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Abstract

Apposite energy is required for body activity. Energy is derived from the oxidation of various biomolecules like carbohydrates, lipids, and proteins. These bio-molecules in the proper amount are essential for the structural and functional activities of any living being. Certain vitamins and enzymes are also needed for the maintenance of biochemical processes. Our daily food is the major source of these biomolecules. From the last few decades, researchers have placed giant effort into searching for a food material that can provide nearly all the essential components required to maintain the energy need and consequently, balancing the body’s homeostasis. Mushrooms have the potential to address the above-raised issues. Besides their pleasant flavor and culinary value, mushrooms are an important source of biomolecules that include large macromolecules (protein, carbohydrate, lipid, and nucleic acid) as well as small molecules (primary metabolites, secondary metabolites, and natural products). This chapter discusses the bioactive compounds in edible mushroom and their activities.

Keywords: mushroom, species, bioactive components, anticancer, antidiabetic

1. Introduction

Mushrooms are a group of fungi with a distinctive fruiting body that can be either epigeous or hypogenous and large enough to be seen with the naked eye and picked by hand [1]. They are either saprophytic, parasitic or mycorrhizal. Out of these three categories, the majority of them are saprophytic and they play an important role in the biodegradation and bioremediation of recalcitrant substances [2]. Notably, there are about 14,000 mushroom species that have been reported to date and a further 126,000 species more are yet to be discovered [3]. The majority of mushroom species are edible and over 400 species are poisonous [4]. Out of these more than 2000 edible species, 5–6 species are grown on a mass scale, 40 species are produced commercially and 80 species are cultivated experimentally (Figure 1). Edible mushrooms have very minimal calorie value as they contain less amounts fat and carbohydrate and are also cholesterol-free. In addition, edible mushrooms are rich in other vital nutrients like niacin, vitamin D, proteins, selenium, potassium, riboflavin. Mushrooms also contain a significant amount of fiber which helps in the appropriate digestion of food (Table 1) [1]. The active
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compounds in common mushrooms and the nutritional value of these mushrooms and their activities were showed in Table 2 and Figure 2.

Oxidative stress (OS) is one of the major causes of any disease such as neurodegenerative (NDs), cardiovascular (CDs) and reproductive diseases (RDs), and diabetes [17]. Inflammation is the progressive result of the severe burden of OS. Any biomolecules with anti-oxidative and anti-inflammatory activity show a better response in the treatment of the above diseases [18]. The polyphenols, terpenoids, alkaloids, and other important biomolecules found in edible mushrooms prove their efficacy in therapeutics with minimal side effects [19]. Mushrooms and their biomolecules are known to have been used to cure diabetes by Indian and Chinese patents from ancient times [20]. The active components in these mushroom species; 

Ganoderma lucidum, Lentinus edodes, Pleurotus ostreatus, Pleurotus sajor-caju, Grifola frondosa, Poria cocos,

have exhibited potent anti-diabetic activity [21]. For example, the polysaccharides derived from Pleurotus ostreatus exhibits potent antidiabetic activity in the streptozotocin-persuaded Diabetic Rat model [22]. β-glucans and several other biomolecules present in edible mushrooms show strong anti-diabetic activity [23]. Recently the edible oyster mushroom Pleurotus fossulatus aqueous extract improved liver and kidney function in the streptozotocin-induced diabetic rats, besides reducing blood glucose levels, total cholesterol (TC), triglyceride (TG), and high-density lipoprotein (HDL) [24].

Disorders related to the heart and blood vessels are grouped into cardiovascular diseases (CVDs) [25]. Mushrooms and their bioactive components can prevent CVDs [26]. Being functional foods, edible mushrooms contain a significant number of bioactive compounds that show strong potential in the treatment of CVDs [27]. The antioxidant and anti-inflammatory biomolecules present in mushrooms reduce the atherosclerosis risk which is directly related to CVDs [28]. Diseases related to the reproductive systems are very common now a day. Abnormalities in the endocrine system are mainly responsible for the progression of reproductive diseases (RDs).
<table>
<thead>
<tr>
<th>Mushroom</th>
<th>Medicinal value</th>
<th>Protein (g/100 g)</th>
<th>Carbo (g/100 g)</th>
<th>Lipid (g/100 g)</th>
<th>Fibers (g/100 g)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clitocybe ne</td>
<td>Anticancer</td>
<td>8.11–12.18</td>
<td>64.47–77.12</td>
<td>1.14–2.04</td>
<td>—</td>
<td>[5]</td>
</tr>
<tr>
<td>Cordyceps</td>
<td>Anti-asthma</td>
<td>21.9</td>
<td>24.2</td>
<td>8.2</td>
<td>—</td>
<td>[6]</td>
</tr>
<tr>
<td>Hericium</td>
<td>Antihypercholesterolic</td>
<td>22.3</td>
<td>57.0</td>
<td>3.5</td>
<td>7.8</td>
<td>[7]</td>
</tr>
<tr>
<td>Trametes</td>
<td>Antidiabetic</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>[8]</td>
</tr>
<tr>
<td>Lentinus</td>
<td>Immunomodulator</td>
<td>26.3</td>
<td>65.1</td>
<td>2.3</td>
<td>—</td>
<td>[8]</td>
</tr>
<tr>
<td>Hypsizygus</td>
<td>Anticancer</td>
<td>19.6–21.0</td>
<td>65–68.5</td>
<td>4.0–5.6</td>
<td>—</td>
<td>[8]</td>
</tr>
<tr>
<td>Flammulina</td>
<td>Immunomodulator, anti-asthma, Antihypercholesterolic</td>
<td>19.3–17.8</td>
<td>86–70.8</td>
<td>1.8–2.9</td>
<td>—</td>
<td>[9]</td>
</tr>
<tr>
<td>Grifioha</td>
<td>Antidiabetic, anti-arthritis, anti-viral, anti-obesity anticancer, anti- osteoporosis,</td>
<td>21.1</td>
<td>58.8</td>
<td>3.1</td>
<td>10.1</td>
<td>[8, 9]</td>
</tr>
<tr>
<td>Agaricus</td>
<td>Anticancer, Immunomodulator, Hepatoprotective, anti-viral, antimitagenicm Antidiabetic, Antihypercholesterolic</td>
<td>56.3</td>
<td>37.5</td>
<td>2.7</td>
<td>—</td>
<td>[10]</td>
</tr>
<tr>
<td>Ganoderma</td>
<td>Antiviral, antithrombotic, Hepatoprotective, anti- osteoporosis, anticancer, Hypoglycemic, anti-aging, Antiallergenic, Hypocholesterolic, Antimitagenic</td>
<td>13.3</td>
<td>82.3</td>
<td>3.0</td>
<td>—</td>
<td>[12]</td>
</tr>
<tr>
<td>Clitocybena</td>
<td>Antihypercholesterolic</td>
<td>18.1–30.5</td>
<td>31.1–52.3</td>
<td>2–6.6</td>
<td>30.1</td>
<td>[14]</td>
</tr>
<tr>
<td>Sarcodona</td>
<td>Anti-aging</td>
<td>12</td>
<td>64.6</td>
<td>2.8</td>
<td>5.1</td>
<td>[15, 16]</td>
</tr>
<tr>
<td>Leucopaxillus</td>
<td>Anticancer</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>[15, 16]</td>
</tr>
<tr>
<td>Tremella</td>
<td>Anticancer, Antidiabetic</td>
<td>40.6</td>
<td>94.8</td>
<td>0.2</td>
<td>1.4</td>
<td>[15, 16]</td>
</tr>
</tbody>
</table>

Table 1. Nutritional values of edible mushrooms and their activities.
<table>
<thead>
<tr>
<th>Mushroom</th>
<th>Common name</th>
<th>Bioactive compounds/ingredients</th>
<th>Health benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Tremella fuciformis</em></td>
<td>Snow Mushroom</td>
<td>propanediol, glycerin, arganiaxispinosa (argan) kernel oil, seawater, sodium hyaluronate, sodium PCA, sodium lactate, 3-O-ethyl ascorbic acid, pentylen glycol, caprylyl glycol, N-prolylalmositol tripeptide-96 acetate, hydroxyethylcellulose, polyglyceryl-4 caprate, diheptyl succinate, capryloylglycerin</td>
<td>Skin health</td>
</tr>
<tr>
<td><em>Agaricus blazei</em></td>
<td>Orivedavr</td>
<td>&gt;27% beta-glucan</td>
<td>Anti-hyperglycemic,</td>
</tr>
<tr>
<td><em>Agaricus blazei</em></td>
<td>Murrill</td>
<td>&gt;0.90% polyphenols</td>
<td>antihypercholestrmic</td>
</tr>
<tr>
<td><em>Ganoderma lucidum</em></td>
<td>Reishi Elixir Mix</td>
<td>Organic Reishi mushroom extract (1500 mg), 18 mg of vitamin C, tulsi, organic mint</td>
<td>Support the body’s sleep cycles as well as</td>
</tr>
<tr>
<td><em>L. edodes</em></td>
<td>Shiitake Goldcapsules</td>
<td>15% Lentinan 60% Polysaccharides</td>
<td>support occasional stress</td>
</tr>
<tr>
<td><em>Ganoderma lucidum</em></td>
<td>ReishiMax capsules</td>
<td>13% Polysaccharides (beta-1,3-glucans) and 6% triterpenes (ganoderic acids and others) nucleosides, fatty acids (oleic acid), and amino acids, Gelatin, Stearic acid</td>
<td>Antidiabetic</td>
</tr>
<tr>
<td><em>Cordyceps sinensis</em></td>
<td>Cordyceps extractcapsules</td>
<td>Amino acids, including L-tryptophan, ergosterol, polysaccharides (β-glucans)</td>
<td>Control blood glucose levels</td>
</tr>
<tr>
<td><em>Ganoderma lucidum</em></td>
<td>GANOHERB Reishi</td>
<td>Organic ganoderma spore powder and extract - balanced blood sugar level diabetes (non-GMO &amp; gluten-free), 100% natural, 400 mg/capsules</td>
<td>Supports healthy glucose metabolism, blood purification, and healthy blood sugar levels</td>
</tr>
<tr>
<td><em>Ganoderma lucidum</em></td>
<td>Pure red reishicapsules</td>
<td>&gt;40% triterpenes</td>
<td>Boost immune system And antidiabetic attribute Levels of blood sugar balanced</td>
</tr>
<tr>
<td><em>Pleurotus eryngii</em></td>
<td>GlucoSANO-Diabetes,</td>
<td>Agaricus blazei, ErgoD2VR</td>
<td></td>
</tr>
<tr>
<td><em>Agaricus blazei</em></td>
<td>Health Formula</td>
<td>(enriched pleurotuseryngii),</td>
<td></td>
</tr>
<tr>
<td><em>Hypsicogus</em></td>
<td>tesellates,</td>
<td>white beech, brown beech,</td>
<td></td>
</tr>
<tr>
<td><em>Cordyceps militaris</em></td>
<td></td>
<td>D2 (ergocalciferol), vegetable capsules, myceliated whole oats, rice, flour, silica</td>
<td></td>
</tr>
</tbody>
</table>
Mushroom; Chemistry, Bioactive Components, and Application
DOI: http://dx.doi.org/10.5772/intechopen.104182

Several RDs like reproductive tract infections, prostate cancer, breast cancer, ovarian cancer, etc. are most common in different populations [29]. Mushrooms and their bioactive molecules show anti-tumor activity which can be immensely beneficial in the treatment of different RDs. RDs commonly lead to different types of cancer and several biomolecules present in edible mushrooms can prevent metastasis toward cancer [1, 26]. Neurodegenerative diseases (NDs) like Huntington’s disease (HD), Alzheimer’s disease (AD), and Parkinson’s disease (PD), etc. have been effectively treated by edible mushrooms through their bioactive components [30]. Progression of the NDs is the main cause of death which can be significantly inhibited by the biomolecules present in edible mushrooms [31]. Polyphenols, alkaloids, and several other biomolecules in edible mushrooms prove their efficacy in the treatment of different neurodegenerative diseases [32]. Similarly, a different form of cancer can also be treated by the biomolecules found in edible mushrooms [23]. This review discusses the role of mushrooms and their biomolecules to be utilized for the treatment of some most common diseases like CVDs, RDs, NDs, diabetes, and the different forms of cancer.

<table>
<thead>
<tr>
<th>Mushroom</th>
<th>Common name</th>
<th>Bioactive compounds/ingredients</th>
<th>Health benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Ganoderma lucidum</em></td>
<td>GanoUltraGanoSuper</td>
<td>Mycelium, primordia, fruitbodies, and extracellular compounds</td>
<td>Anticancerous, anti-stress, antidiabetic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>vegetarian capsule</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(pullulan), 100% organic</td>
<td></td>
</tr>
<tr>
<td><em>Lentinus edodes, Grifola frondosa</em></td>
<td>Agarikon.1</td>
<td>750 mg of high-quality soluble</td>
<td>Anticancer attributes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(growing substrate)</td>
<td></td>
</tr>
<tr>
<td><em>Ganoderma lucidum</em></td>
<td></td>
<td>polysaccharides per table</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(growing substrate)</td>
<td></td>
</tr>
<tr>
<td><em>Pleurotus ostreatus</em> and <em>Agaricus blazei</em></td>
<td></td>
<td>Fruiting body extract, AmylenoneVR, Standardized to contain amylobase including hericenones 1950 mg</td>
<td>Brain health</td>
</tr>
<tr>
<td><em>Hericium erinaceus</em></td>
<td>Amyloban 3399 super lion's mane (tablets)</td>
<td>Extract, polysaccharides</td>
<td>Boost immunity, antidiabetic capsules</td>
</tr>
<tr>
<td></td>
<td></td>
<td>powdered extract, selenium, copper, B vitamins, vitamin D, as well as prebiotics, polysaccharides</td>
<td>Stress relief, liver &amp; brain health, concentrations/focus, brain &amp; immune health, endurance, stamina &amp; immune health, blood sugar &amp; blood pressure control</td>
</tr>
<tr>
<td><em>Ganoderma lucidum</em></td>
<td>E &amp; Rose Wellness’ Magic Milk</td>
<td>Powdered extract, selenium, copper, B vitamins, vitamin D, as well as prebiotics, polysaccharides</td>
<td>Stress relief, liver &amp; brain health, concentrations/focus, brain &amp; immune health, endurance, stamina &amp; immune health, blood sugar &amp; blood pressure control</td>
</tr>
<tr>
<td><em>Cordyceps sinensis, Inonotus obliquus, Grifola frondosa</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Hericium erinaceus</em></td>
<td></td>
<td>što</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Bioactive components in common mushroom.

Several RDs like reproductive tract infections, prostate cancer, breast cancer, ovarian cancer, etc. are most common in different populations [29]. Mushrooms and their bioactive molecules show anti-tumor activity which can be immensely beneficial in the treatment of different RDs. RDs commonly lead to different types of cancer and several biomolecules present in edible mushrooms can prevent metastasis toward cancer [1, 26]. Neurodegenerative diseases (NDs) like Huntington’s disease (HD), Alzheimer’s disease (AD), and Parkinson’s disease (PD), etc. have been effectively treated by edible mushrooms through their bioactive components [30]. Progression of the NDs is the main cause of death which can be significantly inhibited by the biomolecules present in edible mushrooms [31]. Polyphenols, alkaloids, and several other biomolecules in edible mushrooms prove their efficacy in the treatment of different neurodegenerative diseases [32]. Similarly, a different form of cancer can also be treated by the biomolecules found in edible mushrooms [23]. This review discusses the role of mushrooms and their biomolecules to be utilized for the treatment of some most common diseases like CVDs, RDs, NDs, diabetes, and the different forms of cancer.
2. Mushroom active compounds against cardiovascular diseases (CVDs)

Cardio Vascular Diseases (CVDs) are a category of heart and blood diseases, including coronary heart disease, cerebrovascular disease, rheumatic heart disease, and other diseases. CVDs are the leading cause of death worldwide. In the past few decades, researchers have shown the use of mushrooms and their bioactive compounds as therapeutic agents for CVDs. In 2010, Guillamon et al. reported the potentially positive effects of mushroom consumption on risk markers for CVDs and identified some potential bioactive compounds responsible for their therapeutic activity. Several studies have shown the influence of mushroom intake on some metabolic markers (total low-density lipoproteins (LDL), high-density lipoproteins (HDL): cholesterol, fasting triacylglycerol, homocysteine, blood pressure) which could potentially reduce the risk of cardiovascular disease. Relevant nutritional aspects of mushrooms include high fiber content, low-fat content, and low trans isomers of unsaturated fatty acids. Mushrooms also have low sodium concentrations and other significant components, such as eritadenine, phenolic compounds, sterols (such as ergosterol), chitosan, triterpenes, etc., which are considered to be potential agents for some previously healthy properties. The intake of mushrooms has a cholesterol-lowering or hypocholesterolemic effect which has been elucidated by different mechanisms, such as lowering of very-low-density lipoproteins (VLDL), improving lipid metabolism, inhibiting the activity of HMG-CoA reductase and therefore, prevents the development of atherosclerosis (Figure 3). Antioxidants and anti-inflammatory compounds found in mushrooms also reduce the risk of atherosclerosis [26]. *Ganoderma lucidum* play a curricular role in mitigating the toxicity of Adriamycin, where, Adriamycin treatment raised the number of marker enzymes found in serum including aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatine kinase (CK), and lactate dehydrogenase (LDH). In order to increase lipid peroxidation (LPO), adriamycin significantly decreased antioxidant
enzymes in the cardiac tissues, including glutathione-S-transferase (GST), glutathione peroxidase (GPx), catalase (CAT), and superoxide dismutase (SOD). Adriamycin has also been shown to considerably lower glutathione (GSH) levels. This study has shown that *G. Lucidum* extracts have significant antioxidant properties and protect the heart from the free radical-mediated toxicity of adriamycin. *G. Lucidum* extract retrieves free radicals and also increases the levels of glutathione and antioxidant enzymes [33]. Important findings show that the edible mushrooms could be used as possible sources of novel hypocholesterolemia agents. Few studies have identified the levels of sterols, β-glucans, and HMGCoA-red as inhibitors in mushrooms. Ergosterol was the most plentiful sterol recorded in all the samples examined, apart from *G. lucidum*, which had identical levels of ergosterol and ergosta-7,22-dienol. *P. ostreatus*, *G. lucidum*, *A. aegerita*, and *L. edodes* mushrooms had high levels of β-glucan content, whereas *A. Blazeii*, *A. Bisporus*, and *L. procera* had low levels of β-glucan content. Because of the presence of lovastatin, a statin found in mycelia broths and its fruiting bodies, the oyster mushroom (*Pleurotus* spp.) reduces blood cholesterol levels. As a result, a mixture of bioactive supplements improves the nutritional ability of different mushrooms to lower serum cholesterol levels [31]. A study has assessed the effect of different mushroom-like *Lentinus edodes*, *Auricularia polytricha*, and *Flammulina velutipes* preparations on the levels of cholesterol in the rats which showed that the preparation of dried mushrooms significantly reduced plasma cholesterol levels. Lentinus edodes was more effective, while *Auricularia polytricha* (Jews-ear) and *Flammulina velutipes* were less effective than *L. edodes*, Kohshin. However, ergosterol supplements have caused a marked decrease in hepatic cholesterol levels [34]. A previous study, focusing on the hypolipidemic effects of polysaccharides, isolated from *Pholiota Nameko* (PNPS-1) was conducted on hyperlipidemic Wistar rats. The rats were treated with PNPS-1 at different doses which reduced very-low-density: lipoprotein/low-density lipoprotein cholesterol, triacylglycerol, phospholipids, and increased the atherogenic index and high-density lipoprotein cholesterol in the serum. PNPS-1 also improved pathological changes in the coronary arteries of hyperlipidemic rats.
These results suggest that PNPS-1 significantly reduces the development of hyperlipidemia and could be used as a potential therapeutic agent for CVD [35]. Antiatherogenic and antiatherosclerotic effects of different mushrooms belonging to the genera: Armillaria, Agaricus, Boletus, Collybia, Cortinarius, Coriolus, Flammulina, Hirneola, Lentinus, Ganoderma, Lyophyllum, Sarcodon, Pleurotus, Tricholoma, and *Trenella* were detected in human intima aortic culture. The results showed that anti-atherosclerotic, anti-atherogenic, and hypolipidemic effects of certain species of mushrooms allow us to speculate that these edible fungi are beneficial dietary supplements that might be utilized in prophylactics and to a limited extent, in atherosclerotic medicines. Furthermore, the extraction and purification of the active substance from these mushrooms may result in the development of a strong antiatherosclerotic medicine [36]. Among the *Pleurotus* species, *P. ostreatus* was the best candidate for the prevention and treatment of atherosclerosis because it has been shown to contain a large number of antiatherosclerotic agents such as ergothioneine, lovastatin, and chrysin [37].

3. Antidiabetic activity of mushroom biomolecules

Mushrooms are fungi that either grow above or below the ground. These are the macro fungi that can be easily seen with the naked eye. Mushrooms have been used since ancient times by the people of India and China or their medicinal properties. Nowadays many countries are consuming mushrooms for not only their unique flavor but also for their culinary effects. As many studies have revealed that mushrooms are rich sources of: proteins, carbohydrates, vitamins (B1, B2, B12, C, D, and E) and minerals like Mn, Mg, Se, Ca, Na, Cu, K, and Fe [38]. These nutritional factors in mushrooms have made it very efficient to fight diabetes. In vitro and in vivo studies have shown that the extract of mushrooms can reduce the expression of proinflammatory cytokines, induced by lipopolysaccharides which further improved the glucose uptake in skeletal muscle cell lines [39].

One of the most active biomolecules of mushrooms is β-glucans, a polysaccharide that can protect the pancreatic tissue from damage and restore the function of b-cells which helps to lower the blood glucose levels [40]. The low energy, lack of cholesterol and fats, less carbohydrates, and high minerals, proteins and vitamins made mushrooms an ideal food for diabetic patients. The consumption of mushrooms for a few days only can help to manage the low-density lipoproteins, total cholesterol, high-density lipoprotein, triglycerides levels in serum [10]. Besides bioactive molecules, mushrooms are very good in antioxidants activity and are also a good source of dietary fibers and water. Some of the most culinary properties containing mushrooms are *Agaricus bisporus, Agaricus subrufescens, Cordyceps militaris, Cordyceps sinensis, Grifola frondosa, Ganoderma lucidum, Phellinus linteus, Pleurotus flabellatus, Pleurotus citrinopileatus, Pleurotus ostreatus, Poria cocos* [10, 41]. Extracts of *Ganoderma lucidum* contain: polysaccharides, triterpenoids, proteoglycans, and proteins which have been shown to reduce blood glucose levels. The proteoglycans of *G. lucidum* inhibit the tyrosine phosphatase 1B protein in diabetic patients. *G. lucidum* has proven to be very effective in controlling diabetes. Moreover, the triterpenoid from *G. lucidum* inhibits the aldose reductase and a-glucosidase enzymes which are responsible for the elevation of postprandial glucose levels [42]. Polysaccharides from *G. atrum* (PSG-1) increase insulin sensitivity and lower the serum lipid by increasing and decreasing the expression levels of Bcl-2 and Bax, respectively in pancreatic cells [43].
Heteropolysaccharides are one of the bioactive molecules of Pleurotus ostreatus that control diabetes by activating the Glycogen synthase kinase 3 (GSK3) by phosphorylation and facilitating the translocation of glucose transporter type 4 (GLUT4) in streptozotocin-induced diabetic rats [44]. *Lentinula edodes* promote the growth of gut microbiota, which play a very important role to balance the energy in diabetic patients. Another mushroom, *Hirsutella inensis* shows antidiabetic, antiobesogenic effects in high-fat-diet feed-mice by modification of the components of gut microbiota. The polysaccharides and fibers of mushrooms act as prebiotics that helps in the treatment of diabetic patients [45]. Recently, researchers have found the potential effects of mushrooms in diabetic nephropathy conditions. Polysaccharides from *Auricularia auricula* are very helpful in promoting the oxidation of glucose. This polysaccharide protects against diabetic nephropathy by the regulation of creatinine, inflammatory factors, blood urea nitrogen, and urine protein. Polysaccharides isolated from *Flammulina velutipes* provided protection against reactive oxygen species (ROS) and reduced the level of malondialdehyde (MDA) in the kidney. The studies have also revealed that the proteoglycans from *Ganoderma lucidum* can restore kidney function by providing antioxidant activity [46]. According to a study conducted by Chou, Kan, Chang, Peng, Wang, Yu, Cheng, Jhang, Liu and Chuu [47], low molecular weight polysaccharide of *Inonotus obliquus* (LIOP) significantly reduces the expression of NF-κB and Transforming growth factor-beta (TGF-b) in a dose-dependent manner [48]. They find that LIOP treatment can improve glucolipotoxicity induced renal fibrosis in diabetic nephropathy mice. *Hypsizigus marmoreus* have been used to examine its protective effect on the liver, kidney, and pancreas. The spent mushroom compost polysaccharide (SCP), its enzymatic lysates (ESCP), and acid-based hydrolyzed SCP (ASCP) were tested in streptozotocin-induced mice and found that it increased the: catalase, superoxide dismutase, and glutathione peroxidase activity whereas, it reduced the lipid peroxide and malonaldehyde levels [49]. α-glucosidase inhibiting polysaccharide (εPS-F4-1) with triterpenoids had been purified from *Coriolus versicolor*. Another bioactive molecule, MT-α-glucan (polysaccharide) from *Grifola frondosa* increases the expression of Interleukin-2 (IL-2) and prevents the injury of b-cells [50]. Submerged cultured mycelium of *Agaricus brasiliensis* and *G. lucidum* has shown a protective effect on red blood cells (RBCs) in Streptozotocin (STZ)-induced diabetic rats [51].

4. Anticancer activity

Reproductive system diseases are responsible for several types of cancers like: prostate cancer, breast cancer, ovarian cancer, cervical cancer, uterine cancer, colorectal cancer etc. The bioactive compounds present in the mushroom are playing an important role in the treatment of reproductive disease-associated cancers. There are several medicinal mushrooms like *Ganoderma lucidum*, *Trametes versicolor*, *Inonotus obliquus*, *Fomitopsis officinalis*, etc. which are frequently used in the treatment of cancer. Prostate cancer is the third leading cause of cancer deaths in men worldwide and the utmost common male malignancy in several western countries. The incidence rate of prostate cancer is highest in the United States, lower in European countries and lowest in Asia [52]. The common risk factor related to prostate cancer is age, obesity, family history, environmental factors and dietary factors [53]. Retinoblastoma (Rb) and p53 (tumor suppressor gene) play a vital role in the progression of prostate cancer [54]. The anomalous expression
in growth factors and receptors such as: transforming growth factor-a (TGF-a), epidermal growth factor (EGF), transforming growth factor-b (TGF-b), HER-2/neu, and c-erbB-3 oncogenes [41] also lead to the malignant prostate cancer. To combat these problems, natural compounds and fungal metabolites can be used as inhibitors for targeting cancerous cells in certain cancers [55–58]. Ganoderma lucidum belongs to the Ganoderma genus, oriental medicinally mushroom, which have been widely used in Asian countries for centuries to cure different diseases including cancer. Plenty of species of this genus have antiviral, antibacterial, antifungal, anticancer, and immune-stimulating activities [59]. These activities were due to the production of various bioactive compounds present in medicinally mushrooms such as proteins [60–62], terpenes, sterols, and polyphenols, etc. The dried powder of G. lucidum is used as dietary supplements and is also used as a chemotherapeutic agent for cancer therapy. It induced the apoptosis of prostate cancer (PC-3) cells by lowering the expression of NF-jB-mediated Bcl-2 and Bcl-xl expression while the upregulation of the Bax protein [63]. The extracts of G. lucidum suppress the proliferation of cells and induce the G1 cell cycle in prostate cancer and breast cancer cells line [64]. Trametes versicolor, is a medicinal mushroom, belongs to the class Agaricomycetes shows anti-proliferative effects upon hepatocellular carcinoma cells (HCC), prostate cancer (DU145) and human breast cancer (4 T1) [42]. Several studies suggested that in T. versicolor β-glucan-based polysaccharopeptide fraction (PSP) and polysaccharide fraction (PSK) are present which are used as immunotherapeutic anticancer agents [65]. PSP activates cells of the immune system by enhancing the secretion of histamine, chemokines and cytokines such as interleukins (IL-1b and IL-6), TNF-a and prostaglandin E which excites dendrite and T-cell infiltration into tumor and lowers the damaging undesirable effects of chemotherapy [66]. Breast cancer is becoming one of the most common leading causes of mortality among women. The molecular subtypes of breast cancer are identified by gene expression profiles and lead to the identification of biomarkers that may ease the prognosis and treatment of cancer [67]. The molecular and pathological marker for the treatment of breast cancer is based on the presence or absence of progesterone receptors (PR), estrogen receptor (ER), and human epidermal growth factor receptor 2 (HER2) [67]. To overcome this problem, the medicinally mushroom is widely utilized in modern integrative oncology and given to patients regularly. The clinical results suggested that T. versicolor inhibits the human triple-negative breast cancer cells (MDA-MB-231) in the in vitro culture and reduced their growth [68] and is used as a supplement in the treatment of breast cancer. The mushroom Inonotus obliquus, often known as Chaga mushroom, belongs to the Agaricomycetes class and is widely used as traditional medicine for cancer therapy in Korea, China, Japan, and Russia [69]. Scientists illustrated that the water extracts of Chaga mushroom have shown cytotoxic and antimitotic activity on HeLa cells. The polysaccharides from I. obliquus inhibit the migration of cancer cell lines and shows anti-metastatic activities in vitro. The polysaccharide suppressed the NF-jB, PI3K/AKT and MAPKs signaling pathways by blocking activity and the expression of matrix metalloproteinases 2 and 9 (MMP) [70]. The studies confirmed that the Chaga mushroom has Wnt/β-catenin-inhibitory properties due to the presence of one major compound namely inotodiol which suppressed the breast cancer proliferation via the Wnt-dependent signaling pathway in a diabetic rat model [71].

The bioactive compounds present in the Ganoderma species are a viable alternative to fight breast cancer. The aqueous extracts of G. lucidum, G. sinense and
G. tsugae were widely used against breast cancer cells. The data illustrated that the aqueous extract of these species has anti-proliferative activities against MCF-7 cells and MDA-MB-231 cells. However, the aqueous extract of G. tsugae was most effective against MCF-7 cells, although the activity of other Ganoderma species is similar to MDA-MB-231 cells. It also established that the extract did not show any cytotoxic activity against human noncancerous epithelial cells [72]. Several results showed that G. lucidum suppressed the proliferation of MDA-MB-231 cells in a dose and time-dependent manner [64]. The spore powder of G. lucidum also exhibited potent cytotoxic effects in the MDA-MB-468, triple-negative breast cancer cell lines, and SUM-102 cell line and overexpressing the HER2 gene in MDA-MB-435 [73]. Fomitopsis officinalis belongs to the family Polyporaceae and is generally known as ‘Agarikon.’ The fruiting bodies of mushrooms are used as a medicine in Western Europe, North America, and Asian countries for the treatment of gastric cancer, asthma, cough, and pneumonia [74]. Some auspicious evidence illustrated that using fungal extracts can help prevent breast and gastrointestinal cancers. Some studies confirmed antiviral, antibacterial, anticancer, and anti-inflammatory activity of crude extract of F. officinalis in different forms of cancers [75]. In F. officinalis extract, Lanostane-type triterpenoids, was reported which showed promising anticancer activity. Scientists showed that the ethanol extracts of F. officinalis are more effective in comparison with water extract against human breast cancer (MDAMB-231) cells, colon cancer (HCT-116), lung cancer (A549), mouse sarcoma 180 (S-180) and hepatoma (HepG2) cells [75].

Figure 4 shows the therapeutic activity of mushrooms and their biomolecules in the treatment of different forms of cancer. The immune system plays a very contributing role in the progression of tumors toward cancer. Mushroom shows its therapeutic activity by targeting the components of the immune system and also modulates the apoptotic processes. Figure 4 suggests the therapeutic activity of mushrooms by modulating the different components of the immune system and also regulates the apoptotic processes in cancerous cells [76–78].

Figure 4.
Antitumor mechanism of bioactive compounds in medicinal mushroom.
5. Biomolecules of mushrooms in neurodegenerative diseases (NDs)

Bioactive molecules in mushrooms also prevent the progression of different NDs. Motor symptoms linked with Parkinson’s disease (PD) are significantly prevented by a diet rich in mushroom supplements. In addition, the clinical symptoms of PD were also alleviated by mushroom supplements rich in phytochemicals, minerals, and vitamins [79]. Anti-inflammatory and antioxidative activity is exhibited by dietary mushrooms containing significant quantities of carotenoids, polysaccharides, minerals, polyphenols, and vitamins [80]. The two major factors that are responsible for the progression of PD are oxidative stress and neuroinflammation. Thus, the biomolecules present in edible mushrooms offer significant neuroprotection by their antioxidative and anti-inflammatory activity by preventing the progressive degeneration of dopaminergic neurons [79]. One of the major factors responsible for the generation of neuroinflammation in PD is the activation of microglial cells. *Ganoderma lucidum* extract (GLE) inhibited the activation of these microglial cells and ultimately prevented the progressive degeneration of dopaminergic neurons in PD. Tumor necrosis factor alpha (TNF-α) and interleukin-1b (IL-1b) are the examples of some important proinflammatory cytokines whose expression was downregulated by GLE in a dose-dependent manner and can be treated by natural antibiotics reported in [81]. Further progression of PD is prevented by inhibition of these proinflammatory cytokines by GLE. Thus, the treatment of PD, GLE should be utilized as an effective anti-inflammatory medication [82]. For the treatment of PD, niacin-rich food can be very beneficial and offers significant protective activity. Niacin-rich mushroom content offers potential therapeutic efficacy in the treatment of PD [83]. In the rotenone intoxicated model of PD, neuroprotective activity was shown by the *Agaricus blazei* extract (ABE). ABE also improves rotenone-induced non-motor and motor complications in PD. Therefore, for the treatment of PD, ABE might also be utilized as a nutritional supplement [84]. Some herbal plants like *Tinospora cordifolia*, *Withania somnifera*, *Mucuna pruriens* (Mp), and the essential oils also exhibit neuroprotective activity similar to mushrooms in toxin-induced PD mouse models [85–87]. In addition, bioactive components of Mp like Ursolic acid also exhibits potent antioxidative and anti-inflammatory property in toxin-induced PD model [88–90]. Chlorogenic acid also exhibits a similar AntiParkinsonian activity in the mouse model of PD [91]. Similar to PD, in Alzheimer’s disease (AD), nutritional mushroom provides important biomolecules that help to improve the quality of AD patients. Neuroinflammation along with oxidative stress mainly contributes to the pathogenesis of AD. The redox status in the cell of AD is significantly impaired [1]. Mushrooms have all the essential components that restore the normal balance of the redox system in AD models and patients. Proper and accurate functioning of mitochondria is required to maintain energy homeostasis. The synthesis of vital energy equivalents is hampered by abnormal mitochondrial functioning. In the neuroprotective network, inflamasome is an example of a very vital component. In AD, mitochondrial functioning was improved by *Coriolus* and *Hericium*. Normal redox balance was also maintained by these two nutritional mushrooms. Thus, energy homeostasis in AD was maintained by the above-mentioned two mushrooms by their antioxidative and anti-inflammatory properties [92]. One of the best examples of both medicinal and edible mushrooms is the *Hericium erinaceus* (HE). Both in vitro and in vivo model systems show the neuroprotective activity of HE. The aqueous extract of HE rich in a mycelium polysaccharide shows potent anti-apoptotic activity in l-glutamic acid (l-Glu)-induced differentiated PC12 (DPC12) cell lines. The AD mouse model induces by
the combination of AlCl$_3$ with D-galactose. The aqueous extract of HE prevents the further progression of AD by its neuroprotective potential. Behavioral abnormalities were also improved by the aqueous extract of HE in the AD mouse model. In a dosedependent manner, HE is responsible for the enhancement of choline acetyltransferase (ChAT) and acetylcholine (Ach) in serum and hypothalamus. To avert the pathogenesis of AD, the hypothalamus and serum level of Ach and ChAT is very vital. HE could be an efficient neuroprotective agent in AD and for some other neurodegenerative diseases [22]. For the treatment of different diseases, Coriolus versicolor (CV) mushroom is also widely utilized as a nutritional supplement. The oxidative stress and neuroinflammation were considerably reduced by the CV in AD. CV also improve the quality of mitochondria and restores the normal redox balance [92]. Human wellness was effectively maintained by the bioactive molecules present in prebiotics such as legumes [93–95], spirulina [96], biological nanoparticles [93, 97], mushroom [30]. Similar to PD, some herbal plants like Bacopa monnieri, Withania somnifera, Eclipta alba, Moringa oleifera and cucumber also improves cognitive function as suggested by some researchers [98–103]. In addition, the neuroinflammatory pathways are also significantly modulated by a variety of medicinal mushrooms in AD [104]. In Huntington’s disease (HD), the therapeutic efficacy was also shown by medicinal, non-edible, and edible mushrooms and their bioactive components. Cognitive dysfunction is the very basic clinical feature of HD. In the edible mushroom Polyozellus multiplex, Polyozellin is a very important biomolecule having significant therapeutic activity. In the HD model, glutamate-induced mouse hippocampal neuronal HT22 cell death was significantly ameliorated by Polyozellin by apoptosis and the MAPK pathway. In HT22 cells, biochemical anomalies like lipid peroxidation and reactive oxygen species (ROS) were reduced by Polyozellin. Therefore, Polyozellin might be utilized for the treatment of HD patients in near future [105]. In the animal model of multiple sclerosis (MS), the disease conditions were ameliorated by Piwep, a mushroom extract from Phellinus igniarius. The dietary mushrooms and their bioactive components also improve the disease pathology in MS as with other NDs [106]. NFkB and Nrf2 mediated neuroinflammatory pathways are mainly responsible for mitochondrial dysfunction and ultimately cause progressive neurodegeneration in all NDs. Thus, the biomolecules of mushrooms play a very potential role to reduce the pathogenesis associated with NDs. Further studies will need to characterize more biomolecules in mushrooms and test their efficacy in several NDs.
Author details

Ahmed M. Saad*, Mahmoud Z. Sitohy1, Belal A. Omar1, Mohamed T. El-Saadony2 and Basel Sitohy3,4

1 Department of Biochemistry, Faculty of Agriculture, Zagazig University, Zagazig, Egypt

2 Department of Agricultural Microbiology, Faculty of Agriculture, Zagazig University, Zagazig, Egypt

3 Department of Radiation Sciences, Norrlands universitetssjukhus Umeå universitet, Umeå, Sweden

4 Department of Clinical Microbiology, Infection and Immunology, Umeå University, Umeå, Sweden

*Address all correspondence to: ahmedm4187@gmail.com
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