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REVIEW ARTICLE

Medicinal mushroom: boon for therapeutic applications

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Abstract
Medicinal mushrooms are higher fungi with additional nutraceutical attributes having low fat content and a trans-isomer of unsaturated fatty acids along with high fibre content, triterpenes, phenolic compounds, sterols, eritadenine and chitosan. They are considered as the unmatched source of healthy foods and drugs. They have outstanding attractive taste, aroma and nutritional value, so are considered as functional food, which means they are beneficial to the body not only in terms of nutrition but also for improved health. Medicinal mushrooms and their extract have a large number of bioactive components called secondary metabolites. The presence of polysaccharide β-glucans or polysaccharide–protein complexes content in mushroom extract have great therapeutic applications in human health as they possess many properties such as anti-diabetic, anti-cancerous, anti-obesity, immunomodulatory, hypocholesteremia, hepatoprotective nature along with anti-aging. The present review focuses on the comprehensive account of the medicinal properties of various medicinal mushrooms. This will further help the researchers to understand the metabolites and find other metabolites as well from the mushrooms which can be used for the potential development of the drugs to treat various life-threatening diseases.

Keywords Higher basidiomycetes · Medicinal mushrooms · Bioactive compounds · Polysaccharides · Pharmacological activity

Introduction

Mushrooms are filamentous fungi with fruiting bodies showing a huge number of pharmacological aspects in human health. They are considered one of the delicious foods and are commonly produced worldwide. They have been an essential part of the human diet and are used as both food and medicine for centuries. As shown in Table 1, they are a rich source of nutrients and bioactive compounds such as carbohydrates, fibers, proteins, vitamins, minerals and have enormous medicinal attributes such as antibacterial, antiviral, antioxidant, anticancerous, and hypocholesterolemic (Fig. 1) which are valuable for human health. The mushrooms are rich in protein and carbohydrate content, whereas low in lipid content. They contain essential amino acids, which help in meeting the needs of these amino acids in the human body. They are also rich in many essential unsaturated fatty acids, such as linoleic and oleic acids, which are necessary for the proper functioning of the body. Apart from this, they contain many essential minerals, which are responsible for the proper metabolism of many pathways. Mushrooms, unlike plants, lack chlorophyll, therefore, they grow on decayed organic matters, rich in lignin, cellulose, and other important carbohydrates. It is economical, rich in pharmacological properties, easy to cultivate, requires low resources and area, and can be grown all over the world. Nutritional, medicinal, bioremediation and biodegradation aspects of mushrooms are increasing day by day and have gained acceleration in recent years (Singh and Singh 2014; Agarwal et al. 2016; Vaseem et al. 2017).

Mushrooms possess medicinal properties because of the presence of different types of secondary metabolites. These secondary metabolites are bioactive, low molecular weight compounds which are produced in response to stress that help in its survival by signalling and defense but are generally not required by the fungi for their normal growth and reproduction. The most important secondary metabolite in

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Table 1 Nutraceutical value of some edible mushroom

S. no.	Mushroom	Nutritional value				Medicinal value	References
		Protein (g/100 g)	Carbohydrate (g/100 g)	Lipid (g/100 g)	Fibers (g/100 g)		
1	*Pleurotus*	17–42	37–48	0.5–5	24–31	Anticancer, antioxidant, antitumor, antiviral, antibacterial, antidiabetic, antihypercholesterolemic, eye health, anti-arthritic, immunomodulatory, hepatoprotective, anti-obesity	Deepalakshmi and Mirunalini (2014), Elsayed et al. (2014), Lakshmi et al. (2005) and Iuchi et al. (2015)
2	*Ganoderma*	13.3	82.3	3.0	–	Antiviral, hepatoprotective, antioxidant, antiallergenic, anticancer, hypoglycemic, immunomodulatory, hypotensive, antithrombotic, antiinflammatory, hypocholesterolemic, antibacterial, antimutagenic, anti-osteoporotic, anti-ageing	Wachtel-Galor et al. (2011), Kim and Kim (1999), Miyamoto et al. (2009), Weng et al. (2010) and Kalac (2009)
3	*Agaricus*	56.3	37.5	2.7	–	Anticancer, antidiabetic, antihypercholesterolemic, immunomodulatory, hepatoprotective, anti-viral, antimutagenic	Jedinak and Sliva (2008), Jeong et al. (2010), Lau et al. (2014), Johnson et al. (2008), Hsuet al. (2008), Faccin et al. (2007), Menoli et al. (2001) and Kalac (2009)
4	*Tricholoma*	18.1–30.5	31.1–52.3	2–6.6	30.1	Antihypercholesterolemic, anti-ageing	Geng et al. (2016), Ding et al. (2016) and Kalac (2009)
5	*Phellinus*	6.11–10.9	75.04–83.82	0.96–15.86	–	Antiinflammatory, antidiabetic, hepatoprotective	Kim et al. (2010), Lakshmi et al. (2005) and Lee et al. (2010)
6	*Sarcodona*	12	64.6	2.8	5.1	Anticancer	Kobori et al. (2006) and Wang (2014)
7	*Grifola*	21.1	58.8	3.1	10.1	Anticancer, antidiabetic, antihypercholesterolemic, anti-arthritic, anti-viral, anti-osteoporotic, anti-obesity	Griessmayr et al. (2007), Cui et al. (2009), Koichiro et al. (2008), Shingesue et al. (2000), Gu et al. (2007), Saif et al. (2007), Hiroaki (1997) and Cheung (2010)
8	*Leucopaxillus*	–	–	–	–	Anticancer	Ren et al. (2008)
9	*Clitocybene*	8.11–12.18	64.47–77.12	1.14–2.04	–	Anticancer	Pohleven et al. (2009) and Pinto et al. (2013)
10	*Hericium*	22.3	57.0	3.5	7.8	Antihypercholesterolemic	Khan et al. (2013) and Cheung (2010)
11	*Auricularia*	7.2	88.6	1.7	–	Anti-ageing	Zhang et al. (2011) and Hung and Nhi (2012)
12	*Lentinus*	26.3	65.1	2.3	–	Anticancer, immunomodulatory	Lovy et al. (1999), Gunawardena et al. (2014) and Hung and Nhi (2012)
13	*Cordyceps*	21.9	24.2	8.2	–	Anti-asthma	Heo et al. (2010) and Cheung (2010)
14	*Phyllanthus*	–	–	–		Anti-viral	Yang et al. (2005)
15	*Trametes*	–	–	–	–	Antidiabetic, immunomodulatory	Im et al. (2016) and Gunawardena et al. (2014)
16	*Flammulina*	3.9–17.8	86–70.8	1.8–2.9	–	Immunomodulatory, anti-asthmatic	Gunawardena et al. (2014), Lee et al. (2013) and Kalac (2012)
17	*Hypsizygus*	19.6–21.0	65–68.5	4.0–5.6	–	Antihypercholesterolemic	Koichiro et al.(2008), Kalac (2012)

Table 1 (continued)

S. no.	Mushroom	Nutritional value				Medicinal value	References
		Protein (g/100 g)	Carbohydrate (g/100 g)	Lipid (g/100 g)	Fibers (g/100 g)		
18	*Tremella*	4.6	94.8	0.2	1.4	Anticancer, antidiabetic	Chen et al. (2008), Cho et al. (2007) and Cheung (2010)

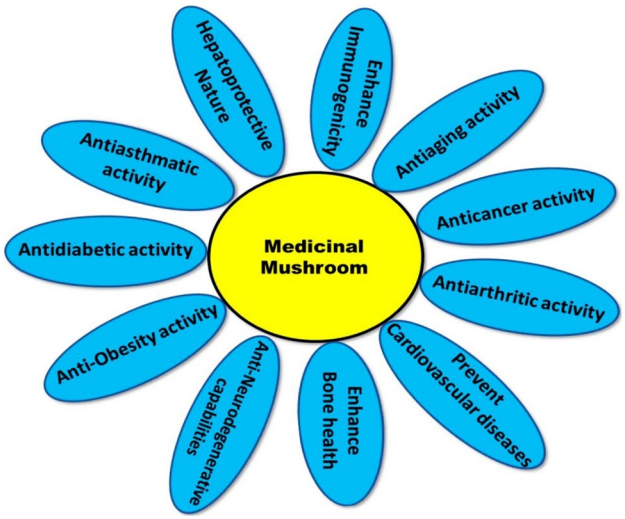

Fig. 1 Schematic illustration of therapeutic applications of edible mushroom

medicinal mushrooms are polysaccharides, which belong to 1,3-β-glucans family, having antitumor activities which are achieved by enhancing and blocking cellular immunity pathway. These polysaccharides exhibit antitumor and immunostimulating properties and generally, glucans with high molecular weight seem to be more effective as compared to low molecular weight. Biologically active polysaccharides have unique structures and they vary from strain to strain and species to species. Generally, the hot-water-soluble fractions from medicinal mushrooms are used to extract these polysaccharides to find out their pharmacological activity.

There are other secondary metabolites as well that confer different pharmacological activities, which include lectins, lactones, terpenoids, alkaloids, antibiotics, and metal-chelating agents.

Several studies had been conducted which reported that these secondary metabolites not only stimulate the immune system but also modulate specific cellular responses by interfering with particular transduction pathways. *Pleurotus ostreatus* is an edible mushroom having the ability to block the cell proliferation of breast and colon cancer, by up-regulation of cell cycle regulatory protein. The extract of *Pleurotus pulmonaris* suppresses liver cancer development by inhibiting PI3k/AKT signalling pathway. Extracted proteoglycans from *Ganoderma lucidum* have a protective effect against liver injury (Wachtel et al. 2011). Methanolic extracts of white button mushroom, *Agaricus bisporus*, exhibit antiproliferative and proapoptotic activities, which inhibit prostate cancer by the regulation of extracellular-regulated kinase (ERK/AKT) and NF-kappa. A fucomannogalactan (FMG-Am) and a (1→3), (1→6)-linked D-glucan (GLC-Am) isolated from *G. lucidum* fruiting bodies activate the cell and humoral immunity by activating NK cell and

inducing gene expression of nitrous oxide in macrophages and interferon-γ (INF-γ) transcription regulation by up-regulation. Ethanolic and proteoglycan extracts from *Pleurotus linteus* illustrate anti-inflammatory effect in collagen-induced arthritis.

There are a large number of bioactive compounds such as α–β-unsaturated polysaccharides, glycoproteins, peptides, phenolics derivatives, hydrolytic, lipids and oxidative enzymes that have been extracted from the crude extract of mycelia and fruiting body of medicinal mushroom that show therapeutic applications, which is depicted in Fig. 2 and Table 2.

The mushrooms with medicinal values are often termed as 'mushroom nutraceuticals'. This mushroom nutraceutical is consumed in the form of capsules or tablets as dietary supplements which is derived from the extract or dried biomass of mycelium or the fruiting body of a mushroom that has potential therapeutic applications. It has been reported that with regular intake of these nutraceuticals, there may be enhancement in the immune response of the human body which helps in increasing resistance to disease and at times improving the condition of the disease state. The review summarizes the knowledge of biologically active compounds of the medicinal mushrooms, their structure, their therapeutical application with pathways that show how they help in suppressing the onset of disease. Some of the medicinal properties exhibited by different mushrooms as studied earlier by different researchers under in vitro conditions are discussed below.

Medicinal properties

Mushrooms showing anticancerous properties

Cancer is one of the leading causes of death worldwide. The most common treatment of cancer is chemotherapy, which usually has side effects. Therefore, it is necessary to find an alternative method which is more effective and non-toxic. In recent years, mushrooms have gained a lot of attention as a source of physiological functional food and drug because of their medicinal value. Bioactive compounds of mushroom such as polysaccharides and polysaccharide–protein complexes have therapeutic attributes, and they cause no harm,

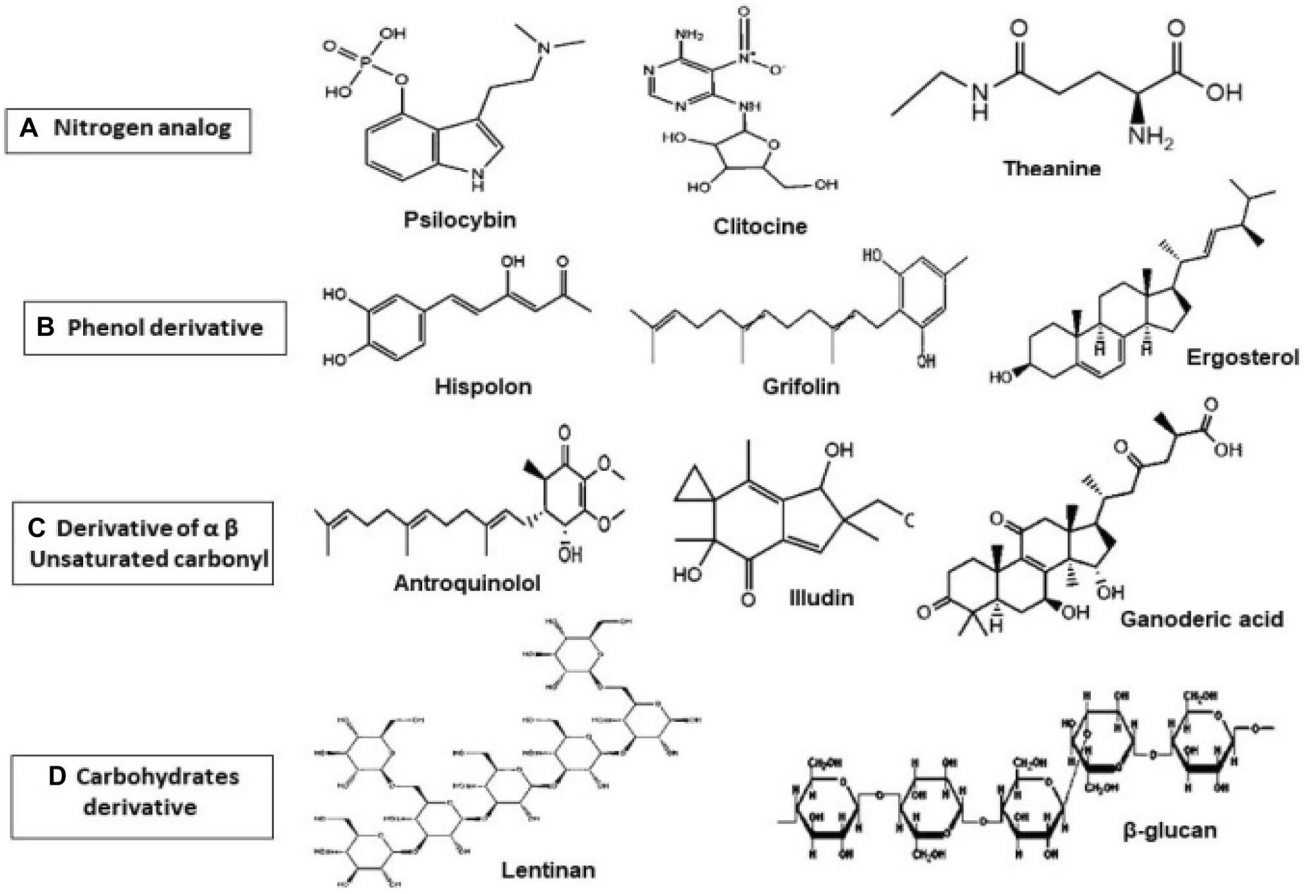

Fig. 2 Structure of bioactive compounds from medicinal mushroom

Table 2 Medicinal properties of different bioactive compounds from mushroom extracts

S. no.	Disease/bioactivity		Bioactive mushroom extract	Mushroom species	Phylum/division/edibility	References
1	Anti-cancer	Colorectal	Methanol extract Polysaccharides extract	*Ganoderma tsugae* *Pleurotus sajor-caju*	Basidiomycota/edible	Hsua et al. (2008) Moharib et al. (2014)
		Leukaemia	Ricin B-lectin PET fraction	*Clitocybe nebularis* *Grifola frondosa*	Basidiomycota/edible	Pohleven et al. (2009) Griessmayr et al. (2007)
		Breast	Ganoderic acid Methanol extract	*Ganoderma lucidum* *Pleurotus ostreatus*	Basidiomycota/edible	Jiang et al. (2008) Jedinak and Silva (2008)
		Oral	Crude extract	*Agaricus brasiliensis*	Basidiomycota/edible	Fan et al. (2011)
		Renal	Ethanol extract	*Ganoderma lucidum*	Basidiomycota/edible	Lu et al. (2004)
		Cervical	Clitocine	*Leucopaxillus giganteus*	Basidiomycota/edible	Ren et al. (2008)
		Gastric	Methanolic extract	*Ganoderma lucidum*	Basidiomycota/edible	Reis et al. (2015)
		Liver	Polysaccharide	*Pleurotus pulmonarius*	Basidiomycota/edible	Xu et al. (2012)
		Prostate	Fruit body powder	*Ganoderma lucidum*	Basidiomycota/edible	Sliva et al. (2002)
		Lung	Ethanol extract	*Tremella mesenterica*	Basidiomycota/edible	Chen et al. (2008)
2	Anti-diabetic		Vanadium Polysaccharides	*Grifola frondosa* *Phellinus linteus*	Basidiomycota/edible	Cui et al. (2009) Kim et. al. (2010)
3	Cardiovascular disease		Crude extract Peptides	*Agaricus bisporus* *Tricholoma matsutakei*	Basidiomycota/edible	Lau et al. (2014) Geng et al. (2016)
4	Immune-function		Lectine Extracts	*Pleurotus ostreatus* *Trametes pubescens*	Basidiomycota/edible	Gao et al. (2013) Im et al. (2016)
5	Asthma		FIP-*fve* Mycelial extract	*Flammulina velutipes* *Cordyceps spheco-cephala*	Basidiomycota/edible Ascomycota/edible	Im et al. (2013) Heo et al. (2010)
6	Rheumatoid arthritis		Polysaccharides extract	*Grifola frondosa*	Basidiomycota/edible	Shingesue et al. (2000)
7	Liver dysfunction		Mycelial extract	*Ganoderma lucidum*	Basidiomycota/edible	Zhang et al. (2002a, 2002b)
8	Anti-viral		Ethanol extracts Glycoprotein Methanol extracts	*Agaricus brasiliensis* *Pleurotus ostreatus*	Basidiomycota/edible	Faccin et al. (2007) Wang and Ng (2000) Yang et al. (2005)
9	Neurodegenerative		Aqueous extract	*Ganoderma lucidum*	Basidiomycota/edible	Rahman et al. (2015)
10	DNA damage		Water extract Polysaccharide	*Agaricus blazei* *Ganoderma lucidum*	Basidiomycota/edible	Guterreza et al. (2004) Kim et al. (1999)
11	Bone studies		Water extract Ganoderic acid	*Grifola frondosa* *Ganoderma lucidum*	Basidiomycota/edible	Saif et al. (2007) Miyamoto et al. (2009)
12	Anti-ageing		Polysaccharide TLH-3 Ergosterol ganoder-masidase	*Tricholoma lobayense* *Ganoderma lucidum*	Basidiomycota/edible	Ding et al. (2016) Weng et al. (2010)
13	Anti-obesity		β-Glucan Water extract	*Pleurotus sajor-caju* *Pleurotus eryngii*	Basidiomycota/edible	Kanagasabapathy et al. (2013) Mizutani et al. (2010)

no additional stress on the body instead they help the body to adapt to environmental and biological stress. Extracted polysaccharides from various medicinal mushrooms show anticancerous activity in human cell lines. Extracted polysaccharides are compounds of β-glucan family. They boost cellular immunity against tumour, because of antitumorigenic property. Proteoglycan isolated from edible mushroom, *Agaricus bisporus*, involves a number of natural killer cells (NK cells) and induces gene expression of nitric oxide (NO) by transcription factor and NF-kappa B (nuclear factor kappa-light-chain-enhancer of activated B cells) downstream signalling, interferon-γ and interleukin, which are responsible for the activation of NK cells.

Colorectal cancer

Colorectal is the second leading cause of cancer causing death and it occurs in about 1 out of 15 people. In the colon,

surface carbohydrate expression changes and this plays a key role in determining the metastatic behavior of tumor cells. Patients with metastatic cancer generally do not survive for more than 5 years after their diagnosis and most patients diagnosed with colorectal cancer usually die all of a sudden due to the disease. The early stage of cancer can be treated by surgery and after that, the patients are treated with adjuvant chemotherapy which results in 40% reduction in risk of relapse. But these methods deteriorate the quality of patient's life and hence it is necessary to treat them with alternative methods to deal with the side effects of chemotherapy. The methanol extract of dried fruiting bodies of *Ganoderma* inhibits colorectal cancer cell accumulation caused by the proliferation of a cell in G2–M cell cycle phase. Methanol extract regulates sp 21 and p 27 and downregulates cyclin A and B kinase proteins (Hsua et al. 2008). Edible mushroom, *Pleurotus ostreatus*, shows antiapoptotic activity because of the presence of low molecular weight polysaccharide, a bioactive compound α-glucan, which is extracted from mycelia by the process of hot water extraction. Proliferation and inhibition are dose dependent. Pro-apoptotic molecules—Bax and cytosolic cytochrome c—inhibit phosphorylation of retinoblastoma (Rb), which can upregulate the growth of colon cancer HT-29 cells (Lavia et al. 2006; Jedinak and Sliva 2008). Recently, it has been seen that the chemically induced colon cancer in HCT-116 cells when treated with polysaccharide extract of *Pleurotus sajor-caju* shows antiproliferative nature (Moharib et al. 2014). Another researcher found that purified sterol 9,11-dehydroergosterol peroxide 9-(11) (DHEP), isolated from the medicinal mushroom *Sarcodona spratus*, selectively suppresses the growth of HT-29 human colon adenocarcinoma cells (Kobori et al. 2006).

Leukaemia

Leukaemia can be divided into two types, lymphocytic and myelocytic, which can be either acute or chronic. The occurrence of the leukaemia is high, about 3–5% and its mortality rate is 4–5%. Significant geographical and racial differences in age-adjusted occurrence and mortality rate of cancer are believed to be influenced by diverse genetic, environmental and dietary factors. It has been found that mushroom-derived extracts have important remedial properties for maintaining health, prevention, and treatment of cancer. In a recent study, Ricin B-like lectin isolated from the extract of medicinal mushroom *Clitocybene bularis* shows anti-proliferative activity against human leukemic T cells. Most lectins contain more than one carbohydrate-binding site, which binds to cell surface glycosylated receptor present in human leukemic T cells, leading to signal transduction pathway activation of antileukemic activity (Pohleven et al. 2009). A sterol 9(11)-DHEP extracted from medicinal mushroom, *Sarcodona spratus*, shows strong apoptosis-inducing activity and is a more effective inhibitor of HL-60 leukaemia cell growth (Kobori et al. 2006). In a research survey, the effect of triterpenes isolated from the mycelial extract of *Ganoderma lucidum* shows arrest of cell cycle in G2–M phase of human leukaemia cancer cell lines HT-29 (Muller et al. 2006). *Grifolan frondosa* PET fraction extracts are used for the treatment of leukaemia in dogs, to induce apoptosis and suppress proliferation of lymphoma C-1 cell lines in vitro (Griessmayr et al. 2007).

Breast cancer

Breast cancer is the major cause of death of women worldwide. It has been found that the reproductive hormone, estrogen, is present in the breast of postmenopausal women and influences breast cancer by affecting cell proliferation and DNA damage as well as the promotion of cancer growth. Aromatase expression occurs in breast tumours which plays a major role in tumour proliferation; this aromatase converts androgen hormone to estrogen. Blocking aromatase with an alternative drug helps to reduce the serum estradiol levels in healthy females. It occurs mainly in women who had early menopause, late or fewer pregnancies by affecting the reproductive hormone. Triterpenes and ganoderic acid extracted from medicinal mushroom, *Ganoderma lucidum*, suppresses the growth of MDA MB breast cancer cell lines by inhibiting cell proliferation and colony formation. Triterpenes inhibit the transcription factors AP-1 and NF-κB resulting in the downregulation of expression of Cdk4 and suppress the secretion of uPA (Johnson et al. 2008). Hydroxylated triterpenes obtained from *Ganoderma lucidum* could be a promising natural agent for the treatment of invasive breast cancers. Extracts from edible mushrooms, *Agaricus bisporus* and *Pleurotus ostreatus*, affect the growth of breast and colon cancer cells by suppressing the proliferation of different breast cancer cell lines (MCF-7, MDA-MB-231) (Jedinakand and Sliva 2008).

Oral cancer

Oral cancer is generally caused by cigarette smoking, chewing of tobacco and alcohol consumption. Apart from that, several nutritional factors are also responsible for oral cancer, such as deficiency of iron and niacin. With niacin deficiency, alimentary tract changes were seen in patients with pellagra. It has been found that with the increased consumption of vitamins A and C, the risk of oral cancer decreases. Retinoids can reduce the occurrence of oral malignancy in patients with oral leukoplakia. During the investigation conducted by Yu et al. in oral cancer studies, 30 rats were divided into 3 different groups to examine oral ulceration induced by phenol. Each group had 10 rats, group 1 contained untreated oral ulceration rats which were used

as control. The second group was isolated polysaccharide-treated low-dose oral ulceration rats, while the third group contained extracted polysaccharide-treated high-dose oral ulceration rats. *Lentinus edodes* polysaccharide (LEP), dose dependently increased serum and oral mucosa IL-1b and TNF-α levels in rats with oral ulceration. These results suggested that the healing of oral ulceration significantly increased with LEP treatment (Yu et al. 2009). In another recent study, crude extract of *Agaricus brasiliensis* induced apoptosis in human oral cancer CAL-27 cells through a mitochondria-dependent pathway (Fan et al. 2011).

Renal cancer

Polysaccharides isolated from the fruiting bodies of *Pleurotus eryngii* show antitumor activity. Its polysaccharides contain mannose, galactose and arabinose which significantly increase relative thymus and spleen lymphocytes proliferation induced by elevated activity of natural killer cells (NK cells) and cytotoxic T lymphocytes (CTL) in spleen and increase serum concentration level of TNF-α and IL-2 in mice bearing renal cancer (Yang et al. 2013). Ethanol extract by *Ganoderma lucidum* mushroom had stronger growth inhibition effect as compared to water extract. Cell cycle analysis showed that the growth inhibition effect was associated with G2/M arrest in urothelial HUC-PC cells and MTC-11 cells (Lu et al. 2004).

Cervical cancer

Cervical cancer is the second most leading cancer in women after breast cancer. It is caused by the infection from human papillomavirus (HPV). Two HPV oncogenic proteins, E6 and E7, induce cervical cancer by interacting with p53 and pRB, and inactivating these cellular regulatory proteins. In the early stages of cancer, radiotherapy is used and for advanced stage, chemotherapy is used, and the rate of the survival increases for 5 years. Apart from this, chemotherapy causes side effects such as immunosuppression and bone marrow depression. The medicinal mushroom, *Leucopaxillus giganteus*, possesses numerous bioactivities including antitumor. The bioactive compound, clitocine, isolated from *Leucopaxillus giganteus*, is responsible for changing the morphology of cells and induces cell death in human cervical cancer cell lines (HeLa cells). Researchers showed that clitocine activates pathway of caspase-3, 8, and 9, mitochondrial-mediated cell death and DNA fragmentation in human cervical cancer (Ren et al. 2008). In another study, it was demonstrated that several medicinal mushrooms such as *Grifola frondosa, Ganoderma lucidum, Lentinula endodus* and *Lentinula aurantiacum* have shown anticancerous activity by inhibiting the growth of human cervical cancer (Lovy et al. 1999) as shown in Fig. 3. The bioactive compounds present in medicinal mushroom have anticancerous as well as other biochemical properties from which the effectivity over different diseases is determined. Table 3 represents the molecular mass, lipophilicity, H bond donors, H bond acceptors and molar refractivity as given by Lipinski rule of different bioactive compounds.

Gastric and other cancer

Gastric cancer is not as common as other cancers. The risk factors associated with gastric cancer are environmental, genetic and infectious. Infection from bacteria *Helicobacter pylori* causes inflammation of gastric mucosa. Environmental factors causing gastric cancers are related to alcohol drinking, smoking, socioeconomic status, dietary habit and refrigerator use. Apart from this, endogenous nitrosamines are responsible for gastric cancer. High-salt diet, smoked meat, high-carbohydrate and -fat diet are also some of the reasons for gastric cancer, whereas consumption of high dietary fibre, fruits, and dairy products reduces the risk of gastric cancer (Wong et al. 2013). *Ganoderma lucidum* is one of the most widely used medicinal mushroom species for treatment of gastric cancer (Rony et al. 2011). The methanolic extract of *G. lucidum* increases cellular autophagy and formation of autophagosomes in the treatment of a gastric adenocarcinoma cell line (AGS) (Reis et al. 2015). Polysaccharide extracted from *Pleurotus pulmonarius* has anticancerous effects. Under in vitro and in vivo conditions, the extracted polysaccharide–protein complex trigger the suppression of PI3K/AKT signalling pathway in liver cancer cell and overexpresses the constitutively active form of AKT, Myr-AKT, which abrogates this effect and inhibits the proliferation of hepatocellular carcinoma (Xu et al. 2012). Medicinal mushrooms show anticancer attribute against prostate cancer (Sliva et al. 2002). Methanol extract of *L. edodes* and ethanol extract of *Tremella mesenterica* induces apoptosis of human lung A549 epithelial cells and skin cells (Gu and Belury 2005; Chen et al. 2008).

Anti-diabetic property of mushrooms

Diabetes is a chronic disease causing several health problems to millions of people worldwide and has become a domestic disease. Diabetes mellitus, or diabetes, is a group of metabolic disease characterized by high blood glucose levels that result from insulin imbalances within the body. Phytochemical screening from *Pleurotus florida* extracts reveal the presence of phenols (61.85 mg catechol equivalent), flavonoids 2.78 mg, alkaloids 1.92 mg, terpenoids 0.08 mg, tannins 0.52 mg, saponins 0.05 mg and glycosides 0.12 mg in 100 g dried powder of mushroom, which shows anti-diabetic activity by reducing blood glucose level (Pohleven et al. 2009). *Grifola frondosa*, mushroom rich in

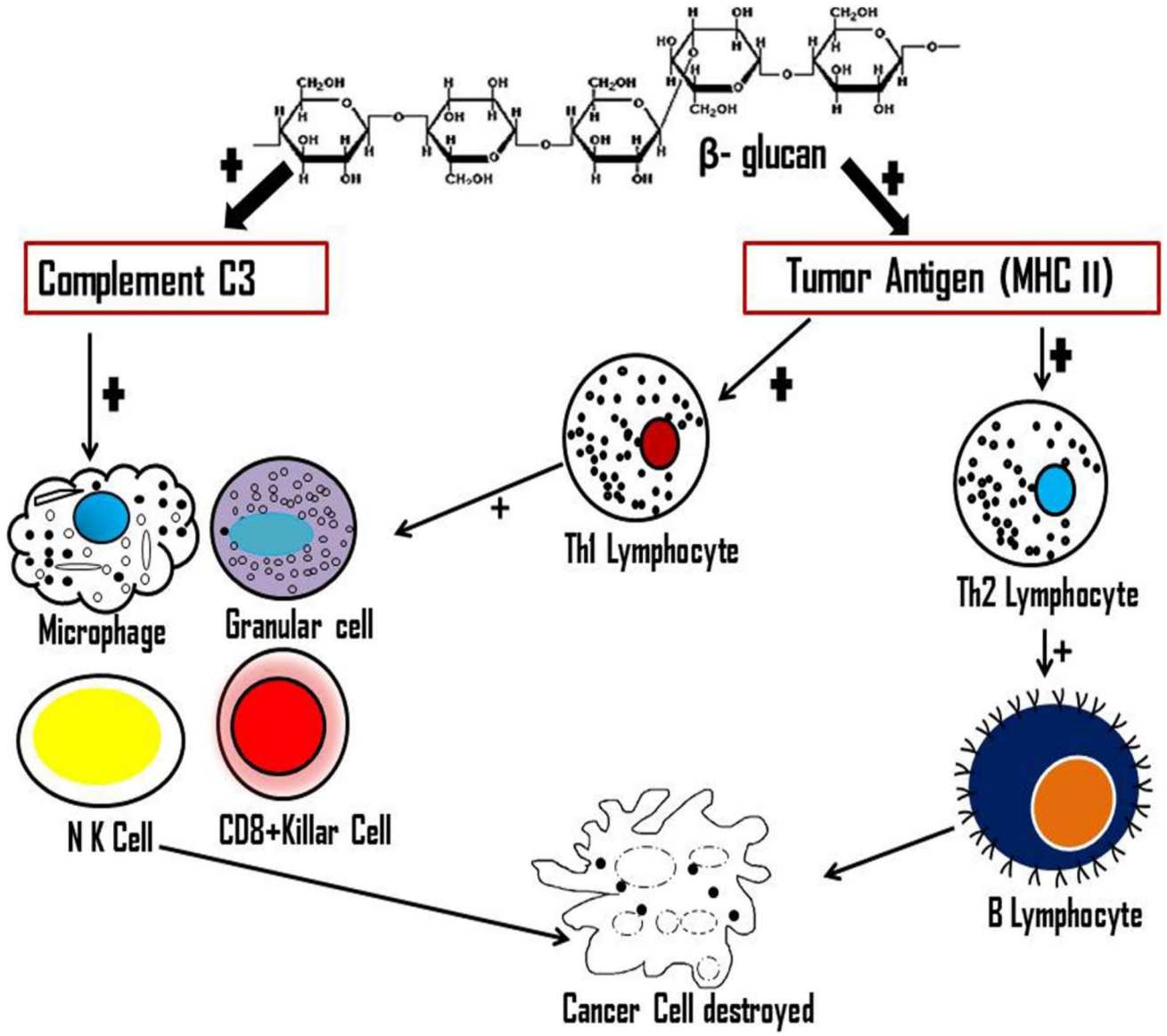

Fig. 3 Mechanism of anticancerous activity of bioactive compound (β-glucan)

vanadium, shows hypoglycemic activity (Cui et al. 2009). The bioactive compound of white button mushroom, *Agaricus bisporus*, decreases the blood glucose level in diabetic rats (Jeong et al. 2010). Extracted polysaccharides of medicinal mushroom, *Phellinus linteus*, show hypoglycaemic activity in non-obese diabetic mice (Kim et al. 2010). *Ophiocordyceps sinensis* is an edible and medicinal mushroom which has been used as novel nutraceuticals drug for diabetes mellitus and antihyperglycemic activity (Sirisidthi et al. 2015). Extract of *Grifola frondosa* (Maitake) fruiting body contains bioactive substances which help in decreasing the blood glucose level in genetically born diabetic mice when given orally (Kubo et al. 1994). Mainly β-glucans and polysaccharides in mushrooms have the ability to restore the function of pancreatic tissues by increasing the secretion of insulin by β-cells, which lowers the blood glucose levels. It has shown to improve the sensitivity of peripheral tissues to insulin (Kaur et al. 2015). Hypoglycemic substances, glycoproteins and β-glucans isolated from the hot water extract of *Agaricus blazei* reduced the blood glucose level in the streptozotocin-induced diabetic rat (Oh et al. 2010; Hwang et al. 2005). *Pleurotus citrinopileatus, P. pulmonarius* and *Grifola frondosa* show similar results of hyperglycaemic activity (Rushita et al. 2013; Badole and Bodhankar 2007; Kurushima et al. 2000). The fruiting body of *Trametes pubescens*, a medicinal mushroom, reduces the blood glucose level and increases the rate of insulin activity (Im et al. 2016). Comparative study of ethyl acetate extract

Table 3 Lipinski rule of different bioactives from medicinal mushroom

S. no.	Name	IUPAC name	Molecular mass (Da)	Lipophilicity (LogP) > 5	H bond donors > 5	H bond acceptors > 10	Molar refractivity (40–130)	Rule of 5 violations
1	Antroquinolol	(4R,5R,6R)-4-Hydroxy-2,3dimethoxy-6-methyl-5-[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrien-1-yl]-2cyclohexen-1-one	390.556	6.60	1	4	114.7 ± 0.4 cm^3	1
2	Clitosin	N-(6-Amino-5-nitro-4-pyrimidinyl)-β-D-ribofuranosylamine	287.229	0.48	6	11	65.7 ± 0.3 cm^3	2
3	Ergosterol	Ergosta-5,7,22-trien-3β-ol	396.648	9.30	1	1	124.2 ± 0.4 cm^3	1
4	Ganoderic acid	(7β,15α,25R)-7,15-Dihydroxy-3,11,23-trioxolanost-8-en-26-oic acid	516.666	2.18	3	7	137.2 ± 0.4 cm^3	1
5	Grifolin	5-Methyl-2-[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrien-1-yl]-1,3-benzenediol	328.488	6.92	2	2	104.3 ± 0.3 cm^3	1
6	Hispolon	(3Z,5E)-6-(3,4-Dihydroxyphenyl)-4-hydroxy-3,5-hexadien-2-one	220.221	0.70	3	4	61.3 ± 0.3 cm^3	0
7	Illudin	(2'S,3'R,6'R)-3',6'-Dihydroxy-2'-(hydroxymethyl)-2',4',6'-trimethyl-2',3'-dihydrospiro[cyclopropane-1,5'-inden]-7'(6'H)-one	264.317	−0.29	3	4	69.2 ± 0.4 cm^3	0
8	Lentinan	β-D-Glucopyranosyl-(1->6)-[β-D-glucopyranosyl-(1->3)-[β-D-glucopyranosyl-(1->6)]-β-D-glucopyranosyl-(1->3)-β-D-glucopyranosyl-(1->3)-β-D-glucopyranosyl-(1->3)]-β-D-glucopyranose	1153.000	−8.11	23	36	239.4 ± 0.4 cm^3	3
9	Psilocybin	3-[2-(Dimethylamino)ethyl]-1H-indol-4-yl dihydrogen phosphate	284.248	0.03	3	6	73.1 ± 0.3 cm^3	0
10	Theanine	(5Z)-5-(Ethylimino)-5-hydroxy-L-norvaline	174.198	−1.02	4	5	43.2 ± 0.3 cm^3	0
11	β-Glucan	β-D-Glucopyranoseglucopyranosyl-(1->4)-β-D-glucopyranoseglucopyranosyl-(1->4)-β-D-glucopyranoseglucopyranosyl-(1->4)-β-D-glucopyranoseglucopyranose	666.578	−5.83	14	21	138.2 ± 0.4 cm^3	3

of *Pleurotus osteratus* (Sayeed et al. 2014) and *Ganoderma lucidum* was used to find out their hypoglycaemic activity in alloxan-induced diabetic mice, and the hypoglycaemic study showed that both mushroom extracts lowered blood glucose level but the better results were observed by oyster mushrooms. The mushroom *Agaricus blazei* Murill is a natural food substance, which has been used as a health promoter, and with a combination of Metformin and Gliclazide, it improves the insulin resistance against type 2 diabetes mellitus (Hsu et al. 2007). *Agaricus blazei* and other medicinal mushrooms are commercially available in the form of mushroom products with claimed antidiabetic and several other medicinal properties as depicted in Table 4. Exopolysaccharides produced by mycelial cultures of two different mushrooms, *Tremella fuciformis* and *Phellinus baumii*, show hypoglycaemic effect by regulating the gene expression of PPAR-γ-mediated lipid metabolism (Cho et al. 2007; Yang et al. 2012a, b).

Mushroom against cardiovascular disease

Cardiovascular disease is marked by the presence of high level of low-density lipoprotein (LDL) and low level of high-density lipoprotein (HDL), thereby increasing the ratio of total cholesterol to HDL cholesterol, which is the main factor for the onset of the cardiovascular disease. Trans-fats are responsible for increasing the total cholesterol level as well as triglyceride levels in the blood. Trans-fats have adverse effects on serum lipids. Risk factors associated with cardiovascular diseases include high blood pressure and high level of glucose and cholesterol in the blood. People with the cardiovascular disease have more chances of

Table 4 Commercially available medicinal mushroom products claimed to have medicinal properties

S. no.	Product name	Mushroom species	Health benefit	References/webpage
1	ORIVEDA® *Agaricus blazei* Murill extract	*Agaricus blazei*	Anti-hyperglycemic, antihypercholesterolemic and anti-lipid peroxidative effects	http://www.chaga.us.oriveda.com/agaricus.php
2	Shiitake Gold capsules	*Lentinus edodes*	For complete physical health	http://www.alohamedicinals.com/shop.html
3	ReishiMax capsules	*Ganoderma lucidum*	Inhibit adipocyte differentiation, stimulate glucose uptake and activate AMPK	Thyagarajan-Sahu et al. (2011)
4	*Cordyceps sinensis* capsules	*Cordyceps sinensis*	Control blood glucose levels	http://curingherbs.com
5	Pure Red Reishi capsules; Organic Reishi tablets _	*Ganoderma lucidum*	Increase the body's resistance to stress and helps to overcome all health challenges more quickly, support the body's normal cellular immune system	https://www.oriveda.com/e-reishi.php
6	GlucoSANO-Diabetes Health Formula	*Agaricus blazei, Pleurotus eryngii, Hypsizygus tessellates, Cordyceps militaris*	Specifically formulated for diabetic health, the nutrients promote increased insulin sensitivity and balanced blood sugar levels	http://www.totalnutraceutical.com/glucosano-diabetes-health-formula
7	GanoUltra GanoSuper	*Ganoderma lucidum*	Anticancerous, anti-stress, antidiabetic	http://www.alohamedicinals.com/gano-ultra.html
8	Agarikon.1	*Ganoderma lucidum, Lentinus edodes, Grifola frondosa, Agaricus blazei* and *Pleurotus ostreatus*	Anticancer properties	http://mykosan.com/agarikon-1-medicinal-mushrooms-cancer/
9	Amyloban 3399 Super Lion's Mane (Tablets)	*Hericium erinaceus*	Brain health	http://www.mushroomwisdom.com/products-brain-health.php
10	Ganoderma herbal antidiabetic capsules	*Ganoderma lucidum*	Enhance human body's overall immunity, accelerate recovery of diabetes, increase the efficacy of medicinal treatments	http://www.globalsources.com/si/AS/FujianXianzhilou/6008823255701/Homepage.htm

heart attack or stroke. Medicinal mushrooms, *Grifola frondosa* (Maitake), *Pleurotus eryngii* (Eringi), and *Hypsizygus marmoreus* (Bunashimeji), are used as biomarkers for atherosclerosis-susceptible C57BL/6J mice, which reduce total cholesterol content in the human body. They contain bioactive elements which prevent cardiovascular diseases in human beings. Oral administration of 30% dried mushroom to atherosclerotic mice reduces the total cholesterol (TC) level in atherosclerosis-susceptible mice in comparison to control mice (Fombang et al. 2016). When these mushrooms' extracts are applied on an atherosclerotic lesion in infected mice, the chances of anti-atherosclerosis decreased (Koichiro et al. 2008). The crude extract of the fruiting body of *Agaricus bisporus* (Lau et al. 2014) and *Tricholoma matsutake* has bioactive inhibitory peptides that inhibit the function of angiotensin, which converts the enzyme responsible for hypertension and cardiovascular diseases (Geng et al. 2016). The ethanol extract of *Hericium erinaceus* improves lipid metabolism by inhibiting platelet aggregation, which is induced by collagen. It also works as a therapeutic agent for various vascular diseases including myocardial infarction and also helps reducing the stock levels of LDL and TGA while increases HDL level and has a hypocholesterolemic effect (Khan et al. 2013; Koh et al. 2003). Hot aqueous extract of *Pleurotus cornucopiae* shows an antihypertensive effect in mice. The extracted D-glucopyranose mannitol from edible mushroom *Pleurotus cornucopiae* inhibits angiotensin I-converting enzyme (ACE), which converts angiotensin I to the potent vasopressor octapeptide angiotensin II, which is responsible for increasing the blood pressure (Hagiwara et al. 2005; Adachi et al. 1988). Mushroom intake has a cholesterol-lowering effect through different mechanisms, such as decreasing very low-density (VLDL) lipoproteins, improving lipid metabolism, inhibiting the activity of β-hydroxy β-methylglutaryl-CoA (HMG-CoA) reductase which takes part in lipid metabolism, and consequently preventing the development of atherosclerosis (Guillamon et al. 2010).

Effects of mushroom on immunity

Immune stimulation by medicinal and edible mushrooms occurs via innate immunity and is typically done by phagocytic cells. Recent studies showed the effect of mushroom extracts on immune function by inhibiting tumour growth. These cells ingest invading pathogens and interact with pathogen components or bioactive element for further stimulation of innate immunity and adaptive immunity by secretion of cytokines and chemokines (Hetland et al. 2008; Harikrishnan et al. 2011). Figure 4 represents the mechanism of immune activation by β-glucan from mushroom. Medicinal mushroom contains efficacious compounds such as 1,6-branched 1,3-β-glucans for stimulation of the immune system by affecting NK cells, macrophages and T cells as well as their cytokine production (Roupas et al. 2012). Oyster mushroom (*Pleurotus* species) is a good source of bioactive compounds, which initiate the complement immune response. Bioactive elements such as polysaccharopeptides, functional proteins ubiquitin-like protein, β-glucans and glycoprotein are responsible for enhancing the immune modulatory pathway as depicted in Fig. 4, by stimulating activity for both innate and adaptive immune systems (Oloke and Adebayo 2015; Elsayed et al. 2014). Medicinal mushroom *Agaricus blazei* Murill (AbM) is reported to have an immunostimulatory effect (Johnson et al. 2008). The oral administration of AbM extract at 0.5–5.0% doses for several days stimulated the release of cytokine in whole blood. Comparative study of various edible mushrooms such as *Pleurotus* spp.(Tanaka et al. 2015), *Pleurotus florida* (Pandimeena et al. 2015), *Trametes pubescens* (Im et al. 2016), *Agaricus bisporus, Flammulina velutipes*, and *Lentinus edodes* species showed anti-inflammatory activity determined by interferon-γ (IFN-γ) and lipopolysaccharide (LPS) which activate macrophages. These raw mushrooms show anti-inflammatory property and their oral administration inhibits the production of NO within the body (Gunawardena et al. 2014). The secondary metabolite lectin, purified from *Pleurotus ostreatus*, enhances immunogenicity by cellular and humoral immunity (Gao et al.2013). *Agaricus blazei* works (Chen et al. 2004) as an adjuvant for hepatitis B virus (HBV) DNA vaccine in HBsAg transgenic mice and the oral administration of its aqueous and alkaline extract inhibits edema induced by nystatin (Padilha et al. 2009).

Antiasthmatic properties of mushrooms

Asthma is a respiratory disease occurring in adults and children. Exposure to allergens causes and increases asthma symptoms. The extract of medicinal mushroom, *Flammulina velutipes*, contains fungal immunomodulatory protein (FIP-*fve*). Oral administration of isolated FIP-*fve* inhibited allergen (OVA)-induced chronic airway inflammation in the mouse asthma model. This allergy is dependent on the balance between type 1 T helper cells (Th1) and type 2 T helper cells (Th2) cells. It has been demonstrated to skew the response to Th1 cytokine production. After intranasal administration of OVA, the resultant rate of inflammation and hyper-responsiveness increased, which is measured by bronchoalveolar lavage fluid (BALF) analysis and ELISA assay (Lee et al. 2013). Oral FIP-*fve* had an anti-inflammatory effect on OVA-induced airway inflammations and might possess a potential for the treatment of an allergic response within the body. Mycelia of *Cordyceps sphecocephala* extract were injected to assess the effects of anti-asthmatic activity on lung cells of ovalbumin-induced asthmatic mice and the results revealed that increasing levels of IL-4, IL-13 and IL-25 expression were controlled (Heo et al. 2010) and

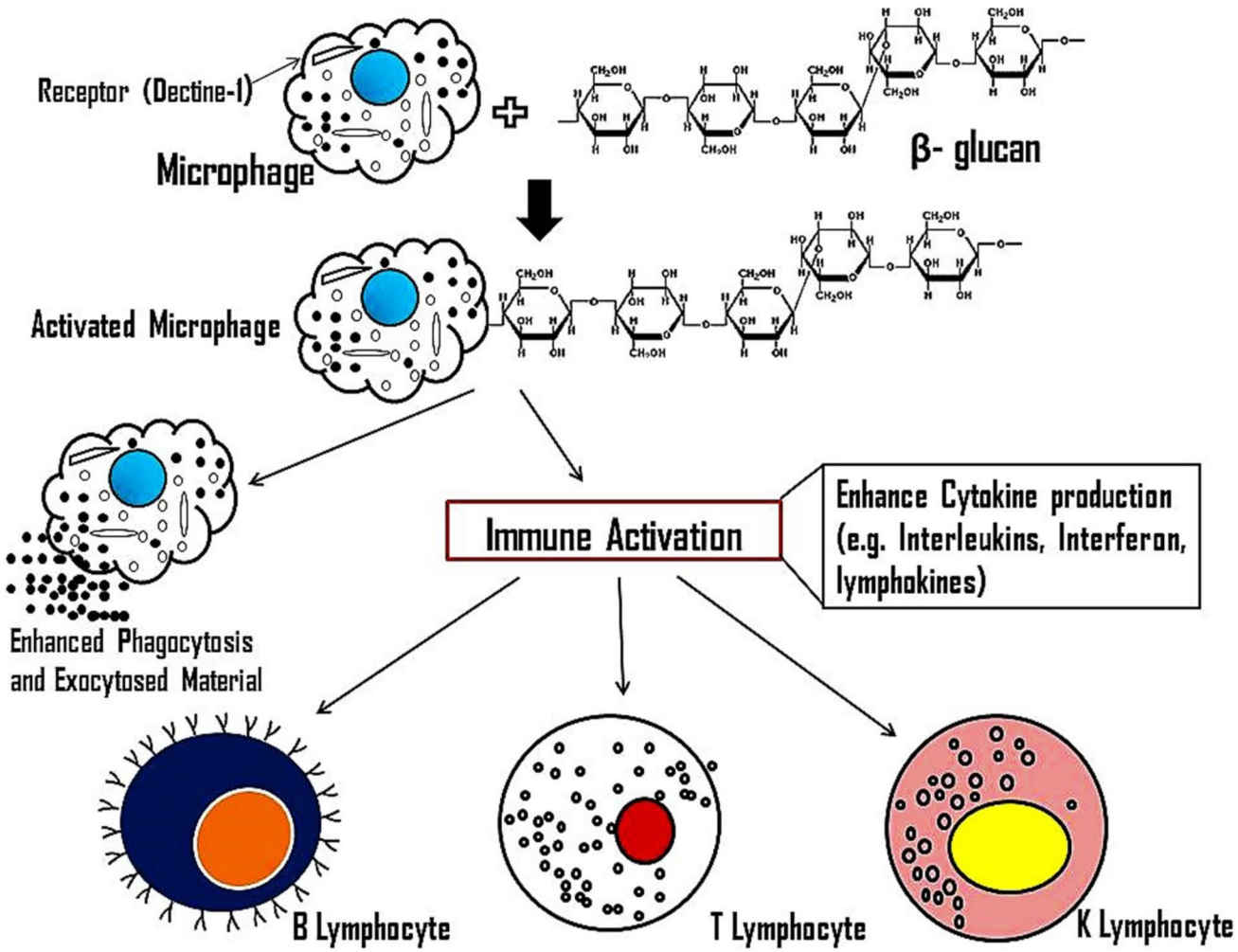

Fig. 4 Mechanism of immune activation by β-glucan from mushroom

reduced immune responses by the inhibition of the expression of cytokine were observed in asthmatic mice.

Rheumatoid arthritis

Rheumatoid arthritis is a joint disease which leads to disability. With increasing age at around 35–45 years inflammation in joints causes loss of shape and function. Women are more affected in comparison to men, which is characterized by chronic inflammation, joint pain and autoimmune disease. The anti-arthritic activity of a poly-branched β-(1,3/1,6)-D-glucan from *P. ostreatus* has been reported (Bauerova et al. 2009; Rovensky et al. 2011) in rat. When the arthritis adjuvant is introduced along with *Mycobacterium butyricum*, it shows immuno-modulating effect on cytokine plasma levels, which changed markedly with arthritis progression. Polysaccharide extract isolated from *Grifola frondosa* shows antiarthritic and immuno-regulating activity by inhibiting the autoimmune response in the collagen-induced arthritic rat (Shingesue et al. 2000).

Hepatoprotective activity of mushroom

The liver plays an important role in metabolism and detoxification of toxic compounds by reducing the exposure to chemical contamination such as drugs during disease within the body. It is, therefore, necessary to develop alternative drugs for the treatment of liver diseases. Secondary metabolites of mushroom such as phenolics, steroids, terpenes and essential cell wall components have protective effects against liver dysfunction. Mycelial extract of medicinal mushroom when tested against exogenous compounds induces liver damage (Soares et al. 2013; Yang et al. 2006). *Ganoderma lucidum* shows hepatoprotective activities against Bacillus Calmette–Guérin (BCG) vaccine-induced liver injury in mice (Zhang et al. 2002a, b). In another study, four patients suffering from hepatitis B and liver damage for more than

3 years were kept under clinical observation for 12 months and were not administered with any drug other than *Agaricu sblazei* Murill (ABM) extract, at a dose of 1500 mg daily for 12 months and the potential benefit of ABM extract was observed in normalizing liver function of patients and the level of aspartate aminotransferase and alanine aminotransferase decreased in comparison to patients suffering from hepatitis B (Hsu et al. 2008). Exposure of liver to radiation induces the generation of reactive oxygen species (ROS) such as hydroxyl radical and peroxyl radical, which are capable of inducing lipid peroxidation. Extracts of the medicinal and edible mushrooms *Pleurotus florida, Ganoderma lucidum, Pleurotus sajor-caju* and *Phellinus rimosus* possessed significant antioxidant activity in liver, measured as radical scavenging activity (Lakshmi et al. 2005).

Antiviral properties of mushrooms

Poliovirus causes poliomyelitis which is characterized by a classic manifestation of flaccid paralysis. Poliomyelitis occurs in developing countries such as African and Asian countries. Aqueous and ethanol extracts of polysaccharide from the fruiting body of Sun mushroom *Agaricus brasiliensis* show antiviral activity against poliovirus type 1 in HEp-2 cells (Faccin et al. 2007). Proteins, peptides and polysaccharopeptides from fresh fruiting bodies of the mushroom have been reported to inhibit human immunodeficiency virus type 1 (HIV-1) reverse transcriptase enzyme, which plays a key role in the life cycle of HIV-1 viruses. Extracted lectin of *Pleurotus citrinopileatus* shows antiviral activity against HIV-1 (Li et al. 2008). The extract of the fruiting bodies of the edible oyster mushroom, *Pleurotus ostreatus*, contained carbohydrate-rich protein (glycoprotein) with a ubiquitin-like N-terminal sequence which showed activities such as inhibition of human immunodeficiency virus-1 reverse transcriptase, translation in reticulocyte lysate of rabbit and cleavage of transfer RNA (Wang and Ng 2000). *Phyllanthus urinaria* is a medicinal plant with many biological activities. Different solvents extracted from *P. urinaria* showed anti-HSV-1 and HSV-2 activities which were investigated by plaque reduction assay under in vitro conditions. Acetone, ethanol and methanol extracts of *P. urinaria* inhibited Herpes simplex virus-2 (HSV-2) (Yang et al. 2005). Antiviral protein was purified from an extract of *Grifola frondosa* fruiting bodies that act as an anti-HSV-1 (Gu et al. 2007; Dine et al. 2008).

Mushroom activity against neuro-degenerative diseases

The recent studies show the effects of mushroom intake on some aspects of neuro-degenerative disease; however, there is insufficient evidence from human studies to confirm clinically relevant outcomes on brain health parameters. Although, it has been found that the consumption of mushroom delays the onset of Alzheimer's disease and shows protective effects of mushroom on β-amyloid peptide toxicity in the brain and mild cognitive impairment (Xu and Beelman 2015). The extracted bioactive compound from medicinal mushroom, *Ganoderma lucidum*, when supplemented as a diet in a mouse model, showed a significantly lowered level of amyloid β deposition in their brain along with increased anti-oxidative enzymatic levels and improved memory-related learning abilities (Rahman et al. 2015). Mental illness is a public health crisis. Millions of people suffer through their days crippled by symptoms of mood, anxiety, and substance abuse disorders. These conditions take large social and economic tolls on our communities. Though helpful to many people, the relative ineffectiveness of traditional drugs is prompting patients and physicians to seek alternatives including psychedelic compound psilocybin which is present in many mushrooms. Clinical trials confirm the therapeutic application of psychedelic mushroom therapies on 53 self-medicating patients suggesting that psilocybin-containing mushrooms are effective in terminating cluster headaches or preventing the regular occurrence of cluster headaches (Sewell et al. 2006). In another study, nine patients with obsessive–compulsive disorder were examined for the effect of oral psilocybin. Doses administered were 0.025, 0.1, 0.2, and 0.3 mg/kg, after a week elapsed between each session. All participants showed substantial symptom reduction in at least one session as assessed by the Yale–Brown Obsessive Compulsive Scale. At a 6-month follow-up, one participant showed long-term improvements. Although these results might suggest psilocybin efficacy, it should be noted that a similar magnitude of symptom reduction was observed at all dose conditions (Moreno et al. 2006).

Antimutagenic activity of mushroom

Agaricus blazei has been a widely consumed mushroom in different parts of the world due to its medicinal power. Butantimutagenic activity has been demonstrated only in *Salmonella*. In this work, the mutagenic and antimutagenic activities of mushroom strains AB96/07, AB96/09 and AB97/11 were evaluated on Chinese hamster V79 cells. Mutagen methyl methane sulfonate induced mutated Chinese hamster V79 cells. 2.5% aqueous extract of *Agaricus blazei* reduces the frequencies of micronuclei and shows antimutagenic activity (Menoli et al. 2001; Oliveira et al. 2002). In vitro study of water extracts of *Agaricus blazei* shows antimutagenicity (Guterrez et al. 2004). Several medicinal mushrooms contain dietary components which prevent chemical-induced DNA damage (Ribeiro and Salvadori 2003). The water-soluble polysaccharide isolated

from the fruiting body of *Ganoderma lucidum* by the hot-water extraction procedure protects against hydroxyl radical-induced DNA strand breaks, indicating that the polysaccharide compound is associated with the protective properties and their pathways are given in Fig. 5 (Kim and Kim 1999).

Mushrooms' effect on bone health

Medicinal mushroom contains many bioactive compound nutrients which take part in bone metabolism in human health, which prevents osteoporosis. Isolated water extract of *Grifola frondosa* stimulates mineralization and ALP activity of human osteoblastic cell cultures (HOS58 and SaOS-2). Total water extract of *Grifola frondosa* (GF) mushrooms stimulates bone formation, bone mineralization as well as enhances the osteogenicity of cultured bone cells (Saif et al. 2007). Vitality and maturation of bone cells are responsible for the activity of alkaline phosphate and mineralization, which are used as indicators for maturation of bone. Mushrooms play a major role in osteoclastogenesis, i.e. reduced break down of bone cells. Ethanol extracts of *Ganoderma lucidum* have preventive effects against the ovariectomized (Ovx) rats. NF-κB ligand (RANKL) is one of the members of tumour necrosis factor (TNF) superfamily and also known as type II membrane protein. The receptor activator of nuclear factor kappa-B ligand (RANKL) has the ability to stimulate bone development, bone density and take part in the formation of the osteoclast. The ethanol extracts of *Ganoderma lucidum* showed response in activating the NF-κB ligand (RANKL) and inhibited signalling of tumour necrosis factor α (TNF-α) (Miyamoto et al. 2009).

Anti-ageing property of mushroom

Recent studies showed that medicinal mushroom *Tricholo malobayense* possesses many bioactive compounds responsible for anti-ageing activity. Extracted polysaccharide TLH-3 isolated from the fresh fruiting body of *Tricholo malobayense* shows anti-ageing capability when measured in D-galactose-induced aged mice model (Ding et al.

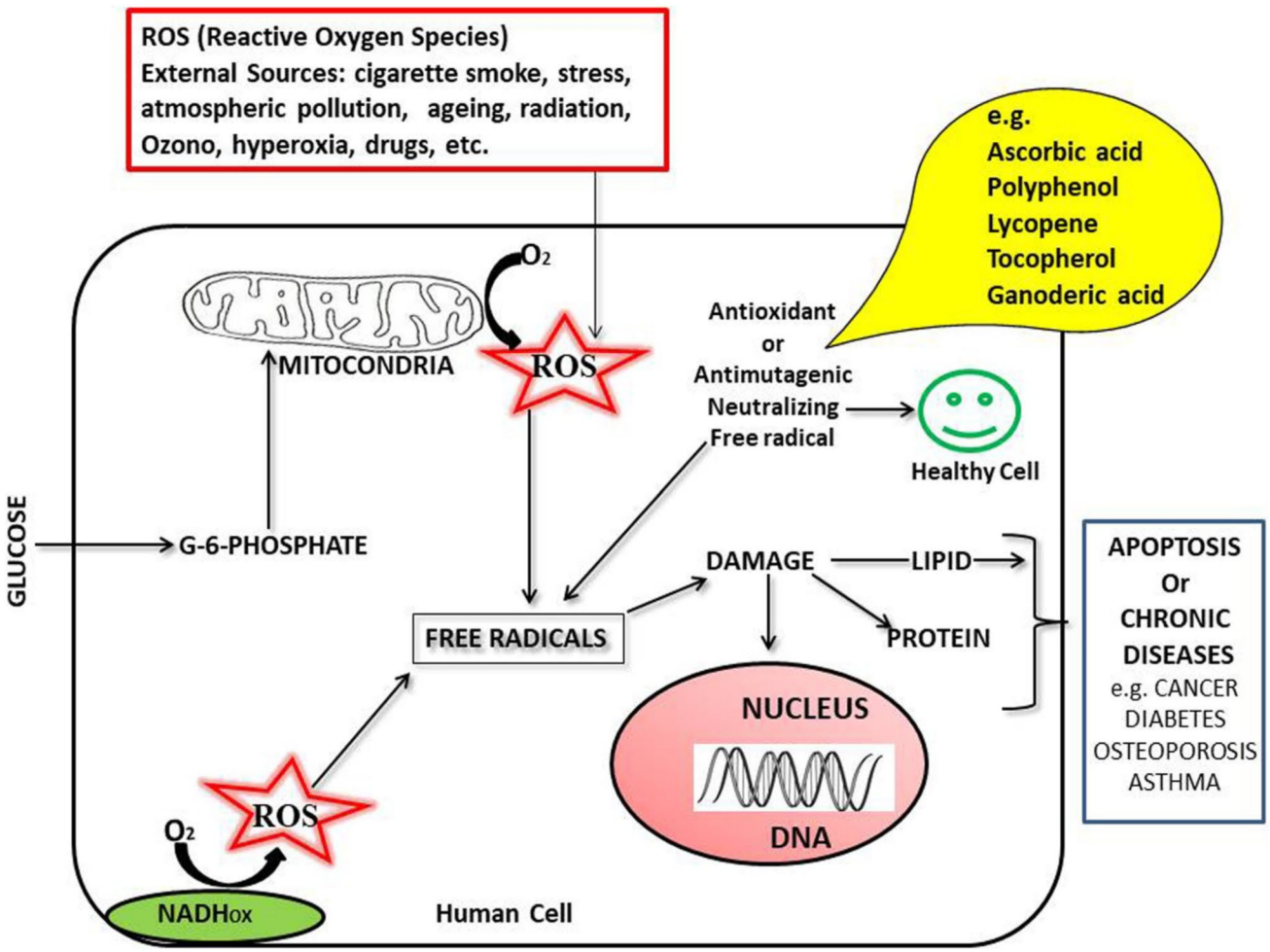

Fig. 5 Antioxidant and antimutagenic activity as shown by different bioactive molecules

2016). The isolated methanol extract of medicinal mushroom, *Ganoderma lucidum*, (Krupodorova et al. 2015) has two novel anti-aging ergosterols, ganodermasidase A and B; these compounds extend the replicative life span of *Saccharomyces cerevisiae* by regulating the expression of UTH1 oxidative stress-responsive genes (Weng et al. 2010). Table 5 depicts the list of patents that confirmed anti-aging/menopause and other symptom relief using *Ganoderma lucidum*s pores with many other therapeutic applications (Chung and Tong 2005). Many extracted ingredients from the fruiting body of medicinal mushroom such as polysaccharides, polyphenolic, phenolics, terpenoids, selenium, vitamins, and volatile organic compounds show tremendous antioxidant, anti-ageing, anti-wrinkle, skin whitening, and moisturizing effects (Hyde et al. 2010; Wu et al. 2016). Water-soluble polysaccharide (AAP I-a) isolated from *Auricularia auricular* prevents oxidative stress in D-galactose-induced aged mice. A paste of polysaccharides is used for the production of antiaging creams or lotions and other skin-related cosmetics in the industry (Zhang et al. 2011). These polysaccharides (AAP I-a) have the ability to delay ageing as they result in the inhibition of the functional enzymes responsible for skin ageing, such as elastase, tyrosinase, hyaluronidase and MMP-1 enzymes. These polysaccharides further help in restoring the skin elasticity and stimulating the expression of collagen synthesis.

Anti-obesity activity of mushroom

Obesity is a major worldwide health problem, and it has been implicated in the development of various diseases, such as diabetes, hyperlipidemia, and atherosclerosis. Extracts of *Pleurotus Florida* showed promising effects against obesity, their administration to high-cholesterol diet rats inhibits their weight gain, reduces total cholesterol level, LDL as well as triglycerides and also reduces fat deposition within the body of high-fat obese mice (Iuchi et al. 2015). β-Glucan found in the extract of *Pleurotus sajor-caju* inhibits obesity in high-fat diet obese mice (Kanagasabapathy et al. 2013). Comparative study of eight different edible mushrooms shows anti-obesity and hypolipidemic activities in fat-loaded (corn oil) mice. In vitro study showed that the water extract of *Pleurotus eryngii* (PEE) reduces pancreatic lipids and *Grifola frondosa* (Hiroaki 1997) inhibits pancreatic lipase by inhibiting hydrolysis of 4-methylumbelliferyl (4-MUO)

Table 5 Patented products of medicinal mushroom for the cure of respective diseases

S. no.	Claimed product/extract name	Patent no.	Activity claimed	Inventors	Sources
1	Glycoprotein with antidiabetic, antihypertensive, antiobesity and antihyperlipidemic effects from *Grifola frondosa*, etc.	US 7214778	Antidiabetic	Zhuang et al. (2007)	http://www.freepatentsonline.com
2	Mushroom extracts having anticancer activity	US 7258862	Anticancerous	Mahajna et al. (2007)	
3	Anti-cancer combination treatment and kit-of-parts	US 9072776	Anticancerous	Kristiansen (2015)	
4	Mushroom extracts from *Agaricus, Hericium erinaceum*, and *Hypsizigus marmoreus* as insulin secretion stimulators and health foods for prevention and therapy of diabetes mellitus	JP 2012077004A	Antidiabetic	Takeshi et al. (2012)	
5	Antiviral and antibacterial activity from medicinal mushrooms	US 8765138	Antiviral, Antibacterial	Stamets (2014)	
6	Basidiomycetes, Basidiomycetes extract composition, health foods, and immunopotentiators	US 7517682	Immune Function	Watanabe (2009)	
7	Method to prepare *Ganoderma lucidum* polysaccharides possessing anti-obesity properties and uses there of	US 9758595	anti-obesity	Ko et al. (2017)	
8	Process for producing, methods and compositions of glucuronoxylomannan as nutriceutical agent from higher basidiomycetes mushroom	US 6383799	Control hyperglycaemia	Wasser and Reshetnikov (2002)	
9	Antimutagenic effects of Ganoderma lucidum spores	US 7087233	Antimutagenic	Chung and Tong (2006)	
10	Anti-aging/menopause symptoms relief using *Ganoderma lucidum* spores	US 6908614	Anti-ageing	Chung and Tong (2005)	

and trioleoylglycerol emulsified with lecithin (Mizutani et al. 2010).

Conclusion

The administration of an extract of medicinal mushrooms can help to treat the patients or protect people from a large number of diseases. The extract of mushroom can be incorporated into the diet as a nutritional supplement. The bioactive compounds in both fruiting bodies and mycelial extract of medicinal mushroom show positive response in human health. The mushroom production and extraction of their bioactive metabolites are key features for the development of efficient biotechnological methods. Chemically defined molecules isolated from medicinal mushroom may develop as functional foods and as a source of new innovative drugs. Nowadays, many countries develop industries which use mushroom mycelia as a medicinal substance for the production of tonics to treat diseases. From the higher class of fungi Basidiomycetes, mushroom extracts are developed as a source of novel pharmaceutical agents against a variety of diseases by biotechnological processes. Further studies including clinical trials of bioactive compounds can be used against infection and other diseases. We hope with this review, there is an increased use of mushroom in medicinal research, with the long-term objective of developing effective therapies for several diseases.

Future prospects

Mushrooms and their biologically active substances can be promising source materials in future for the pharmaceutical industry to treat various diseases with minimum toxicity, unlike today's available drugs, which have severe side effects. Mushrooms can be used as functional foods and can be increased in the diet of the people to protect them from life-threatening disorders. Till now most of the studies have been performed on animals or in cell culture models and human experimental studies are very less and generally, the results are not always supportive towards in vitro studies. Therefore, more experiments need to be done with reliable experimental and clinical data from human trails to clarify whether the reports related to health are valid and significant. Further strategies are required for enhancing quality control procedures to standardize mushroom preparations to understand better the mechanisms of action and to characterize the active components of maximum medicinal mushrooms. Further research should be done to analyze the polysaccharide composition, particularly its components which form dietary fibers and which have positive health effects. Information regarding effects of storage, preservation and culinary treatment on mushroom constituents is necessary to further help the researchers to work on it efficiently.

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Compliance with ethical standards

Conflict of interest The authors declared no conflict of interest with respect to the research, authorship and publication of this article.

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