha-rides (WSPS), extracted from submerged fermented medium</td>
<td>diet</td>
<td>diabetic rats</td>
<td>glucose levels</td>
<td></td>
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<tr>
<td>28. <strong>Pleurotus eryngii</strong> (DC.) Quel. (Pleurotaceae) King trumpet mushroom, French horn mushroom, King oyster mushroom, King brown mushroom, Boletus of the steppes, Trumpet royale</td>
<td>Freeze-dried, powdered fruiting body</td>
<td>Diet containing 5% freeze dried mushroom</td>
<td>Male db/db mice</td>
<td>Reduced total cholesterol, triglyceride levels, and increased high density lipoprotein cholesterol levels with improved insulin sensitivity [80]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29. <strong>Pleurotus ostreatus</strong> (Jacq.) P. Kumm. (Pleurotaceae) Oyster mushroom</td>
<td>Powdered fruiting bodies</td>
<td>Diet containing 4% mushroom</td>
<td>Type 2 diabetic rats</td>
<td>Significantly lower basal and postprandial glycaemia. [81]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ethanol extract of fruiting bodies</td>
<td>250, 500 and 1000 mg/kg</td>
<td>Alloxan induced diabetic rats</td>
<td>Dose dependent decrease in blood glucose and cholesterol effects [82]</td>
<td></td>
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<tr>
<td></td>
<td>Ethanol extract of fruiting bodies</td>
<td>100 and 200 mg/kg for 30 days, p.o.</td>
<td>STZ - induced diabetic rats</td>
<td>Significant decrease of blood glucose levels, genetic alterations and sperm abnormalities [83]</td>
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<tr>
<td></td>
<td>Suspension of freeze-dried and powdered fruiting body</td>
<td>250, 500, 750, 1000, and 1250 mg/kg, p.o.</td>
<td>Normal and alloxan-induced diabetic Wistar rats</td>
<td>Significantly reduced levels of serum glucose. Hypo-glycemic effect comparable with metformin and glibenclamide [84]</td>
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<tr>
<td></td>
<td>Ethanol extract of fruiting bodies</td>
<td>380, 760 and 1140 mg/kg, i.p.</td>
<td>Alloxan-induced diabetic rats</td>
<td>Significant reduction in blood glucose levels [85]</td>
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<tr>
<td></td>
<td>Ethanol extract of fruiting bodies</td>
<td>-</td>
<td>Normal and alloxan-induced diabetic mice.</td>
<td>Significant decrease in serum glucose level; reduced serum cholesterol, triglyceride and LDL-cholesterol levels [86]</td>
<td></td>
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<tr>
<td>30. <strong>Pleurotus pulmonarius</strong> (Fr.) Quel (Pleurotaceae) Indian Oyster, Italian Oyster, Phoenix Mushroom, Lung Oyster</td>
<td>Aqueous extract of fruiting bodies</td>
<td>250, 500, and 1000 mg/kg, p.o.</td>
<td>Normal and Alloxan-induced diabetic mice</td>
<td>Antihyper-glycemic effect (increased glucose tolerance in both normal and diabetic mice) [2]</td>
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<tr>
<td>No.</td>
<td>Name</td>
<td>Description</td>
<td>Glucan Component</td>
<td>Effect</td>
<td>Notes</td>
<td></td>
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<tr>
<td>31</td>
<td><em>Sparassis crispa</em> (Wulfen) Fr. (Sparassidaceae) Cauliflower fungus</td>
<td>Freeze dried fruiting body samples</td>
<td>-</td>
<td>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</td>
<td></td>
<td></td>
</tr>
<tr>
<td>32</td>
<td><em>Stropharia rugosoannulata</em> Farl. ex Murrill. (Strophariaceae) Wine cap, Burgundy mushroom King stropharia</td>
<td>Extracellular polysaccharide (EPS)</td>
<td>-</td>
<td>Increase in the migration of macrophages and fibroblasts, and directly increased synthesis of type I collagen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>33</td>
<td><em>Trametes gibbosa</em> (Pers.) Fr. (Polyporaceae) Lumpy bracket</td>
<td>Exopolysaccharide (EPS)</td>
<td>-</td>
<td>Decrease in plasma levels of adiponectin; decreased blood glucose levels, serum triglycerides and total cholesterol levels</td>
<td></td>
<td></td>
</tr>
<tr>
<td>34</td>
<td><em>Tremella aurantia</em> Schwein. (Tremellaceae) Golden ear</td>
<td>Acidic polysaccharide (TAP) solution and TAP-H (degradation products of TAP) solution</td>
<td>TAP solution- 0.5 g/l; TAP-H solution- 1.5 g/l, p.o.; for 10 weeks</td>
<td>Reduced serum glucose levels, total cholesterol and triglyceride levels; Significant decrease in plasma lipoperoxide level</td>
<td></td>
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</tr>
<tr>
<td>35</td>
<td><em>Tremella fuciformis</em> Berk. (Tremellaceae) Snow fungus, Silver ear fungus, White jelly mushroom</td>
<td>Exopolysaccharides (EPS) produced by submerged mycelial culture</td>
<td>Normal and STZ- induced diabetic mice</td>
<td>Significant dose-dependent hypo-glycemic activity</td>
<td></td>
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</tr>
<tr>
<td>36</td>
<td><em>Tremella mesenterica</em> (Schaeff.) Retz. (Tremellaceae) Yellow brain mushroom, Golden jelly fungus, Yellow trembler, Witches' butter</td>
<td>Tremellastin, containing 40-45% acidic polysaccharide glucuronoxylomannan, obtained by alcoholic precipitation of culture broth after submerged cultivation</td>
<td>STZ-induced hyperglyc-emic mice</td>
<td>Statistically significant and dose-dependent reduction of intrinsic blood glucose levels as well as significantly decreased triglyceride levels</td>
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</tbody>
</table>
Table 2. Clinical studies carried out with mushrooms for management of DM.

<table>
<thead>
<tr>
<th>S.no.</th>
<th>Biological source</th>
<th>Extract/Fraction/Isolate</th>
<th>Dose</th>
<th>Type of trial</th>
<th>Observations</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td><em>Agaricus sylvaticus</em> Schaeff. (Agaricaceae) Sun Mushroom</td>
<td>Fruiting bodies</td>
<td>30mg/kg; Dietary supplementation</td>
<td>Randomized, double-blind, placebo-controlled clinical trial on 56 patients with colorectal cancer</td>
<td>Significant reduction of fasting plasma glucose, total cholesterol, creatinine, aspartate aminotransferase, alanine aminotransferase, systolic blood pressure</td>
<td>[98, 99]</td>
</tr>
<tr>
<td>2.</td>
<td><em>Grifola frondosa</em> (Dicks.) Gray (Fomitopsidaceae) Hen of the woods, Maitake</td>
<td><em>Grifola frondosa</em> polysaccharide caplets (MFCs) containing active SX-fraction</td>
<td>-</td>
<td>5 patients with type 2 diabetes</td>
<td>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</td>
<td>[8]</td>
</tr>
<tr>
<td>3.</td>
<td><em>Pleurotus ostreatus</em> (Jacq.) P. Kumm. (Pleurotaceae) Oyster mushroom</td>
<td>Powdered fruiting bodies</td>
<td>Dietary supplementation</td>
<td>120 patients with type 2 diabetes</td>
<td>Significant association between mushroom supplementation and gradual reduction in hyperglycemia in type 2 diabetic subjects</td>
<td>[100]</td>
</tr>
</tbody>
</table>
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.

REFERENCES


