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An overview on mushroom: Chemical constituents and pharmacological activities

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Abstract
Mushrooms have been valued as a traditional source of natural bioactive compounds for centuries and have recently been exploited for potential components in the cosmetics industry. Numerous mushrooms and their ingredients have been known to be beneficial to the skin and hair. The representative ingredients are as follows: phenolics, polyphenolics, terpenoids, selenium, polysaccharides, vitamins, and volatile organic compounds. These compounds show excellent antidiabetic, antioxidant, anti-aging, anti-wrinkle, skin whitening, and moisturizing effects, which make them ideal candidates for cosmetics products. Lectins play crucial role in various biological processes such as cellular signaling, scavenging of glycoproteins from the circulatory system, cell–cell interactions in the immune system, differentiation and protein targeting to cellular compartments, as well as in host defence mechanisms, inflammation, and cancer. Among all the sources of lectins, plants have been most extensively studied. However, more recently fungal lectins have attracted considerable attention due to their antitumor, antiproliferative and immunomodulatory activities. Given that only 10% of mushroom species are known and have been taxonomically classified, mushrooms represent an enormous unexplored source of potentially useful and novel lectins. In this review we provide an up-to-date summary on the biochemical, molecular and structural properties of mushroom lectins, as well as their versatile applications specifically focusing on mushroom lectin bioactivity.

Keywords: mushrooms, antidiabetic, anti-aging, antioxidant, skin whitening

Introduction

Mushrooms are an assemblage of fleshy macroscopic fungi. They possess a distinctive fruiting body that could by hypogenous or epigeous, large enough to be seen by naked eyes & to be picked by hands. Edible mushrooms are ideal low calorie foods for diabetic patients since they contain very low amounts of fats cholesterol low levels of carbohydrates, high content of protein, vitamins & minerals. Mushrooms are known to contain compounds which help in proper functioning of the liver, Pancreas & other endocrinal gland thereby promoting formation of insulin & related hormones which ensure healthy metabolic functioning. Polysaccharides, such as beta glucans contained in mushrooms have the ability to restore the function of pancreatic tissues by causing increased insulin output by beta-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, & low- density lipoproteins & increase the level of high- density lipoproteins [1]. Medicinal mushrooms and their constitutive active compounds have been described to have reducing many diseases including cancer, hypertension, metabolic syndrome and cardiovascular diseases. Many studies have focused on their immunomodulatory and anti-tumor effects because mushrooms may contain a diverse array of biologically active metabolites (β-D-glucans, immunomodulatory proteins, secondary metabolites) with well-known immune enhancing capabilities. Some chemical and biochemical hypoglycemic agents (anti-diabetes agents), such as insulin, Metformin, tolbutamide, gliclazide, phenformin, troglitazone and rosiglitazone, exenatide are the mainstay in the treatment of diabetes and are effective in controlling hyperglycemia. However, these anti-diabetes agents may have harmful side-effects, fail to significantly alter the course of diabetic complications and there is insufficient knowledge on the pharmacological management of the disease .Therefore, natural antidiabetic drugs from medicinal plants have attracted a great deal of attention. Admittedly, diabetes is a metabolic disorder which should be controlled or prevented with appropriate lifestyle adaptations including exercise, appropriate food and health relevant environments. Indeed healthy foods rich in various medicinal properties provide a means to good health. 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. *Agaricus bisporus* is a popular edible mushroom worldwide. The mushroom has potential anti-inflammatory, hypoglycemic and hypocholesterolemic effects due to presence of high amounts of acidic polysaccharides, dietary fibre, and antioxidants, such as vitamins C, B12, and D; folate, ergothioneine; and polyphenol. The increased intake of white button mushrooms may promote innate immunity against tumors and viruses High concentrations of blood cholesterol levels, hypercholesterolemia, can lead to a progression of hyperglycemia/ type 2 diabetes in humans and animals. Cholesterol directly effects β-cell metabolism and opens a novel set of mechanisms that may contribute to β-cell dysfunction and the onset of diabetes. Epidemiological studies suggest that higher levels of dietary fibre intake play a significant protective role with respect to diabetes, in lowering the dietary glycemic load and shows potent hypocholesterolemic effects. Diabetic rats fed *A. bisporus* fruiting bodies exhibited significant anti-glycemic and anti-hypercholesterolemic effects. Moreover, the mushrooms had a positive influence on lipid metabolism and liver function. Although soluble dietary fibre is the most likely candidate in lowering blood glucose levels and cholesterol levels, other constituents, such as anti-oxidants (polyphenol, vitamin C, and ergothioneine), proteins, and polysaccharides may also play an important role [2].

Agaricus -Taxonomic position

Division	:	Mycota
Sub-division	:	Eumycotina
Class	:	Basidiomycete
Subclass	:	Homobasidiomycetidae
Series	:	Hymenomycetes
Order	:	Agaricales
Family	:	Agaricaceae.
Genus	:	Agaricus
Species	:	Bisporus

Fig 1: Mushroom

Most widely cultivated species for food purposes is *Agaricus bisporus* in India [3].

Cultivation and Cllection

Favorable season: Oct. to March (for plains of India) Required temp. and humidity:14-22^{0}C and 80-85%

Cultivation process involves four major steps

a. Preparation of compost
b. Spawning of compost
c. Casing (Covering the spawned compost)
d. Cropping and crop management

Preparation of compost

Unlike other traditional crops soil is not the appropriate substrate for mushroom cultivation. Rather, the substrate for mushroom called compost, is prepared from agro wastes like straw, stem, shoot, apices etc. with organic manure. Mushroom substrate may be simply defined as a lingo-cellulosic material that supports the growth, development and fruiting of mushroom mycelium. This compost is pasteurized by various micro-organisms and at appropriate temperature range. Essential supplement are also added/ supplemented to the compost. The whole process is termed as composting. Generally composting refers to the piling of substrates for a certain period of time and the changes due to the activities of various micro-organisms, which result in a composted substrate that is chemically and physically different from the starting material. The compost provides nutrients, minerals, vitamins and ions required for proper growth of mushroom. This compost supports the growth of only the mycelium of button mushroom and prevents that of other competitive moulds.

Methodology for compost preparation

Compost is an artificially prepared growth medium from which mushroom is able to derive important nutrients required for growth and fructification. Cemented floors are required for making good quality compost. There are two main methods for compost preparation:

1. Long method of composting: This is an outdoor process and takes around 28 days in its completion with a total of seven turnings.
Before making compost, wheat straw is spread on cemented floor and is turned many times with water being spread at regular intervals.

Day 0: At the stage, there should be around 75% humidity content in the wheat straw, to which wheat bran, calcium ammonium nitrate, urea, murate of potash, and super phosphate are mixed thoroughly and evenly. The material is then piled 1.5m thick x1.25m high with the help of wooden rectangular block. The blocks are removed. Once the entire material has been stacked up or piled up. Water is sprayed twice or thrice to keep the substrate moist. Temperature should be in the range of 70-75^{0}C.

1st turning Day 6: On the sixth day first turning is given to the stack. The purpose of turning is that every portion of the pile should get equal amount of aeration and water. If the turnings are not given, then anaerobic condition may prevail which may lead to the formation of non-selective compost. In the stack, the central zone is fermenting at its peak and has maximum temperature rest of the portion is either not at all fermented or ferments improperly. The correct method of turning is as: Removing about 15cm of compost from the top and spread it on one side of the floor, the rest part of compost on the other side of the floor. Now turning is done by shaking the outer (top most) part and the inner part of the compost, first separately and then missing them altogether thoroughly with the help of wooden buckets.

2nd turning (Day 10): On the tenth day, again the top most part and the inner part of the compost is separated, water is sprayed on the top part. Again the two parts are piled up together in such a way that now the top part is inside and the inner part is on the top of the stack.

3rd turning (day 13): it is also done in the same way as described earlier. Gypsum and furadan are mixed at this stage.

4th turning (day 16): The same process of turning is followed.

5th turning (day 19): The compost is turned in the same manner and B.H.C. is added.

6th turning (day 22): The same process of turning is followed.

7th turning (day 25): if no ammonia persists in the compost, spawning is done

2. Short method of composting

Compost prepared by short method composting is superior in production quality and the chances of infection and disease is quite low.

This method is accomplished in two phases:

Phase I: Outdoor composting

Wheat straw mixed with chicken manure is sprayed with water and a 45cm high pile is made on the fourth day and first turning is made. On 7th day, wheat bran, gypsum and urea is mixed thoroughly and piled up to 1.25-1.50 m height with a width ranging from 1.25 -1.5 m. The internal temperature of the compost should be maintained at 70-75^{0}C within 24hr. Second turning is done on this day where as third turning is done on 8th day with subsequent mixing of gypsum. On the 10th day, the compost is transferred to the pasteurization tunnel. Compost is filled in the pasteurization tunnel to a height of 7'. Filling height depends upon the size of the tunnel.

Phase II: Indoor composting

This is the pasteurization procedure which is done in a closed environment. Pasteurization has got many purposes.

1. If the temperature during composting has been low and the compost is heterogeneous, many parasites (nematodes, pathogens, flies and mites etc.) will survive in the compost mass, therefore, pasteurization is the best means with which these parasites can be destroyed.
2. To end fermentation and to convert compost into a chemical and biological state favourable to the development of the mycelium and unfavourable to moulds.
3. Conversion of ammonia into microbial protein.

Compost is filled in the pasteurization tunnel and as soon as the compost in the tunnel is completely filled the doors and fresh air damper are properly closed and blower is put on for recirculation of air @ 150-250 cubic metre/ 1000 kg compost/ hour. The phase II process is completed in three stages:

1. **Pre-peak heat stage:** After about 12-15 hours of compost filling, the temperature of compost starts rising and once 48-50^{0}C is obtained, it should be maintained for 36-40 hours with ventilation system. Normally such temperature is achieved by self generation of heat by the compost mass without steam injection.
2. **Peak heat stage:** raise the temperature of compost to 57-58^{0}C by self generation of heat from microbial activity if it is not obtained. Injecting the live steam in the bulk chamber and maintain for 8 hours in order to ensure effective pasteurization. Fresh air introduced by opening of the fresh air damper to 1/6 or 1/4 of its capacity and air outlet too is opened to the same extent.
3. **Post- peak heat stage:** lower down the temperature gradually to 48-52^{0}C and maintain till no traces of ammonia are detected in compost. This may take 3-4 days in a balanced formulation. When the compost is free from ammonia, full fresh air is introduced by opening the damper to its maximum capacity and cool down the compost to around 25^{0}C which is considered as the favourable temperature for spawning.

Spawning

The process of mixing of the spawn in the compost is known as spawning. Spawn is thoroughly mixed in the compost at the rate of 600-750 gm per 100 kg of compost (0.6 - 0.75%). The spawned compost is filled in tray or polypropylene bags covered with formalin treated news papers. In case of bags, they should be folded at the top and covered up. After spawning, temperature and humidity of crop room should be maintained at 18-22^{0}C and 85-90%, respectively. Water should be sprayed over the covered news papers, walls and floors of the crop room. After 12-14 days of spawning white mycelial growth is seen running the entire length of the tray/bag. This is then covered with casing soil on the surface.

Casing soil

The significance of casing soil is to maintain the moisture content and exchange of gases within the surface of the compost which helps in the proper growth of the mycelium. The pH of the casing soil should be 7.5-7.8 and must be free from any infection or disease.

Pasteurization of casing soil

The casing soil is piled on cemented floor and is treated with 4% formalin solution. Thorough turning of the soil is done and it is covered with polythene sheet for the next 3-4 days. Pasteurization of casing soil at 65^{0}C for 6-8 hours is found to be much more effective.

Using the casing soil

3-4cm thick layer of casing soil is being spread uniformly on the compost when the surface has been covered by white mycelium of the fungus. Formalin solution (0.5%) is then being sprayed. Temperature and humidity of the crop room should be maintained at 14-18^{0}C and 80-85%, respectively. Proper ventilation should be arranged with water being sprayed once or twice a day.

Harvesting of crop

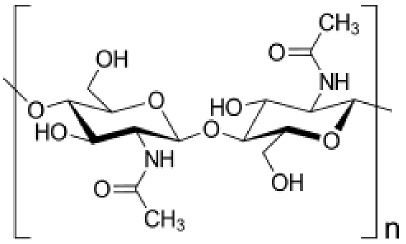
Pin head initiation takes place after 10-12 days of casing and the fruiting bodies of the mushroom can be harvested for around 50-60 days. The crops should be harvested before the gills open as this may decrease its quality and market value.

Productivity

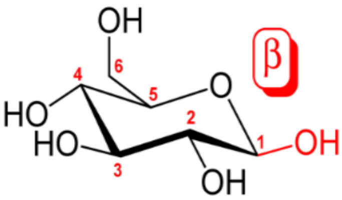
From 100 kg compost prepared by long method of composting 14-18 kg of mushroom can be obtained. Similarly, 18-20 kg mushroom can be obtained from pasteurized compost (Short Method Compost) [4].

Phytochemical compounds

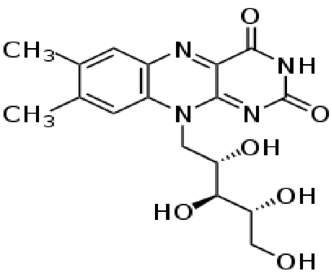
Literature indicates that mushrooms have phytochemicals compound such as Alkaloid, Carbohydrates, steroids, glycosides, flavonoids, protein, amino acids, phenols, Saponins, triterpenoids presented [5, 6] Pantothenic acid [7], Riboflavin [7], Niacin [7], Vitamin C [7], Chitin [8], Beta glucan [8], Vitamin D [9].



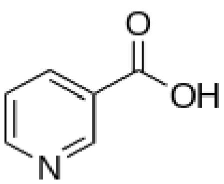
Chitin



Beta-glucan



Riboflavin



Niacin

Pharmacological Activities

Anti diabetic

Mushrooms are known to contain compounds which help in proper functioning of the liver pancreas and other endocrinal glands, thereby promoting formation of insulin and related hormones which ensure healthy metabolic functioning. 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 [10].

Antioxidant

Mushrooms also contain antioxidant compounds such as polyphenols and flavones that are involved in antioxidant defence for humans, Such compounds have the ability to block reactive oxygen species involved in lipid peroxidation, oxidative stress that leads to DNA, cell membrane proteins and cellular organelles damage. Oxidative stress arises from an imbalance between the production of reactive oxygen species and antioxidant systems in the human body, when the ability to inactivate these compounds is low [11].

Antimicrobial and antiviral activity

The ethanolic extract of fruiting bodies of *A. bisporus* contains various components with antimicrobial activity. The freeze-dried extract of this species displays activity towards *Escherichia coli* CBAB 2 (Minimum Inhibitory Concentration – MIC – 5 mg/mL), and also against *Staphylococcus aureus* ATCC 6588 (Gram negative). On the other hand, *Pseudomonas aeruginosa* ATCC 15442 has proved to be the most resistant strain, with a MIC value of 15 mg/mL. The antimicrobial action of numerous mushroom species (including *A. bisporus*) is due to high contents of chitosan and chitin. Chitin and its deacetylated derivative – chitosan, are polysaccharides whose molecular weight is relatively high (similar to the ones found in crustaceans), which could suggest that their antibacterial properties are reduced. The antimicrobial effect of chitin and its derivatives increases with a decrease in the molecular weight. The activity is based on decreasing bacterial adhesion to the culture medium into *Agaricus campestris*, a species closely related to *A. bisporus*, has shown the presence of agarodoxin – a benzoquinone derivate. This substance is an antibiotic and shows activity against *Staphylococcus aureus* (golden staph).

Anti-carcinogenic

A.bisporus, including hydroxybenzoic acid and protocatechuic acid, are also characteristic for this species. These substances, apart from their typical anti-carcinogenic activity. The application of *A. bisporus* to anticancer therapy should, therefore, be feasible and inexpensive [12]

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 [10].

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

S. No.	Biological source	Extract/Fraction/ Isolate	Dose	Experimental Models	Observations
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 %
		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
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
		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
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
		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
		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
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
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
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
		Hot water extract from fruiting bodies	Diet containing 5% extract	Genetically diabetic (type 2) KK-Ay	Reduced postprandial hyperglycemia
		Dried mycelia powder	0.5 and 1.0g/kg, p.o.	Genetically diabetic mice	Significant reduction of plasma glucose, total cholesterol and triglyceride levels
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
		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
		4,5- Dihydroxy-2- methoxybenzalde hyde (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
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)
		Aqueous fruiting body extract	0.5 g/kg in diet	Type 2 diabetic rats	Amelioration of insulin resistance and improved insulin secretion
		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

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
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
		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)
11	*Fomitopsis pinicola* (Sw.) P. Karst. (Fomitopsidaceae) Red Banded Polypore	Water extract (WE) and an alkali extract (AE) from the fruit body	Dietary supplementation	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.
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
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
	(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
		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
		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
		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
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
		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
		Powdered fruiting bodies	20% maitake solid feed	Type 2 diabetic Female KK-Ay mice	Inhibition of increase in blood glucose levels
		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
		Fermented *G. frondosa* rich in vanadium (GFRV)	i.g. route	Alloxan- and adrenalin-induced hyperglycemic mice	Significant decrease in blood glucose levels
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

16.	*Inonotus obliquus* (Ach. ex Pers.) Pilat (Hymenochaetace- ae) Chaga mushroom	Protein- containing polysacchari-des, extracted from sclerotia and mycelia	-	-	Hypo-glycemic effect
		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
		Dried matter of culture broth	500 and 1000 mg/kg, in diet	Alloxan induced diabetic mice	Significant antihyper-glycemic; antilipid- peroxidative and antioxidant effects
		Ethyl acetate fraction	-	Alloxan-induced diabetic mice	Significant antihyper- glycaemic and antilipidperoxidative effects
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
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
		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
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
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).
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
		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
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
		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
		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
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
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

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
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
27.	*Pleurotus*	Water-soluble	0.4 g/kg, in	STZ- induced	Reduced fasting blood
	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
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.
		Ethanol extract of fruiting bodies	250, 500 and 1000 mg/kg	Alloxan induced diabetic rats	Dose dependent decrease in blood glucose and cholesterol effects
		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
		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
		Ethanol extract of fruiting bodies	380, 760 and 1140 mg/kg, i.p.	Alloxan-induced diabetic rats	Significant reduction in blood glucose levels
		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
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)
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
		Freeze dried fruiting body samples	Dietary supplementati on	Diabetic KK-Ay mice	Increased plasma levels of adiponectine; decreased blood glucose levels, serum triglycerides and total cholesterol levels
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
33.	*Trametes gibbosa* (Pers.) Fr. (Polyporaceae) Lumpy bracket	Extracellular Polysaccharide (EPS)	-	STZ- induced diabetic mice	Decreased plasma glucose, total cholesterol and triacylglycerol concentrations

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
35.	*Tremella fuciformis* Berk. (Tremellaceae) Snow fungus, Silver ear fungus, White jelly mushroom	Glucuronoxylom annan (AC) from the fruiting bodies	Oral administrat- ions of the AC solution	Normal and STZ- induced diabetic mice	Significant dose- dependent hypo-glycemic activity
		Exopolysacch-arides (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
36.	*Tremella mesenterica* (Schaeff.) Retz. (Tremellaceae) Yellow brain mushroom, Golden jelly fungus, Yellow trembler, Witches' butter	Tremellastin, containing 40-45% acidic polysaccharide glucuronoxy- lomannan, 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
		Fruiting bodies	-	STZ-induced	Significant reduction in
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
		Freeze dried fruiting body samples	Dietary supplementati on	Diabetic KK-Ay mice	Increased plasma levels of adiponectine; decreased blood glucose levels, serum triglycerides and total cholesterol levels
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		Fruiting bodies	-	STZ-induced	Significant reduction in

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

S.no.	Biological source	Extract/Fraction/ Isolate	Dose	Type of trial	Observations
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
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
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

Conclusion

The review demonstrates that *Agaricus bisporus* have a great potential for the production of useful bioactive metabolites and those they are a prolific resources for drugs. The responsible bioactive compounds belong to several chemical groups. *Agaricus bisporus* possess a high variety of bioactive compounds, and therefore of pharmacological effects.

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References

1. Amandip Kaur, Gurpaul Singh Dhingra, Richa Shri; Antidiabetic potential of mushrooms; Asian J Pharma. Res. 2015; 5(2):111-125.
2. Dilani D. De Silva, Sylvie Rapior, Kevin D Hyde, Ali H Bahkali. Medicinal mushrooms in prevention and control of diabetes mellitus Fungal Diversity. 2012; 56:1-29.
3. Dr. V Venkatash Gobi1. Bio-Chemical Extraction of Active Compounds of Agaricus (Mushrooms) and it's Antioxidant Activity**.** IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) e-ISSN: 2279-0853, p-ISSN: 2279-0861. 2015; 14(9):36-39.
4. Ulrike Lindequist, Timo HJ, Niedermeyer, Wolf-Dieter Jülich. The Pharmacological Potential of Mushrooms, Evid Based Complement Alternat Med. 2005; 2(3):285-299.
5. Ram Chandra, Pandey VN, Singh HB. Extract of white button mushroom (*Agaricus bisporus*) for bio-medicinal molecules; CIB Tech Journal of Pharmaceutical sciences. 2012; 1(1):9-11.
6. Mariappansenthi Kumar, Vinayagam Srividhya, Durai Mahalakshmi. Phytochemical screening of bioactive compounds from pleurotus ostreatus kumm., An wild edible mushroom, wjpr. 2015; 4(05):1603-1618.
7. Dhamodharam G, Mirunalini S. A Novel medicinal characterizatio of *Agaricus bisporus*; Pharmacologyonline. 2010; 2:456-463.
8. Nasiri F, Ghiassi Tarzi B. Annals of Biological Research. 2012; 3(12):5677-5680.
9. Katherine M Phillips, Ronald L Horst, Nicholas J Koszewski, Ryan R Simon. Vitamin D_4 in mushrooms. Plos one. 2012; 7(8).
10. Amandip Kaur, Gurpaul Singh Dhingra, Richa Shri. Antidiabetic potential of mushrooms; Asian J Pharma. Res. 2015 5(2):111-125.
11. Liu J1, Jia L, Kan J, Jin CH. In vitro and in vivo antioxidant activity of ethanolic extract of white button mushroom (*Agaricus bisporus*)., Food Chem Toxicol. 2013; 51:310-6.
12. Bożena Muszyńska1, Katarzyna Kała1, Jacek Rojowski, Agata Grzywacz1. Włodz imierz Opoka Composition and Biological Properties of *Agaricus bisporus* Fruiting Bodies – a Review, Pol. J Food Nutr. Sci. 2017; 67(3):206-9.