Edible Mushrooms as Myco-Therapeutics

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Polysaccharides (essentially β-D-glucans), chitinous substances, heteroglycans, proteoglycans, peptidoglycans, alkaloids, lactones, lectins, alkaloids, flavonoids, steroids, terpenoids, terpenes, phenols, nucleotides, glycoproteins, proteins, amino acids, antimicrobials, and minerals are the major bioactive compounds in these mushrooms. These bioactive compounds have chemo-preventive, anti-obesity, anti-diabetic, cardioprotective, and neuroprotective properties. Consumption of edible mushrooms reduces plasma triglyceride, total cholesterol, low-density lipoprotein, and plasma glucose levels. Polysaccharides from edible mushrooms suppress mRNA expression in 3T3-L1 adipocytes, contributing to their anti-obesity properties. Therefore, edible mushrooms or their active ingredients may help prevent obesity and other chronic ailments.

edible mushroom obesity body mass index gut microbiota anti-obesity agent

1. Introduction

Mushrooms are spore-bearing fruiting bodies of fungi that grow above the ground. They are rich in starches and proteins but are a poor source of fat [1]. Many researchers have reported the nutritional value of various mushrooms. Reis et al. reported the composition of *Agaricus bisporus* as 14.1% protein, 2.2% fat, and 74.0% carbohydrates, while another mushroom *Pleurotus ostreatus* contains 7.0% protein, 1.4% fat, and 85.9% carbohydrates [2]. Mushrooms also contain micronutrients, mainly various types of vitamin B such as riboflavin, niacin, and pantothenic acid [3]. The consumption of 100 g of mushrooms provide 22 calories. Oyster mushrooms are common in South Asian countries. They are used to make oyster sauce in Chinese cuisine. The cremini mushroom is also known as the baby Bella mushroom. The portobello mushroom is mainly used for highly woody flavours and has immunomodulatory properties [4]. Aromatic shiitake mushrooms in Italian foods have antiviral properties [5]. Maitake mushrooms have immune-protective and anti-tumour properties [6][7]. The pioppino mushroom (*Cyclocybe aegerita*) is a good source of nutrients (amino acids, malic acid, and sugars) and has anticancer, antifungal, and antiviral properties [8][9].

Mushrooms are used as food and nutraceuticals. They are essential nutrient supplements that play a vital role in health and illnesses. They have low polyunsaturated fat. Therefore, eating mushrooms helps to reduce weight, as a low fat, low glucose, and high mannitol diet can prevent diabetes [10]. Mushrooms also have low sodium and no cholesterol, which prevents hypertension [11]. Mushrooms have high levels of antioxidants. Few researchers have reported their preventive effect against cancer [12][13]. Mushrooms possess antioxidant properties, which aids in the antioxidant defence mechanisms of cells [14]. They have anti-inflammatory properties and reduce the risk of obesity-related dyslipidaemia and hypertension [4][5][15][16][17][18][19][20][21][22][23][24][25]. Mushroom consumption on a

regular basis is useful in curing metabolic disorders that include obesity. Therefore, they could be nutraceuticals of choice in the future for anti-obesity treatment. *P. ostreatus*, frequently called the oyster mushroom, is one of the world's most widely consumed mushrooms after white button mushrooms (*A. bisporus*). *P. ostreatus* is especially significant since it can colonise and make use of a broad range of lignocellulosic substrates from natural deposits. It grows more rapidly than other edible mushrooms. In addition, *P. ostreatus* contains bioactive substances, including β-glucans, which aid in cardiometabolic health [26][27]. *P. ostreatus* has two-fold more β-glucan content compared to *A. bisporus*. They are nutritional fibres that have gained popularity due to their ability to reduce insulin obstruction, hypertension, dyslipidaemia, and obesity. β-glucans are exceptionally good supplements for human gastrointestinal health, and their fermentation is believed to contribute to the wellbeing of the intestine. These effects have been widely reported in studies with oat and grain β-glucans. Mevinolin, also known as lovastatin, has an inhibitory effect on 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase and is also involved in decreasing cholesterol synthesis. In addition, in vitro digestion of *P. ostreatus* produces bioactive peptides that inhibit angiotensin-converting enzymes [28]. *P. ostreatus* contains abundant phenolic compounds which may be involved in lowering the blood pressure [29][30]. *P. ostreatus* has been used in animal studies and showed hypoglycaemic, hypolipidemic, and antioxidant effects. Animals consuming *P. ostreatus* exhibited reduced food intake and weight gain, suggesting the anti-obesogenic potential of this edible mushroom [29][30][31][32][33][34].

Ergosterol peroxide is a compound found in mushrooms that decreases the accumulation of fatty acids in 3T3-L1 cells (**Figure 1**) [35]. This compound inhibits the mRNA upregulation of sterol regulatory element binding protein-1c (SREBP-1c). SREBP-1c is a sterol response limiting protein that regulates the response of sterol in the body. In addition, ergosterol peroxide treatment inhibits the expression of unsaturated fat synthase, unsaturated fat translocase, and acetyl-coenzyme A carboxylase involved in the synthesis and transportation of long-chain unsaturated fatty acids. Since it aids in the prevention of obesity and related metabolic conditions, these reports suggest that ergosterol peroxide obtained from *G. lucidum* might be a potential drug for anti-obesity treatment [35]. AMP-activated protein kinase (AMPK) is a key regulator of homeostasis. Increased AMPK activity showed antihyperglycemic and anti-hyperinsulinemic effects which resulted in reduced obesity in mice. Consumption of *H. erinaceus* (a mushroom) powder reduced total plasma cholesterol and leptin levels in mice that were fed a diet containing the amount of fat tissue [36].

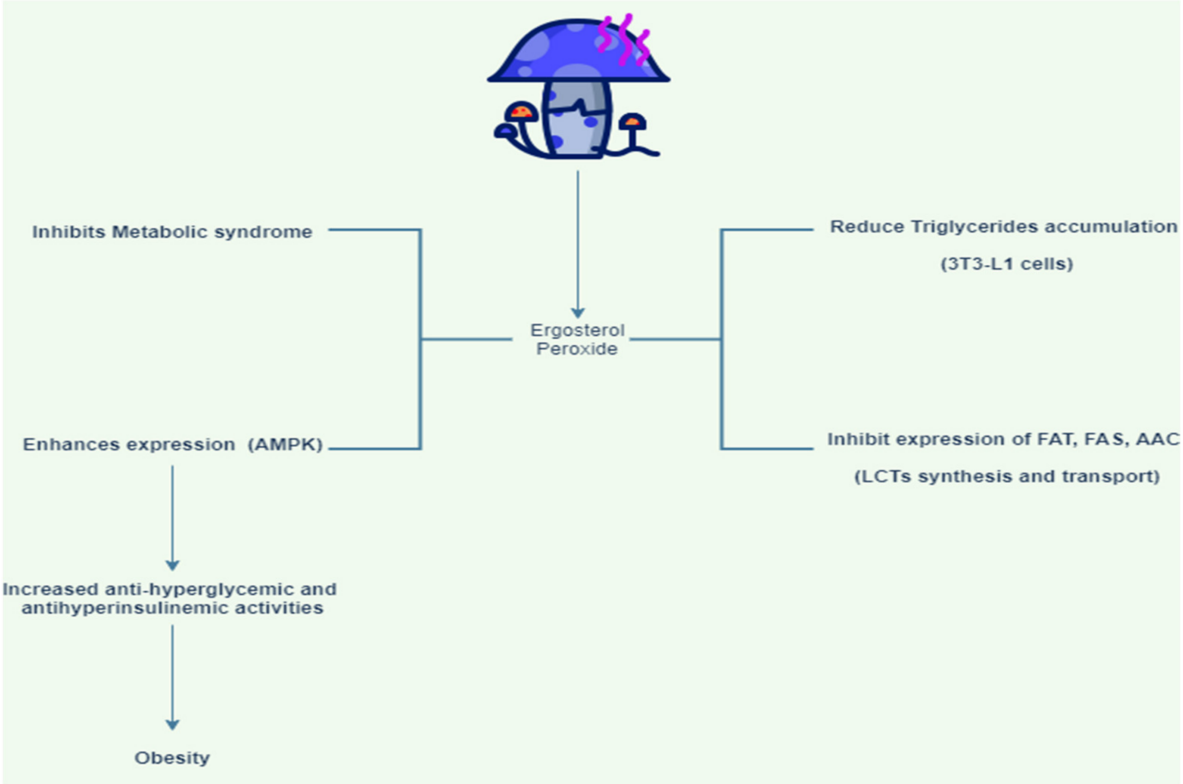

Figure 1. Pharmacological effects of ergosterol peroxide derived from mushrooms on obesity [35]. Ergosterol shows anti-obesity effect by reducing triglycerides accumulation, inhibiting expression of FAT, FAS, AAC, inhibiting metabolic syndrome, enhancing AMPK expression, increasing antihyperglycemic, and anti-hyperinsulinemic activities.

G. lucidum has anti-diabetic properties and has been used in conventional Chinese medicine. In mice following a high-fat diet (HFD), administration of water concentrate of *G. lucidum* mycelium (WEGL) reduced bodyweight, irritation, and insulin obstruction [37]. Along with reducing HFD-induced gut dysbiosis (as seen by lower Firmicutes-to-Bacteroidetes ratio and increased abundance of endotoxin producing proteobacteria), WEGL administration alleviates metabolic endotoxemia [38]. The weight-reducing and microbiota-regulatory effects can be passed on from WEGL-treated mice to HFD-administered ones by faecal exchange. In addition, high molecular weight polysaccharides (>300 kDa) present in the WEGL have shown anti-obesity and microbiota-regulating properties. *G. lucidum* and its high atomic weight polysaccharides can be used as prebiotics in overweight individuals to treat gut dysbiosis and metabolic disorders [37].

Pleurotus citrinopileatus is another potential source of bioactive mixtures and therefore, can be used in anti-obesity treatment [39][40][41]. One study assessed the anti-obesity and hypolipidemic effects of *P. citrinopileatus* water extract (PWE) in high-fat diet-induced obese (DIO) C57BL/6J mice. They were administered with PWE in gradually increasing concentrations (400 to 800 mg/kg of body weight, independently) along with a high-fat diet for 12 weeks [42]. Within 12 weeks, the weight gain, fat build-up, and food utilisation of DIO mice were drastically reduced in mice administered with PWE. PWE also decreased fatty acid, cholesterol, and low-density lipoprotein levels in the blood, simultaneously increasing the activity of aspartate transaminase, non-esterified unsaturated fats, creatinine levels,

and high-density lipoprotein levels. Moreover, PWE also enhanced glucose tolerance in HFD mice and showed a high potential for managing obesity and other metabolic diseases [42].

2. Effect of Mushroom Consumption on Gut Microbiota

The beneficial effects of edible mushrooms and their polysaccharides on the gut microbiota, which are closely linked with the body weight, are currently a major focus in the field. A study in mice reported that administering the concentrates of *G. lucidum* reduced the body weight by modifying the microbiota, suggesting that mushrooms might be used as a potential probiotic for weight reduction [37]. The effect of HFD on gut microflora is more pronounced than the effect on energy balance. HFD-induced changes in the gut microbiota have been shown to reduce Firmicutes to Bacteroides ratio, which is related to high energy accumulation, fat storage, and intestinal homeostasis over time. Through the provocative rundown and platelet markers, obesity negatively affects the immunity. Several studies have examined the anti-obesity effects of polysaccharides from various mushrooms in vitro and in vivo [43][44][45]. Polysaccharides from *Coriolus versicolor* initiated an immunomodulatory effect in mice splenocytes through the MAPK-NF-B pathway [46]. A polysaccharide from *Tremella fuciformis* hindered the differentiation of 3T3-L1 adipocytes by reducing the mRNA expression, suggesting that this polysaccharide could be a potential prebiotic for obesity [47]. Cure of adipocytes with *G. lucidum* diminished adipogenic record factor articulation, which increases glucose and lipid transport and activates AMPK pathway, suggesting its potential as an anti-obesity drug [48].

Being overweight could cause several other illnesses and result in a reduced lifespan. A recent study suggests that changes in the gut microbiota are associated with obesity and other related metabolic syndromes [49][50][51]. The gut microbiota comprises trillions of microorganisms that perform several functions, including nutrient metabolism, maintaining the gastrointestinal cells, modulating the immune system, protecting against the invasion of pathogens, and balancing the endotoxins. The gut microbiota generate energy from food and can cause overweight and type 2 diabetes mellitus (T2DM). It has been observed that in overweight mice, the gut microbiota draws out more energy from food than lean mice [52]. In healthy people, vancomycin treatment for one week modifies the gut microbiota, which results in reduced insulin sensitivity [53]. Additionally, the transfer of gut microbiota of any lean person to an overweight person leads to the development of insulin sensitivity in the recipient. These results suggest that changes in gut microbiota could cause obesity and T2DM.

In HFD animals, the levels of proteins that play a role in maintaining tight junctions of the intestine are lower than those in chow-fed animals. Administration of *G. lucidum* extract could recover the levels of those proteins, which resulted in the maintenance of the integrity of the intestine and prevention of the translocation of pro-inflammatory endotoxins from gut bacteria to blood (for example, lipopolysaccharides) [37]. Using a mouse obese model, it has been observed that feeding of high-fat diet for eight weeks increased the body weight, liver weight, fat accumulation, and lipid deposition in hepatocytes and adipocytes compared to the control group that were fed with chow. Supplementation with the water extract of *G. lucidum* reduced the weight gain and accumulation of fats in HFD mice. *G. lucidum* also improved glucose tolerance and insulin sensitivity. Compounds in *G. lucidum* that reduce obesity are high molecular weight polysaccharides (greater than 300 kDa). Fungal polysaccharides cannot

be digested in the stomach or small intestine. However, the large intestine can digest them and produces short-chain fatty acids, consequently secreting GLP-1. GLP-1 and short-chain fatty acids ultimately enter the blood and affect the brain, muscles, adipose tissues, and liver. Additionally, GLP-1 reduces gastric emptying and thereby, the appetite. It also reduces the deposition of fats, resistance to insulin, and inflammation. It also upregulates the proliferation and downregulates apoptosis in β-cells [37]. This suggests that *Escherichia coli* in the large intestine releases proteins that enhance or aid in the production of GLP-1 and peptide YY, which increases satiety [44]. These results indicate that the water extract of *G. lucidum* could be a potential prebiotic agent that can be used for the treatment of obesity and related complications [37]. Button mushrooms (*A. bisporus*) and *L. edodes* contain several polysaccharides, indicating their potential to stimulate the growth of beneficial bacteria in the gut.

Hirsutella sinensis is the asexual form of *Ophiocordyceps sinensis*. It modifies the composition of the gut microbiota and is beneficial in reducing obesity, inflammation, and diabetes in HFD mice. **Table 1** presents the effects of various mushrooms on gut microbiota.

Table 1. Effect of various mushrooms on gut microbiota.

Name of Mushroom	Effect on Gut Microbiota	References
Pleurotus eryngii	*P. eryngii* polysaccharides altered the abundance of SCFA producing gut bacteria	[54]
Pleurotus sajor-caju	Growth of SCFA producing bacteria was reduced, and *E.Shigella* was decreased by *Pleurotus sajor-caju.*	[48]
Flammulina velutipes	increase in lactic acid-producing bacteria (*Lactobacillus, Lactococcus, and Streptococcus*) and SCFA-producing bacteria (*Allobaculum, Bifidobacterium, and Ruminococcus*)	[55]
Hypsizygus marmoreus		
Lentinusedodes		
Grifola frondosa		
Pleurotus eryngii		
Ganoderma lucidum	*G. lucidum* enhanced SCFAs producing bacteria and abridged sulfate-reducing bacteria in a time-dependent manner	[56]
Lentinula edodes	LESDF-3 was found to stimulate the synthesisof Bacteroides	[57]
Bulgaria inquinans	increase of *Faecalibaculum* and Parabacteroides abundance and the decrease of *Allobaculum*, *Candidatus_Saccharimonas,* and *Rikenella* abundance at the genus level	[58]
Ganoderma lucidum	There was an increase in *Bacteroides/Firmicutes ratio, Clostridium clusters IV, XVIII,*	[37]

Name of Mushroom	Effect on Gut Microbiota	References
	XIVa (*Roseburia* spp.), *Eubacterium* spp.) SCFAs production bacteria, reduction in *Oscillibacter* spp. and *E. fergusonii*.	
	Increase in *Alloprevotella, Barnesiella, Parabacteroides, Bacteroides, Bacteroidales S24-7 and Alistipe.* Decrease in *Blautia, Roseburia, and Enterorhabdus.*	[59]
	Increase in *Blautia, Bacteroides Dehalobacterium,* and *Parabacteroides,* *Decrease in Proteus, Aerococcus, Ruminococcus, and Corynebactrium.*	[60]
	Increase in *Alloprevotella, Prevotella, Ruminococcus and, Alistipes, Peptococcaceae, Alloprevotella, and Defluviitalea,;* Decrease in *Turicibacter, Clostridium XVIII and Phascolarctobacterium*.	[61]
Grifola frondosa	Increase in *Akkermansia muciniphila, Bacteroidetes/Firmicutes, Porphyromonas gingivalis, Lactobacillus acidophilus, Roseburia intestinalis, Tannerella forsythia, and Bacteroides acidifaciens.*	[60]
	Increase in Barnesiella Helicobater, Intestinimonas, Defluvitalea, Flavonifractor and Paraprevotella and Ruminococcus. *Decrease in Butyricicoccus, Clostridium-XVI, and Turicibacter.*	[62]
	Increase in Alistipes. *Decrease in Streptococcus, Enterococcus, Staphlococcus, and Aerococcus.*	[63]
	An increase in Bacteroidetes/Firmicutes ratio increased the abundance of Oscillibacter, Defluvitalea, and Barnesiella.	[64]
	Increase in Intestinimonas and Butyricimonas. *Decrease in Turicibacter and Clostridium XVIII.*	[65]
Phellinus linteus	Increase in *Lachnospiraceae-NK4A136, Roseburia, Prevotella Lachnospiraceae-UCG-006, Anaerotruncus, Blautia, Eubacterium_xylanophilum, Ruminiclostridium-9, and Oscillibacter.*	[66]
Coriolus versicolor	Increase in *Akkermansia muciniphila*	[67]
Hericium erinaceus	Increase *in Bifidobacterium, Coprococcus, Desulfovibrio, Lactobacillus, Parabacteroides, Prevotella; Decrease in Corynebacterium, Dorea, Roseburia, Ruminococcus, Staphylococcus, Sutterella*	[68]

Name of Mushroom	Effect on Gut Microbiota	References
Ganoderma lucidum	Increase in *Firmicutes, Proteobacteria (Helicobacter), Rikenella;* Decrease in *Acinetobacter, Actinobacteria (Arthrobacter, Corynebacterium), Bacteroidetes (Bacteroides, Parabacteroides, Prevotella), Blautia, Brevundimonas, Clostridium, Coprobacillus, Cyanobacteria, Facklamia, Jeotgalicoccus, Sporosarcina, Staphylococcus, Streptococcus*	[69]
*Boletus edulis, Boletus pinophilus, Boletus aureus (*Porcini*), Armillaria mellea(Honey fungus), Lactarius piperatus (blancaccio), Pleurotus eryngii (King oyster)*	Increase in *Bifidobacterium* and *Lactobacillus* genera	[70]
*Cyclocybe cylindracea (*poplar mushroom*), Hericium erinaceus, Pleurotus eryngii, Pleurotus ostreatus (*Oyster mushroom*)*	Increase in *Bifidobacterium spp. Faecalibacterium prausnitzii (Ruminococcaceae), Eubacterium rectale/Roseburia* spp.	[71]
*Flammulina velutipes (*Enoki*), Hypsizygus marmoreus, (*White beech mushroom*), Lentinula edodes (*Shiitake*), Grifola frondosa, (*Maitake*) Pleurotus eryngii* [73]	Increase in *Allobaculum, Bifidobacterium, Ruminococcus, Lactobacillus, Lactococcus, Streptococcus* [72]	[55]

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of mushroom (*G. lucidum*)- 100 mg/kg in the low-fat diet group, (3) high dose of mushroom (*G. lucidum*)- 300 mg/kg in the low-fat diet group, (4) high-fat diet control group, (5) low dose of mushroom (*G. lucidum*)- 100 mg/kg in the high-fat diet group, (6) high dose of mushroom (*G. lucidum*)- 300 mg/kg in the high-fat diet group. Mice in each group were divided into two cages, with three mice in each cage. The temperature was maintained at 25–28 °C. *G. lucidum* was administered once a day to each mouse for 12 weeks, and weight and food intake were monitored regularly. Weight was significantly reduced in the low-fat diet group [74].

4. Recommendations and Implications for the Future

Different clinical trials have been conducted on mushrooms in various forms and their beneficial effects on health have been analysed. They include fresh, cooked, and powdered forms. Herein concluded in vitro and in vivo studied on the anti-obesity effects of edible mushrooms by modulating gut microflora. The findings of the clinical trials suggest that edible mushrooms can be used as alternative to vegetables; they contain several bioactive compounds and could be used as nutraceuticals. They also contain essential nutrients such as vitamins and minerals and have low sodium and cholesterol contents. Therefore, it is an excellent alternative food source for patients with hypertension. They also contain trace elements such as selenium which aids in improving human health. Therefore, edible mushrooms are potential candidates for preventing obesity and several other chronic ailments.

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