# Biological Activities of Some Edible Mushrooms

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**Abstract** Since ancient times, mushrooms have been a valuable food source and traditional medicine worldwide. Edible mushrooms possess high nutritional value and medicinal significance due to the presence of a large number of active ingredients that cause the development of therapeutic functions. They are used to treat severe diseases like microbial and viral infections, cancer, tumors, inflammation, and cardiovascular and immune diseases. Mushrooms contain various bioactive compounds, including α- and ß-glucans, proteoglycan, lectin, phenolic compounds (flavonoids, flavonoids, phenolic acids), polysaccharides, triterpenoids, steroids, lentinan, schizophyllan, lovastatin, pleuran, glycopeptides, alkaloids, dietary fiber, and others. The biological activities of some well-known edible mushrooms are discussed in this chapter.

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## Abbreviations

| | |
|---|---|
| ABTS | Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) |
| AChE | Acetylcholinesterase |
| AD | Alzheimer's disease |
| CAT | Catalase |
| CDK | Cyclin-dependent kinase |
| COX | Cyclooxygenase |
| DPP-4 | Dipeptidyl peptidase-4 |
| DPPH | 2,2-Diphenyl-1-picrylhydrazyl |
| EtOH | Ethanol |
| FRAP | Ferric reducing antioxidant power |
| GLP | Glucagon-like peptide-1 |
| GSH | Glutathione |
| $H_2O$ | Water |
| HDL | High-density lipoprotein cholesterol |
| IFN-γ | Interferon-γ |
| IL | Interleukin |
| iNOS | Inducible nitric oxide synthase |
| JNK | c-Jun N-terminal kinases |
| LDL | Low-density lipoprotein cholesterol |
| LPS | Lipopolysaccharide |
| MDA | Malondialdehyde |
| MMK | Matrix metalloproteinase |
| NF-κB | Nuclear factor kappa-light-chain enhancer of activated B cells |
| NK | Natural killer |
| NLRP3 | Nod-like receptor protein 3 |
| NO | Nitric oxide |
| Nrf2 | Nuclear factor-E2-related factor 2 |
| PGE2 | Prostaglandin E2 |
| PSK | Polysaccharide K/Krestin |
| PSP | Polysaccharopeptide |
| SOD | Superoxide dismutase |
| TC | Total cholesterol |
| TG | Triglyceride |
| TLR4 | Toll-like receptor 4 |
| TNF | Tumor necrosis factor |

## 1 Introduction

Macrofungi are important natural sources that benefit human health and prevent various diseases. Different mushroom species contain bioactive chemicals (mainly phenolic compounds, such as phenolic acids, flavonoids, and terpenoids). Due to their enormous biological activities, polysaccharide-protein complexes in medicinal mushrooms have attracted researchers' attention worldwide. However, their chemical composition mostly depends on their microhabitat's specific environmental conditions, particularly the surrounding mycelia's physicochemical properties (Raseta et al. 2020). The mushrooms' bioactive compounds exhibit immunomodulatory, anticancer, antidiabetic, antihyperlipidemic, microbiota-modulating, anti-inflammatory, antimicrobial, and antioxidative properties. Prepared extracts from individual mushrooms are used to produce dietary supplements as immunomodulatory agents and cosmetics (as regenerating cosmetics (regenerating the skin and treating atopic dermatitis)). They can be used as natural preservatives or probiotics (Golak-Siwulska et al. 2018b). In the following sections, we have selected some important mushroom species and described their biological activities.

## 2 *Agaricus bisporus* (J.E. Lange) Imbach

*Agaricus bisporus* (J.E. Lange) Imbach (Fig. 1a) (*Agaricaceae*) is known as button mushroom, common mushroom, cultivated mushroom, etc. It is one of the world's most common and widely consumed mushrooms.

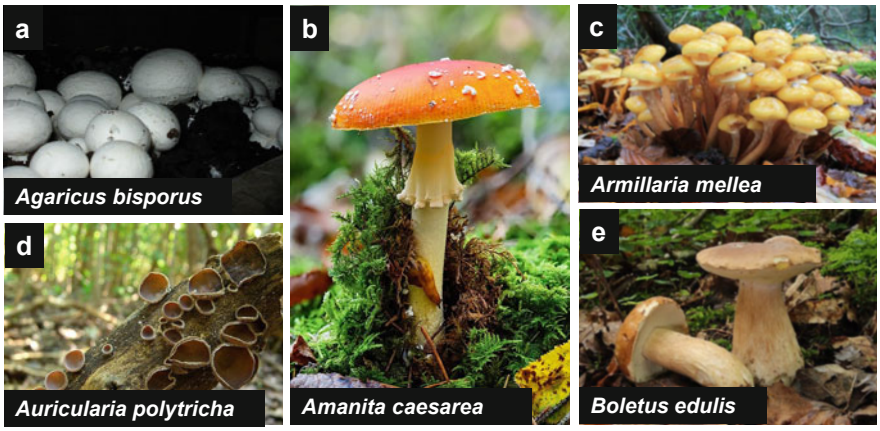


**Fig. 1** (**a**) *Agaricus bisporus*; (**b**) *Amanita caesarea*; (**c**) *Armillaria mellea*; (**d**) *Auricularia polytricha*; (**e**) *Boletus edulis*. Attrition: CC-BY-4.0; https://commons.wikimedia.org

*A. bisporus* exhibits an antioxidant effect higher than a lot of edible mushrooms. This effect is attributed to its phenolic compounds, serotonin, and tocopherol content (Liu et al. 2013; Reis et al. 2012).

Extracts, polysaccharides, lectins, and propionate of *A. bisporus* showed antidiabetic activity in different test models. It (200 mg/kg) reduced plasma glucose levels by 25% in streptozotocin-induced diabetic rats. It also decreased plasma triglyceride levels by 39%. This mushroom possesses antidiabetic and antihyperlipidemic properties. *A. bisporus* contains not only phytosterols, like all mushrooms, but also lovastatin, which lowers the cholesterol levels in the body to reduce the development of cardiovascular diseases (Ekowati et al. 2018; Jeong et al. 2010; Yamaç et al. 2010; Xu et al. 2013).

Water-soluble extract of *A. bisporus* suppressed the progression of liver fibrosis by the antioxidant, anti-inflammatory, and antiapoptotic mechanisms in vitro and in vivo. The anti-inflammatory action of this mushroom is related to a decrease in toll-like receptor 4 (TLR4) expression and a downregulation of Nod-like receptor protein 3 (NLRP3) inflammasome activation (Gallego et al. 2021). *A. bisporus* α-glucan increased nitric oxide and tumor necrosis factor (TNF)-α production by bone marrow-derived macrophages from mice in vitro (Volman et al. 2009). *A. bisporus* β-glucan inhibited the expression of interleukin (IL)-1β and cyclooxygenase (COX)-2, suggesting that different components of this mushroom exhibit anti-inflammatory action (Smiderle et al. 2013).

*A. bisporus* extracts or different components inhibited proliferation of cancer cells, including PC3, DU145 prostate cancer, HL-60 leukemia cells, MCF-7 breast cancer cell, and sarcoma 180, and induced apoptosis. Moreover, *A. bisporus* extract inhibited aromatase at the estrogen receptor in vitro in MCF-7 cells and also in vivo in rats (Chen et al. 2006; Golak-Siwulska et al. 2018b; Jeong et al. 2012). *A. bisporus* polysaccharides also possess anticancer effect via immunomodulatory effects. They stimulated the production of nitric oxide (NO), IL-6, and TNF-α and activated nuclear factor kappa-light-chain enhancer of activated B cells (NF-κB) pathway in macrophages but had no effect on the proliferation of human colon cancer cells or murine sarcoma cells. However, it reduced tumor growth in sarcoma 180-inoculated mice (Jeong et al. 2012).

Thus, *A. bisporus* is not only a good source of food but also exhibits medicinal values. It exhibited antioxidant, antidiabetic, antihyperlipidemic, anti-inflammatory, and anticancer properties.

## 3 *Agaricus blazei* Murill

*Agaricus blazei* Murill (synonym *Agaricus brasiliensis*) belongs to the *Agaricaceae* family. It is commonly known as almond mushroom, mushroom of the sun, or God's mushroom. It is edible, with a sweet taste and a fragrance of almonds. This mushroom gets much attention due to its immunomodulatory effect. Especially there is a commercial mushroom extract, namely, Andosan, containing 82%

*A. blazei*, 15% *Hericium erinaceus*, and 3% *Grifola frondosa*. Many clinical trials have tested the immunomodulatory, anticancer, and anti-inflammatory effects of Andosan.

*A. blazei* extracts and polysaccharides showed anti-inflammatory activity in many studies. *A. blazei* extract rich in cerevisterol suppressed IL-6 secretion and expression of the cyclooxygenase (COX)-2 in vitro (Song et al. 2012). *A. blazei* polysaccharides have anti-inflammatory activity interfering in the biosynthesis and secretion of inflammatory mediators. Oral administration suppressed the expression of NF-κB and intercellular adhesion molecule 1 (ICAM-1). It reduced the serum levels of IL-1β, TNF-α, COX-2, and inducible nitric oxide synthase (iNOS) in vivo (Wang et al. 2013b). The anti-inflammatory effect of *A. blazei*-based extract, Andosan, has been reported in a placebo-controlled clinical study in patients with ulcerative colitis or Crohn's disease. The extract showed a partial reduction in pro- and anti-inflammatory cytokines (Therkelsen et al. 2016). Thus, *A. blazei* possesses anti-inflammatory activity in vitro and in vivo, associated with decreased biosynthesis and secretion of inflammatory mediator expression of enzymes, the polysaccharides, the main responsible for this activity.

The antioxidant effect of *A. blazei* is one of the main underlying mechanisms of this mushroom that is well-documented. It scavenged 2,2-diphenyl-1-picrylhydrazyl (DPPH); azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radicals also exhibited antioxidant action in ferric reducing antioxidant power (FRAP) assay and lipid peroxidation assay in vitro (Bach et al. 2019; Carneiro et al. 2013; Wei et al. 2020). *A. blazei* extracts also exhibited antioxidant effect in vivo by reducing malondialdehyde (MDA) (a marker of lipid peroxidation) and alleviated glutathione (GSH) level, enhancing superoxide dismutase (SOD) activity (Al-Dbass et al. 2012).

Oral administration of *A. blazei* polysaccharides reduced the triglyceride (TG), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL) and increased high-density lipoprotein cholesterol (HDL) plasma levels. Furthermore, it upregulated the expression of CYP7A1. This enzyme limits the conversion of CH to bile acid in the liver and inhibits the transcription factor SREBP-1C, a factor associated with TG metabolism and lipid deposition in cells (Ji et al. 2014; Li et al. 2020b).

Different extracts of *A. blazei* inhibited α-glucosidase in a dose-dependent manner. They also improved the glucose uptake by insulin-resistant HepG2 cells and alleviated postprandial hyperglycemia (Al-Dbass et al. 2012). *A. blazei* extract decreased reduced serum glucose levels as well as HbA1C compared to control in streptozocin-induced diabetes (Ji et al. 2014; Vitak et al. 2015). In addition, *A. blazei* extracts ameliorated diabetic neuropathy by reducing TNF-α and IL-1β levels, suppressing inflammation, and increasing antioxidant status (Ji et al. 2014). It also exhibited antidiabetic effects in human studies. In a randomized, double-blind, placebo-controlled clinical study, *A. blazei* extract improved insulin resistance among subjects with type 2 diabetes and increased adiponectin concentration after 12 weeks of oral treatment compared to control (Hsu et al. 2007).

*A. blazei* extract exhibited an antimicrobial effect against several common pathogens. It showed a higher antimicrobial effect against gram-positive bacteria than

gram-negative ones. The antimicrobial effect of *A. blazei* is attributed to the phenolic content (Bach et al. 2019).

Oral administration of hydroalcoholic extract of *A. blazei* exhibited anxiolytic-like activity in mice, similar to positive control diazepam (Ali et al. 2021). Ethanol extract of *A. blazei* suppressed the rotenone-mediated decrease in dopamine transporter and vesicular monoamine transporter 2 expressions, inhibited apoptosis, and showed neuroprotection (Gobi et al. 2019).

Many studies have mainly focused on cancer-related activities of *A. blazei*. Extracts and different components of this mushroom inhibited the proliferation of various cancer cell lines related to the modulation of cyclin-dependent kinases and their inhibitors, cell cycle proteins. *A. blazei* activated caspases, stimulated release of cytochrome c and radical oxygen species production, modulated proapoptotic and antiapoptotic proteins in turn, and stimulated apoptosis associated with NF-κB and c-Jun N-terminal kinase (JNK) signaling (Jin et al. 2006; Kim et al. 2011; Matsushita et al. 2018; Yu et al. 2009). A. *blazei* also reduced tumor size and volume in animal models (Ito et al. 1997; Yu et al. 2009). *A. blazei* acts as immunostimulants, both in the proliferation and activation of lymphocytes (NK cells and T cells) and macrophages. These stimulated cells can produce cytokines, mainly IL-8 and IL-6 TNF-$\alpha$ (Bernardshaw et al. 2005; Johnson et al. 2009; Lima et al. 2011). Furthermore, randomized controlled trials also proved the immunomodulating effect of *A. blazei* (Tangen et al. 2015; Therkelsen et al. 2016). According to the literature, *A. blazei* contains compounds, including polysaccharides, proteins, steroids, nucleosides, and phenols, that may modulate tumorigenesis and carcinogenesis through different mechanisms. Anticancer activity seems to be associated with polysaccharides chiefly. The effects of different polysaccharides are likely to be mediated by various cell-surface receptors. The combination of such responses mediated from different polysaccharides conceivably provides greater tumor inhibition than if induced by a single polysaccharide.

In conclusion, *A. blazei* possesses anti-inflammatory, antidiabetic, antihyperlipidemic, anxiolytic, neuroprotective, hepatoprotective, anticancer, and immunomodulatory properties. It seems that *A. blazei* exhibited these biological effects mainly related to anti-inflammatory action. Unlike many other edible mushrooms, there is a commercial product of this mushroom. Current clinical trials have shown promising results in using this mushroom as an immunomodulator agent. However, adequately designed, further clinical studies on standardized extracts are needed.

## 4 *Amanita caesarea* (Scop.) Pers.

*Amanita caesarea* (Scop.) Pers. (*Amanitaceae*) (Fig. 1b) is a popular edible mushroom with good flavor and taste. *A. caesarea* methanol extract scavenged DPPH radical stronger than positive controls, butylated hydroxytoluene, and butylated hydroxyanisole with an $IC_{50}$ value of 0.7615 mg/mL. It inhibited the peroxidation

of linoleic acid in β-carotene-linoleic acid assay. The inhibition values of *A. caesarea* extract were higher than those of Trolox, similarly to butylated hydroxytoluene, and lower than butylated hydroxyanisole. Methanol, chloroform, and acetone extracts of *A. caesarea* possess an antimicrobial effect with MIC values of 312.5–39 mg/mL against several common pathogens. This mushroom exhibited the highest antimicrobial effect against *Candida albicans* and the lowest antimicrobial effect against *Klebsiella pneumoniae* (Doğan and Akbaş 2013).

An *A. caesarea* polysaccharide, APCS, molecular weight 18,620 Da and 33,500 Da, exhibited good in vitro activity in Alzheimer's disease (AD). Treatment with APCS prior to L-glutamic acid (L-Glu) co-exposure reversed the decreased cell viability, inhibited apoptosis, decreased the accumulation of intracellular ROS, and alleviated mitochondrial membrane potential in HT22 cells (Li et al. 2019). APCS and another polysaccharide, ACPS2, with an average molar mass of 16.6 kDa isolated from *A. caesarea* alleviated Alzheimer's disease-like symptoms in APP/PS1 and BALB mice. Both polysaccharides reduced amyloid deposition, tau hyperphosphorylation, neuroinflammation, and brain damage. These effects were mainly related to its suppression of endoplasmic reticulum stress and oxidative stress through regulation of nuclear factor-E2-related factor 2 (Nrf2) signaling and NF-κB activation (Hu et al. 2021; Li et al. 2019).

## 5 *Armillaria mellea* (Vahl) P. Kumm

*Armillaria mellea* (Vahl) P. Kumm (*Tricholomataceae*) (Fig. 1c) is known as a honey mushroom. It is an edible mushroom used for its medicinal and health-promoting properties worldwide. *A. mellea* was used to treat palsy, headache, hypertension, insomnia, dizziness, vertigo, neurasthenia, insomnia, and convulsion. It is also a component of traditional Chinese medicine "Tianma" (Sun et al. 2020).

The phenolic contents of the hydromethanolic extract and ethanolic extract of *A. mellea* were 21.68 and 5.70 mg/g. The hydromethanolic extract exhibited DPPH, 2,2'-ABTS free radical scavenging and reducing abilities with $EC_{50}$ values of 452.60, 140.57, and 129.45 g/mL, respectively (Zavastin et al. 2015). The ethanolic extract was more effective in 15-lipoxygenase, α-glucosidase, and ferrous ion chelation assays ($EC_{50}$ = 67.93, 290.93, and 8.54 g/mL, respectively).

Water extract of *A. mellea* induced maturation of human dendritic cells without induction of cytokine expression (Kim et al. 2008). *A. mellea* and some secondary metabolites of this mushroom possess anticancer properties. Armillarikin induced cell death of human leukemia K562, U937, and HL-60 cells and hepatocellular carcinoma HCC, Huh7, HA22T, and HepG2 cells. It also induced apoptosis by activating procaspase-3, procaspase-8, and procaspase-9, inducing cleavage of PARP (Chen et al. 2014, 2016). 5′-Methoxy-armillasin, 5-hydroxyl-armillarivin, armillaridin, armillartin, armillarin, melleolide B, armillarilin, armillasin, armillarigin, and melleolide exhibited highly cytotoxic activity on HepG2 cells (4.95–37.65μg/mL). Melleolide was the most cytotoxic compound, with an $IC_{50}$

value of 4.95μg/mL. It induced apoptosis by activating different caspases like armillarikin (Li et al. 2016).

Different extracts, as well as metabolites of this mushroom, have an anti-inflammatory effect. Ethanol extract of *A. mellea* protected lipopolysaccharide (LPS)-induced cell death in THP-1 cells. It attenuated LPS-induced nitric oxide (NO) and prostaglandin E2 (PGE2) production and reduced levels of pro-inflammatory cytokines, including TNF-α, IL-4, and IL-8. This extract suppressed the LPS-induced expression of COX-2 and iNOS but did not change COX-1 (Wu et al. 2007). Similarly, a fraction obtained from a sub-ethyl acetate extract of crude ethanol extract of *A. mellea* significantly suppressed the production of inflammation mediator NO and inflammatory cytokines TNF-α, IL-6, and IL-1 β in a dose-dependent manner. Moreover, the same fraction downregulated the phosphorylation levels of NF-κB p65, inhibitory κB-α (IκB-α), and JNK pathways in BV-2 cells. 5-Hydroxymethylfurfural, 2-furoic acid, 4-hydroxybenzoic acid, vanillic acid, syringate, daidzein, and genistein were isolated from this fraction (Geng et al. 2017). In addition, sulfated polysaccharides containing fucose, galactose, glucose, and mannose as major sugars inhibited TNF-α and IL-6 production associated with suppression of NF-κB (Chang et al. 2013). Different compounds isolated from this mushroom, namely, dehydroarmillylorsellinate, arnamial, armillarin, and melleolide D, inhibited 5-lipoxygenase with $IC_{50}$ values of 0.3 ± 0.1, 1.0 ± 0.2, 5.2 ± 1.4, and >10 mM in neutrophils (König et al. 2019).

Protoilludane sesquiterpenoid aromatic esters of *A. mellea* ameliorated depressive behaviors in depressive mice induced by chronic unpredictable mild stress. They reduced hypothalamic-pituitary-adrenal axis hyperactivity by restoring GR negative feedback regulation caused by chronic unpredictable mild stress. These compounds may enhance synaptic plasticity and function by controlling levels of related proteins CREB, brain-derived neurotrophic factor, and synaptic-related protein PSD95. They may have anti-inflammatory effects on the central nervous system by reducing levels of inflammatory cytokines and NLRP3 protein and inhibiting neuronal apoptosis (Sun et al. 2020).

Oral administration of polysaccharide-enriched *A. mellea* fruiting body extract reduced fasting blood glucose and improved glucose intolerance and insulin resistance in type 2 diabetes mellitus. This extract also modulated lipid metabolism by enhancing lipolysis and suppressing lipogenesis (Yang et al. 2019).

Overall, *A. mellea* is a popular delicious mushroom. Besides, it possesses various biological effects, including anti-inflammatory, antioxidant, cytotoxic, antidepressant, and antidiabetic effects.

## 6 *Auricularia* Species

*Auricularia* species are known as wood ears or jelly ears due to their ear-shaped gelatinous fruiting bodies. They are growing widely and also cultivated. They have been widely consumed as edible medicinal mushrooms for thousands of years.

*Auricularia* species exhibited antioxidant effects both in vitro and in vivo. Antioxidant effect of these mushrooms involved mechanism of action of different effects (Agbor et al. 2022; Chellappan et al. 2016; Chiu et al. 2014; Wu et al. 2010). *A. auricula* extract scavenged ABTS ($EC_{50} = 1.2$ mg/mL), DPPH ($EC_{50} = 3.3$ mg/mL), superoxide ($EC_{50} = 0.7$ mg/mL), and hydroxyl radicals ($EC_{50} = 9.0$ mg/mL) and inhibited peroxidation of egg yolk homogenate ($EC_{50} = 0.1$ mg/mL) (Zeng et al. 2012).

Administration of 200 mg/kg of a β-glucan fraction of *A. polytricha* (Fig. 1d) reduced serum oxidative stress markers, glial cell aggregation, and inflammatory infiltrate compared to streptozotocin-induced diabetic rats and exhibited a neuroprotective effect (Agbor et al. 2022). Different polysaccharides of *Auricularia* species were studied. *A. auricula* polysaccharide comprising mannose, rhamnose, glucuronic acid, glucose, galactose, arabinose, and fucose with a molecular weight of 23.51 kDa increased the NO production and the phagocytosis of RAW264.7 macrophages at 0.5 mg/ml. It also induced the secretion of TNF-α and IL-6 from macrophages (Bao et al. 2020). Another *A. auricula* polysaccharide induced endotoxin tolerance by downregulating NF-κB and altering cytokine secretion (Perera et al. 2020). Oral administration of *A. auricula* polysaccharide fraction also increased the weights of the spleen and thymus in aged mice after oral administration, which suggested a possible effect on the activation and differentiation of the thymus lymphocyte and modulating the immune functions of aged mice (Wu et al. 2010). It has been reported that *Auricularia* polysaccharides bind different membrane receptors like toll-like receptor 4 and Dectin-1, activating the expression of pro-inflammatory cytokines and iNOS. It activated the innate immune system and effector cells, including macrophages, B and T1 lymphocytes, and natural killer (NK) cells (Liu et al. 2022).

Treatment with *A. auricula* polysaccharides for 40 days decreased the serum TC, TG, LDL, and MDA levels. It increased serum SOD and GSH-Px activity dose dependently. Also, it ameliorated left ventricle ejection fraction and left ventricular short axis fraction shortening and improved heart function in aged mice (Wu et al. 2010). *A. auricula-judae* polysaccharides also affect plasma TG, TC, and LDL cholesterol in dietary-induced hyperlipidemic rats. Moreover, polysaccharides of this mushroom downregulated liver adipogenic-related gene expressions, suppressed cholesterol synthesis-related gene levels, upregulated fatty acid oxidation-related gene expressions, and induced cholesterol efflux-related gene expressions, thus improving mice hepatic lipid metabolism (Liu et al. 2022; Zeng et al. 2013). The level of matrix metalloproteinase (MMP)-13 expression in atherosclerotic plaques is related to the progression of plaques. *Auricularia* polysaccharides inhibited atherosclerosis development by reducing the expression of MMP-13 in plaques and decreasing the production of collagen fibers (Wang et al. 2007).

*A. auricula* polysaccharide treatment at 100 and 400 mg/kg decreased blood glucose levels by promoting glucose metabolism. It prevented diabetic nephropathy by regulating blood urea nitrogen, creatinine, uric protein, and inflammatory-related factors. These effects were associated with modulations of the antioxidative system and NF-κB signaling (Hu et al. 2017).

Due to their antioxidant effects, water extract of *A. polytricha* attenuated paracetamol-induced hepatotoxicity and hepatic lipid accumulation in rat models (Chellappan et al. 2016; Chiu et al. 2014).

A water-soluble *A. auricula-judae* polysaccharide extract enhanced wound healing by promoting fibroblast and keratinocyte proliferation, migration, and invasion, increasing collagen synthesis and decreasing E-cadherin expression (Mapoung et al. 2021).

Protein extracts of *A. auricula-judae* exhibited antimicrobial activity with MIC values of 5μg/mL against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Bacillus subtilis*, and *Candida albicans.* They showed the best antimicrobial effect against *Escherichia coli* with a MIC value of 2.5μg/mL (Oli et al. 2020).

*Auricularia* species exhibited a cytotoxic effect on different cancer cells, including HCT-15, Huh-7, SK-MEL-5, SNU-213, A-549, and SNU-484. *A. auricula* induced PARP cleavage; activated caspases 3, 7, and 9; downregulated Bcl-xL; upregulated proapoptotic proteins Bak, Bid, and Bik; and caused apoptosis. Also, it downregulated PRDX1 expression, causing inactivation of antioxidant enzymes (Kang et al. 2020). *A. polytricha* suppressed cell proliferation and induced apoptosis. *A. polytricha* polysaccharides caused cell cycle arrest at the G0/G1 phase and upregulated the expression of cyclin-dependent kinase (CDK) inhibitors p53 and p21, whereas downregulated the expression of cyclin A, cyclin D, and CDK2 in A549 cells (Yu et al. 2014).

*Auricularia* species possess antioxidant, cardioprotective, antihyperlipidemic, antidiabetic, immunomodulatory, anticancer, antimicrobial, hepatoprotective, and neuroprotective effects. Research on this species mainly focused on *A. auricula-judae* and *A. polytricha* polysaccharides.

## 7 *Boletus edulis* Bull

*Boletus edulis* Bull. (Boletaceae) (Fig. 1e) is widely distributed across Europe, Asia, and North America in the Northern Hemisphere. It is one of the most popular edible mushrooms due to its flavor and taste.

Antioxidant activity of *B. edulis*, extracts, fractions, or some components has been studied widely. It scavenged DPPH, ABTS, and ·OH radicals. It also exhibited antioxidant activity in β-carotene bleaching and FRAP, reducing power, ferrous ion chelating, cupric reducing antioxidant capacity assay (Garcia et al. 2022; Guo et al. 2012, 2020a; Heleno et al. 2015; Luo et al. 2012). *B. edulis* polysaccharides enhanced the activity of antioxidant enzymes SOD, GSH, and GSH-Px and reduced MDA levels (Xiao et al. 2018, Zheng et al. 2019).

*B. edulis* polysaccharides ameliorated carbon tetrachloride-induced hepatic damage revealed by smaller hepatocyte lesions, decreased ALT and AST serum levels, and increased antioxidant capacity (Zheng et al. 2019). *B. edulis* polysaccharides reduced fasting blood glucose, ALT and AST levels, and serum lipid profile, similar

to metformin in high-fat-induced and streptozocin-induced diabetes. They exhibited anti-hepatotoxic effects associated with decreased sterol regulatory element-binding protein 1, NF-κB and TNF-α expressions and increased CYP7A1 expression (Xiao et al. 2018).

*B. edulis* polysaccharides suppressed ovalbumin asthma, reduced airway resistance, reduced lesion degree and mucosubstances, reduced pro-inflammatory responses (lower IL-4 and interferon-γ (IFN-γ) level), and increased anti-inflammatory responses (higher proportion of anti-inflammatory CD4+CD25+-FOXP3+ Treg cells) significantly increased in mouse models of asthma (Wu et al. 2016).

*B. edulis* extracts, different components including polysaccharides, lectins, and biopolymers (composed of polysaccharides and glycoproteins), exhibited anticancer effects by boosting the immune system and exhibiting toxicity to cancer cells. *B. edulis* polysaccharides increased the spleen and thymus indices, enhanced splenocytes proliferation, increased NK cell and CTL activities in the spleen, and stimulated the secretion of the cytokines IL-2 and TNF-α in Renca tumor-inoculated mice (Wang et al. 2014a). A polysaccharide purified from *B. edulis* exhibited an anticancer effect on non-small cell lung cancer A549 in vitro and in vivo. Moreover, it inhibited A549, MDA-MB-231 human breast cancer cell, and Ca761 mouse breast cancer cell proliferation associated with G1 or S phase cell cycle arrest and downregulated CDK4 level. It also arrested apoptosis by activating the expression of PARP, caspase-3, caspase-8, and caspase-9 and upregulated the Bax/Bcl-2 (Meng et al. 2021; Zhang et al. 2021). *B. edulis* lectin inhibited the proliferation of MCF-7 cells, hepatoma Hep G2 cells, and colorectal cancer HT29 cells and reduced the migratory ability of Runt-related transcription factor 2 expressing melanoma cells in a xenotransplanted zebrafish model (Bovi et al. 2013; Valenti et al. 2020). *B. edulis* biopolymer exhibited an antiproliferative effect in colon cancer cells (LS180) associated with a cell cycle arrest in $G_0/G_1$ phase by altering the p16/cyclin D/CDK4–6/pRb pathway. It also induced apoptosis in a p53-dependent manner (Lemieszek et al. 2013, 2016).

Water extract of *B. edulis* exhibited antimicrobial and anti-biofilm properties against multidrug-resistant pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter species*) in different test systems. This extract contains phenolics, including gallic acid, catechin, 2,4-dihydroxybenzoic acid, 2,5-dihydroxyphenylacetic acid, and protocatechuic acid. It is recommended for use in the prevention of wound infection, particularly by multidrug-resistant pathogens (Garcia et al. 2022).

*B. edulis* is one of the most delicious mushrooms with multiple health benefits. It possesses antioxidant, antidiabetic, anti-inflammatory, antimicrobial, anti-hepatotoxic, and anticancer properties.

## 8 *Coprinus comatus* (O.F. Müll.) Pers.

*Coprinus comatus* (O.F. Müll.) Pers. (*Agaricaceae*) (Fig. 2a) is an edible and medicinal fungus widely distributed in most parts of the world.

Antidiabetic effects of *C. comatus* have been shown in many studies. *C. comatus* extracts or some components like comatin or polysaccharides decreased blood sugar levels by increasing plasma insulin levels through enhanced glucagon-like peptide-1 (GLP-1) and suppression of dipeptidyl peptidase-4 (DPP-4). This mushroom protected the pancreas, decreased blood sugar, and raised insulin and GLP-1 levels by inhibiting DPP-4 and reducing ROS (Ding et al. 2010; Husen et al. 2021; Ratnaningtyas et al. 2019, 2022). Furthermore, *C. comatus* polysaccharides inhibited α-amylase (Cao et al. 2019). Additionally, *C. comatus* also suppressed diabetic nephropathy. It ameliorated dysfunction in the kidney and relieved the renal oxidative stress and inflammation by modulating the PTEN/PI3K/Akt and Wnt-1/β-catenin pathways (Gao et al. 2021).

*C. comatus* was found to possess antioxidant properties in DPPH scavenging, hydroxyl scavenging, β-carotene bleaching and reducing power tests (Cao et al.

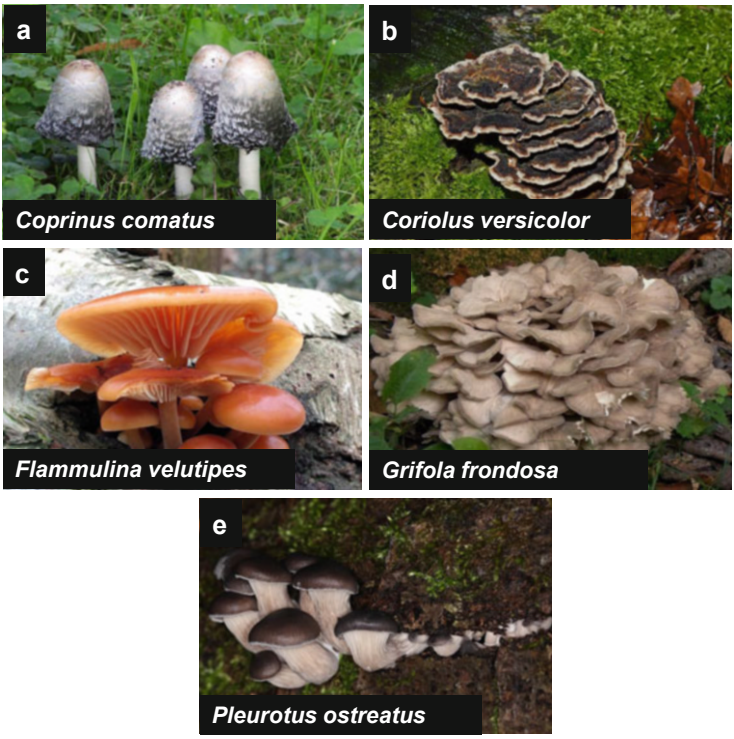


**Fig. 2** (**a**) *Coprinus comatus*; (**b**) *Coriolus versicolor*; (**c**) *Flammulina velutipes*; (**d**) *Grifola frondosa*; (**e**) *Pleurotus ostreatus*. Attrition: CC-BY-4.0; https://commons.wikimedia.org

2019; Sihoglu Tepe 2021). It significantly enhanced the GSH-Px, SOD, and catalase (CAT) activities (Gao et al. 2021). *C. comatus* also has an anti-hepatotoxic effect. Oral administration of this mushroom alleviated carbon tetrachloride-induced hepatic damage through increasing antioxidant capabilities, decreasing serum aminotransferase levels, and lipid peroxidation intensity (Stilinović et al. 2020).

This mushroom has beneficial effects on lipid metabolism. *C. comatus* polysaccharides inhibited adipocyte differentiation of 3 T3-L1 cells and high-fat diet-given mice. It caused a significant decrease in lipid accumulation through the downregulation of a major transcription factor involved in the adipogenesis pathway, including PPARγ related to the regulation of the Akt pathway (Park et al. 2020). Moreover, *C. comatus* polysaccharides diminished TC, TG, and LDL-C levels and increased HDL-C levels, indicating that oral administration of *C. comatus* polysaccharides alleviated lipid metabolism (Gao et al. 2021).

Like most mushroom polysaccharides, *C. comatus* polysaccharides have prebiotic effects on normal mice and mice with acute alcoholic liver injury by increasing relative abundance of *Firmicutes* and *Lactobacillaceae* and decreasing the abundance of *Rikenellaceae* (Li et al. 2020a).

*C. comatus* exhibited an anticancer effect in vitro. It inhibited proliferation and induced apoptosis of LNCaP (androgen-sensitive human prostate adenocarcinoma), U87MG and LN-18 glioblastoma cells, and ovarian cancer cells (ES-2). It induced extrinsic and intrinsic apoptotic pathways by reducing procaspases-3, procaspases-8, and procaspases-9 (Dotan et al. 2011; Nowakowski et al. 2021; Rouhana-Toubi et al. 2015). This mushroom reduced the androgen levels and prostate-specific antigen gene expression in LNCaP cells (Dotan et al. 2011).

In conclusion, *C. comatus* is an edible mushroom with health-promoting effects. Especially antidiabetic effect of this mushroom has been reported in several studies. It also regulated lipid metabolism, reduced hyperlipidemia, and inhibited the proliferation of cancer cells. Like most mushroom polysaccharides, it modulates gut microbiota. Thus, it could be regarded as healthy food. Health-promoting products can be produced from this mushroom. However, current research is limited, and more in vitro and in vivo studies are needed.

## 9 *Coriolus versicolor* (L. ex Fr.) Quel.

*Coriolus versicolor* (L. ex Fr.) Quel. (Fig. 2b) also named as *Trametes versicolor* (L.) Lloyd and *Polyporus versicolor* L. belongs to the genus *Coriolus* (*Polyporaceae*) (Cruz et al. 2016). *C. versicolor* is a saprotrophic mushroom species that commonly grows on dead logs, bark, stumps, tree trunks, and branches and lives by using lignocellulosic wastes in the temperate zones of Asia, Europe, and North America (Jo et al. 2010). It was named turkey tail mushroom because of its structural similarity. *C. versicolor* has been a well-known traditional medicine in the east for over 2000 years. It has been reported that *C. versicolor* fungus has antiradical, antioxidant, cytotoxic, anticancer, immunostimulant, and neurological effects. In

Japan and China, due to its immunostimulatory properties, it is used in the treatment of gastric cancer patients as an adjuvant. It is approved and has licensed products and food supplements (Dou et al. 2019; Hobbs 2005; Janjusevic et al. 2018). Recently, its neurological and synergistic effects with other drugs have been investigated.

Physiologically active polysaccharopeptide (PSP) and polysaccharide K (PSK, Krestin) from *C. versicolor* are isolated. 4-Isobutoxyphenyl palmitate, 2-hydroxyheptanoic-1-*O*-β-D-glucopyranosyl-9-methyl-4,8-sphinga-dienine (cerebroside), 3β-linoleyloxyergosta-7,22-diene, 3β-linoleyloxyergosta-7-ene, betulinic acid, terpenoids, flavonoids, and other many phenolic compounds derived from cinnamic acid also have been identified in this mushroom (Habtemariam 2020; Wan 2013).

The anticancer effects of *C. versicolor* were investigated in vivo, in vitro, and in clinical studies. PSK and PSP do not have only cytotoxicity; they also have an immunostimulating effect. At 100μg/ml and less, PSK and PSP concentrations were found to have cytotoxic activity. The extracts can inhibit carcinogenesis and tumor cell growth by activating cancer cell apoptosis. The underlying mechanism of this effect is caspase 3 activation, the key enzyme of apoptosis. As expected, markers of apoptosis induction have been stimulated while suppressing cancer cell survival-associated genes and proteins (antiapoptotic Bcl-2 Bcl-xL, etc.). In addition to the metastasis in cancer patients, inhibition of key angiogenic enzymes such as metalloproteases (MMP-9 or MMP-2) suppresses cell migration and invasion. It can reverse myelosuppression, which is a side effect of medications with chemotherapeutics. In myelosuppressive mice, especially in granulocyte colonies with stimulating factor (GCSF) or IL-3 were reversed myelosuppression by PSK1. In myelosuppressive mice, especially in granulocyte colonies with stimulating factor (GCSF) or IL-3 were reversed by PSK. Generally, it has a proliferative effect, including lymphocytes, monocytes, macrophages, and splenocytes on many cells. In addition, human peripheral blood mononuclear cells increased interleukin 1 production. In many more ways, the immune system positively affects the system (Habtemariam 2020).

Sun et al. (2012) reported that PSK possesses clinical benefits with limited side effects in several cancers, e.g., colorectal, gastric, and lung cancer, as an additive to other conventional adjuvant treatments.

The methanol and the aqueous extract have been tested in the DPPH scavenging experiment. They showed a dose-dependent response. $IC_{90}$ values were found as 178.83, 518.06, and 332.98μg/ml, for methanol extract, aqueous extract, and ascorbic acid, respectively. In the extract, catechin (5.91 mg/ml) and quercetin (29.90 mg/ml) were found, and catechin was more effective in biological activity (Hossen et al. 2021; Janjusević et al. 2017). Another study on the $H_2O$ extract expressed better antioxidant scavenging potential than EtOH, showing the highest activity for the *T. versicolor* ($IC_{50} = 5.6$μg/mL, $IC_{50} = 0.6$μg/mL for DPPH and OH radicals, respectively) (Raseta et al. 2020). It was found that the conformation of the polysaccharides was more important for DPPH radical scavenging activity than monosaccharide composition (Kozarski et al. 2012).

In vitro acetylcholinesterase (AChE) inhibitor activity tests showed that the inhibition was concentration-dependent. A strong degree of inhibition was found

at the dose of 100μg/ml, compared to donepezil (89.05%) used as an AChE inhibitor (60.53%). The EtOH extract at 500μg/ml had 44.35% inhibition. AChE inhibitory activity of $H_2O$ and EtOH extracts were found $IC_{50}$ = 78.01μg/ml and $IC_{25}$ = 383.96μg/ml, respectively. This inhibitory effect is due to the major flavonoids in the extracts, baicalein (21.6μg/g) and quercetin (31.2μg/g). It has also been found that this inhibitory effect is due to synergistic effects of the flavonoids, terpenoids, phenolic compounds, and polysaccharides in the aqueous extract, but the strongest effect belongs to baicalein (Fang et al. 2015; Janjusević et al. 2017).

In light of the literature, there seems to be a need for more research on the anticancer and neurological effects of *C. versicolor*. PSK and PSP from *Coriolus* appear safe and effective as long-term adjuvant immunotherapy in conjunction with or after standard chemotherapy and/or radiation. They may increase survival time, immune function, and tumor-associated symptoms in patients with various types of cancer.

## 10 *Flammulina velutipes* (Curtis) Singer

*Flammulina velutipes* (Curtis) Singer (*Physalacriaceae*) (Fig. 2c) is an edible mushroom with many biological activities. It is widely consumed and the world's fifth most cultivated mushroom (Karasoy et al. 2019).

According to several reports, the antioxidant effect is one of the main mechanisms underlying the activities of *F. velutipes.* The ethanol extract of *F. velutipes* exhibited strong antioxidant properties in DPPH and ABTS radical scavenging activities and reducing power. It protected PC12 cells from $H_2O_2$-induced injury by reducing the LDH release, ROS production, and MDA generation. The extract also enhanced the activities of antioxidant enzymes such as GSH level and SOD. Several phenolic and polyphenolic compounds, including arbutin, epicatechin, phillyrin, apigenin, kaempferol, and formononetin, were isolated from this extract (Hu et al. 2016). Likewise, polysaccharide fraction *F. velutipes* boosted glutathione peroxidase (GSH-Px) and SOD activity against oxidative stress in $H_2O_2$-stimulated L929 cells. Moreover, they inhibited the production of hydroxyl radicals by chelating metal ions such as $Fe^{2+}$ and $Cu^{2+}$ (Wang et al. 2016).

*F. velutipes* polysaccharides attenuated carbon tetrachloride-induced acute liver injury revealed by histopathological examination of the liver. They also decreased levels of serum aspartate transaminase (AST), alanine aminotransferase (ALT), triglyceride (TG), total cholesterol (TC), total bile acid (TBA) content, hepatic MDA, and protein carbonyl levels. *F. velutipes* polysaccharides enhanced the activities of antioxidant enzymes CAT and SOD. They reduced pro-inflammatory cytokines (including IL-6, IL-1β, and TNF-α). *F. velutipes* polysaccharides changed the gut microbiota according to 16S rRNA, suggesting that their gut microbiota modulating effect is also involved in anti-hepatotoxic action (Xu et al. 2022).

*F. velutipes* polysaccharides possess anti-inflammatory properties associated with their immunomodulatory and gut microbiota modulatory effects. They regulated

CD4+, CD8+, ICAM-1, and myeloperoxidase in the serum and colon of rats. It also changed NF-α, IFN-γ, IL-1β, IL-6, and iNOS levels in ulcerative colitis mice. It regulated intestinal microorganisms to reduce inflammation by increasing beneficial bacteria (*Lactobacillus*, *Bifidobacterium*) and decreasing harmful bacteria such as *Clostridium* (Zhao et al. 2020). *F. velutipes* polysaccharides prevented scopolamine-induced learning and memory impairment by mediating gut microbiota composition and inhibiting inflammation (Su et al. 2018). Notably, *F. velutipes* polysaccharides in combination with ginsenosides enhanced cognitive functions in Alzheimer's disease model (Zhang et al. 2018).

Several studies showed that *F. velutipes* polysaccharides stimulate the immune system. They stimulated macrophages, T cells, B cells, and NK cells and increased splenocyte proliferation and antibody release to boost humoral immunity. They boosted the secretion of TNF-α, IL-1β, and IL-6 from macrophages and induced cellular nitric oxide formation. Additionally, it showed that there was a considerable increase in the quantity of beneficial flora as well as the concentration of two types of fecal short-chain fatty acids, namely, isobutyric acid and butyric acid. Apart from these, *F. velutipes* polysaccharides stimulate the immune system through mitogen-activated protein kinases (MAPKs), autophagy, and Akt/NF-κB signaling pathways via TLR4 receptor in vitro and in vivo (Meng et al. 2018; Ye et al. 2020; Yin et al. 2010). *F. velutipes* polysaccharides have anticancer action mainly by immunomodulatory effect rather than toxicity to cancer cells. A polysaccharide fraction of *F. velutipes* reduced tumor weight in sarcoma 180-inoculated mice. However, it did not reduce the proliferation of sarcoma 180 cells in vitro. Our literature survey found no other study reporting direct toxicity to cancer cells or tumors of *F. velutipes* or polysaccharides (Leung et al. 1997).

Thus, *F. velutipes* improves learning and memory ability, regulates cognitive function, and protects the liver. But the most notable effect of it is immunomodulation. Compared to other widely cultivated mushrooms, studies on *F. velutipes* are limited and need more research.

## 11 *Grifola frondosa* (Dicks.)

*Grifola frondosa* (Dicks.) Gray (Fig. 2d) is an edible and medicinal mushroom belonging to the *Grifolaceae* family. It is known as maitake (Japan) and gray tree flower (China). This mushroom is mainly distributed in northern temperate regions in Japan, Europe, and America, but it also grows at high altitudes in the subtropics with a temperate climate. It is also cultivated due to high demand. It is used as healthy food and food flavoring agent, and some polysaccharide-containing fractions of *G. frondosa* are commercially available as healthcare products like D-fraction. Apart from D-fraction, a proteoglycan, other polysaccharide fractions, such as MD-fraction, X-fraction, grifolan, and MZ-fraction, also possess a wide range of bioactivities. The China Food and Drug Administration approved some patent drugs

containing *G. frondosa* polysaccharides, and also there are many clinical trials on these fractions in different countries (He et al. 2017; Wu et al. 2021).

Antidiabetic effects of *G. frondosa* extracts or polysaccharides have been reported in several studies (Chen et al. 2018; Guo et al. 2020b; Jiang et al. 2020; Ma et al. 2014; Shen et al. 2015; Su et al. 2013). Some studies have shown that *G. frondosa* polysaccharides exhibit antidiabetic effects through the insulin signal pathway. They affected insulin receptors, enhanced insulin sensitivity, and ameliorated insulin resistance. They enhanced glucose uptake by cells, activated the insulin receptor protein in the cell membrane, induced phosphorylation of increased Akt, and overcome insulin resistance. In addition to Akt-GSK-3 signaling, upregulation of phosphorylation of insulin receptor and downregulation of phosphorylation of insulin receptor substrate 1 are also involved in fasting serum glucose level decreasing effect of *G. frondosa* polysaccharides (Ma et al. 2014; Xiao et al. 2015). The antidiabetic effect of *G. frondosa* polysaccharides is also related to their α-glucosidase inhibition. Not only polysaccharides but also nonpolar fractions, ergosterol, oleic and linoleic acid, and pyrrole alkaloids of *G. frondosa* possess α-glucosidase inhibitory potential (Chen et al. 2018; Shen et al. 2015; Su et al. 2013). The antidiabetic effect of this mushroom is also associated with its modulatory potential for gut microbiota (Guo et al. 2020b). *G. frondosa* also ameliorated renal function and attenuated renal inflammatory responses in diabetic mice by decreasing IL-6, IL-1β, TGF-β1, and TNF-α levels, suppressing apoptosis and fibrosis. TLR4/NF-κB signaling is associated with the diabetic nephropathy effect of maitake (Jiang et al. 2020).

*G. frondosa* has an antihypertensive effect and is associated with the renin-angiotensin system (Preuss et al. 2010). Several researchers also reported antihyperlipidemic effect of maitake mushroom. Dried *G. frondosa* powder reduced serum cholesterol, triglyceride, and phospholipid levels 0.3–0.8 times compared to the control group and increased cholesterol excretion approximately 1.8 times by feces. *G. frondosa* also reduced serum total cholesterol concentration and very low-density lipoprotein levels. The total cholesterol-lowering effect was attributed to increased fecal cholesterol excretion. In addition, *G. frondosa* prevented hyperlipidemia in diabetic mice by altering gut microbiota and regulating hepatic glycolipid metabolism-related genes (Kubo and Nanba 1997; Fukushima et al. 2001; Guo et al. 2020b).

*G. frondosa* also possesses antiviral effects against hepatitis B virus (HBV), enterovirus 71 (EV71), herpes simplex virus type 1 (HSV-1), and human immunodeficiency virus (HIV). A combination of D-fraction of *G. frondosa* with interferon-alpha (IFN-α) synergistically inhibited HBV. The effect was nine times higher than that of IFN-α (Gu and Sivam 2006; Mayell 2001).

In general, mushroom polysaccharides regulate gut microbiota. Gut microbiota-regulating effects of *G. frondosa* involve various biological effects, including antidiabetic, antihyperlipidemic, and against nonalcoholic fatty liver disease (Gangarapu et al. 2014; Guo et al. 2020b; Friedman 2016). *G. frondosa* polysaccharides modulate intestinal microflora by significantly increasing the relative abundance of *Alistipes* and *Bacteroides* and reducing *Enterococcus* and *Firmicutes* to

*Bacteroidetes* ratio, the latter suggested possessing fat-lowering effects (Guo et al. 2020b; Friedman 2016). Moreover, *G. frondosa* polysaccharides significantly boosted the proportion of *Allobaculum*, *Bacteroides*, *Bifidobacterium*, and other microbial groups in the cecal microbiota, which may improve the immune system of the host and the defense against nonalcoholic fatty liver disease (Liu et al. 2019).

*G. frondosa* extracts and polysaccharides also exhibited an antioxidant effect. They scavenged DPPH, hydroxyl, and superoxide radicals in vitro and enhanced the antioxidant status and activities of endogenous antioxidant enzymes (He et al. 2017; Wu et al. 2021).

Different extracts and components of *G. frondosa* possess anticancer properties by suppressing tumor growth or modulating the host immune system. *G. frondosa* polysaccharides and ergosterol derivatives exhibited antiproliferative effects on cancer cells (Chen et al. 2018; Cui et al. 2007; Wang et al. 2013a). They also induced apoptosis associated with altering transmembrane potential, activating different caspases, upregulating proapoptotic proteins like Bax, and downregulating antiapoptotic proteins like Bcl-2, Notch1/NF-κB/p65 signaling (Cui et al. 2007; Wang et al. 2013a; Wu et al. 2021). A heteropolysaccharide fraction also exhibited an antiangiogenic effect (Wang et al. 2014b). *G. frondosa* D-fraction reduced the effective dosage of the chemotherapeutic agent by enhancing cisplatin's antitumor and antimetastatic activities. It also reduced the myelosuppression and nephrotoxicity induced by cisplatin (Masuda et al. 2009a).

*G. frondosa* polysaccharides enhanced phagocytic activity of macrophages, activated T cells, B cells, and NK cells and promoted the release of cytokines IL-1, IL-2, TNF-α, and IFN-γ (Masuda et al. 2009a; Wang et al. 2013c). D-fraction stimulated the differentiation into Th-1 or Th-2 cells of CD4+ T cells by enhancement of IL-12p70 and IFN-γ secretion (Harada et al. 2003; Kodama et al. 2002). D-fraction boosted a Th-1 dominant response, including the cell-mediated immunity related to cytotoxic T cell activation. Furthermore, D-fraction also induced a Th-2 dominant response through macrophage activation, enhancing humoral immunity rather than cell-mediated immunity (Inoue et al. 2002; Kodama et al. 2004). Other than many mushroom polysaccharides, which may become ineffective if administered orally, D-fraction and MD-fraction can be given orally, making them easy to use.

In conclusion, *G. frondosa* can regulate blood lipids and glucose levels and improve fat metabolism and weight loss. It also exhibits anticancer effects by inhibiting tumor growth and metastasis and modulating the immune system. Most of the activities of *G. frondosa* come from polysaccharides. Such as the Gut microbiota regulating effect of *G. frondosa*. Some of these polysaccharides are commercially available as a dietary supplement and undergo clinical trials for the treatment of cancer. However, well-designed randomized controlled clinical trials are needed.

## 12 *Pleurotus ostreatus* (Jacq. Ex Fr) P. Kumm.

There are about 40 species in the *Pleurotus* genus, including those with high economic significance, such as *P. ostreatus* and *P. pulmonarius*. Many species contain medicinal components, including polysaccharides, proteins, terpenoids, fatty acids, and polyphenols. It is also reported that oyster mushroom contains phenolic compounds with antioxidative effects. Bioactive substances in this genus exhibit immunostimulatory, antineoplastic, antidiabetic, anti-atherosclerotic, anti-inflammatory, hepatoprotective, and antioxidative properties (Golak-Siwulska et al. 2018a; Piska et al. 2017).

*Pleurotus ostreatus* (Jacq. Ex Fr) P. Kumm. (*Pleurotaceae*) (Fig. 2e), also known as the oyster mushroom, is found on all continents except Antarctica. These mushrooms grow on various lignocellulosic substrates and form shell-shaped fruiting bodies. It has been cultivated commercially on a large scale since World War I. *P. ostreatus* is an important dietary mushroom with many biological activities. It is also rich in proteins, vitamins, minerals, and oleic and linolenic acids. Flavonoids and phenolic acids such as myricetin, naringenin, hesperidin, formononetin, biochanin A, and p-hydroxybenzoic are also found in sinapic, ferulic, p-coumaric acids, etc. (Piska et al. 2017). These species contain high levels of lovastatin, an approved hypolipidemic drug, and pleuran, an immunomodulating polysaccharide (β-glucan) (Golak-Siwulska et al. 2018a; Piska et al. 2017). It was found to possess an anticancer effect due to its polysaccharides and glucans (Jedinak et al. 2010; Jedinak and Sliva 2008; Wu et al. 2011); antiviral and antibacterial properties due to its proteins (laccase, ribonucleases) and $\beta$-glucans, respectively (Erjavec et al. 2012; Gashaw et al. 2020; Golak-Siwulska et al. 2018a; Iwalokun et al. 2007; Patel et al. 2012; Wang and Ng 2000), anti-inflammatory and antioxidant activities due to its polysaccharides and phenolics (Mitra et al. 2013; Jayakumar et al. 2007, 2011; Venkatakrishnan et al. 2010); and anti-atopic dermatitis effect due to pleuran (Park et al. 2016). The hypoglycemic activity of *P. ostreatus* has been indicated in various in vivo studies on animals (Piska et al. 2017).

Zhang et al. (2012) isolated two polysaccharide fractions from *P. ostreatus* and showed their potent antioxidative effects. Extracts of *P. ostreatus* increased the activities of known potent antioxidant enzymes in aged rats (Jayakumar et al. 2007).

Gu and Sivam (2006) have found water-soluble proteins or polypeptides from *P. ostreatus* cytotoxic effect and induced cytotoxicity on various cell lines. However, it has the most significant cytotoxicity on human androgen-independent prostate cancer PC-3 cells. Both cytotoxicity and apoptosis-inducing effects were dose-dependent. Furthermore, linear insoluble α-glucan *P. ostreatus* exhibited high cytotoxic activity on HeLa cell lines (Wiater et al. 2011). *P. ostreatus* exhibited an antiproliferative effect on the colorectal cancer cell lines COLO-205 and SW 480 and induced apoptosis of monocytic leukemia THP-1 (Piska et al. 2017; Wu et al. 2011). Facchini et al. (2014) proved that polysaccharides extracted from the *P. ostreatus* mycelium successfully inhibited the development of neoplastic cells of Ehrlich tumor (ET) and sarcoma 180 (S-180). *P. ostreatus* extracts have inhibited the

growth of HL-60 cells by arresting the cell cycle related to the inducement of apoptosis (Venkatakrishnan et al. 2010).

*P. ostreatus*, which contains lovastatin, is known to be effective in preventing cardiovascular disorders because it reduces cholesterol. It was reported that oyster mushroom has antioxidant, immunomodulatory, and antitumor activity and affects breast and colon cancer treatment and prevention.

## 13 Conclusion

Edible mushrooms are important products in the global trade. They have gradually attracted the attention of the food, pharmaceutical, and cosmetic industries regarding their use as food supplements and in searching for new drug candidates.

The biological activities of edible mushrooms are mainly attributed to the presence of polysaccharides, but the contribution of other chemical constituents, such as proteins, triterpenes, steroids, and phenols, are also responsible for these effects. Edible mushrooms possess promising bioactivities, including antitumor and immunomodulation, antioxidant, anti-hyperglycemia, and anti-inflammatory effects (Table 1).

Mushroom polysaccharides regulate gut microbiota, and this regulation involves most of the bioactivity of mushrooms. Arguably, the immunomodulatory effects of mushroom polysaccharides are one of the most studied and well-known bioactivity. Some polysaccharide fractions are commercially available such as *G. frondosa* D-fraction or Andosan, making them easy to use for health promotion.

Although several randomized clinical trials on some edible mushrooms, including *A. blazei*, *G. frondosa*, and *T. versicolor*, have been conducted; larger randomized studies are required to confirm these interesting findings and potential health benefits.

**Table 1** Major biological activity of some well-known edible mushrooms

| Mushroom name | Biological activity | Application | References |
|---|---|---|---|
| *Agaricus bisporus* (J.E. Lange) Imbach | – Antioxidant | In vitro, in vivo | Liu et al. (2013) |
| | – Antidiabetic | In vivo | Ekowati et al. (2018) |
| | – Antihyperlipidemic | In vivo | Jeong et al. (2010) |
| | – Anti-inflammatory | In vitro, in vivo | Gallego et al. (2021), Smiderle et al. (2013), Volman et al. (2009) |
| | – Cytotoxicity against cancer cells | In vitro, in vivo | Chen et al. (2006), Jeong et al. (2012) |
| *Agaricus blazei* Murill | – Antioxidant | In vitro, in vivo | Al-Dbass et al. (2012), Bach et al. (2019), Carneiro et al. (2013), Wei et al. (2020) |
| | – Antidiabetic | In vivo | Al-Dbass et al. (2012), Ji et al. (2014), Vitak et al. (2015) |
| | – Antihyperlipidemic | In vivo | Ji et al. (2014), Li et al. (2020b) |
| | – Anti-inflammatory | In vitro, in vivo, clinical study | Song et al. (2012), Therkelsen et al. (2016), Wang et al. (2013b) |
| | – Antimicrobial | In vitro | Bach et al. (2019) |
| | – Anxiolytic | In vivo | Ali et al. (2021) |
| | – Immunostimulant | In vitro, in vivo, clinical study | Bernardshaw et al. (2005), Johnson et al. (2009), Lima et al. (2011), Tangen et al. (2015), Therkelsen et al. (2016) |
| | – Cytotoxicity against cancer cells | In vitro, in vivo | Ito et al. (1997), Jin et al. (2006), Kim et al. (2011), Matsushita et al. (2018), Yu et al. (2009) |
| *Amanita caesarea* (Scop.) Pers. | – Antioxidant | In vitro | Doğan and Akbaş (2013) |
| | – Antimicrobial | In vitro | Doğan and Akbaş (2013) |
| | – Anti-Alzheimer | In vitro, in vivo | Hu et al. (2021), Li et al. (2019) |
| *Armillaria mellea* (Vahl) P. Kumm | – Antioxidant | In vitro | Zavastin et al. (2015) |
| | – Antidiabetic | In vivo | Yang et al. (2019) |
| | – Antidepressant | In vivo | Sun et al. (2020) |
| | – Anti-inflammatory | In vitro | Chang et al. (2013), Geng et al. (2017), König et al. (2019), Wu et al. (2007) |
| | – Cytotoxicity against cancer cells | In vitro, in vivo | Kim et al. (2008), Li et al. (2016) |
| *Auricularia* species | – Antioxidant | In vitro, in vivo | Agbor et al. (2022), Chellappan et al. (2016), Chiu et al. (2014), Wu et al. (2010) |
| | – Antidiabetic | In vivo | Hu et al. (2017) |
| | – Antihyperlipidemic | In vivo | Liu et al. (2022), Zeng et al. (2013) |
| | – Anti-inflammatory | In vitro, in vivo | Bao et al. (2020), Perera et al. (2020), Wu et al. (2010) |
| | – Antimicrobial | In vitro | Oli et al. (2020) |

(continued)

**Table 1** (continued)

| Mushroom name | Biological activity | Application | References |
|---|---|---|---|
| | – Cytotoxicity against cancer cells | In vitro | Kang et al. (2020), Yu et al. (2014) |
| | – Wound healing | In vivo | Mapoung et al. (2021) |
| *Boletus edulis* Bull. | – Antioxidant | In vitro | Garcia et al. (2022), Guo et al. (2012, 2020a), Heleno et al. (2015), Luo et al. (2012), Xiao et al. (2018), Zheng et al. (2019) |
| | – Antidiabetic | In vivo | Xiao et al. (2018) |
| | – Anti-hepatotoxic | In vivo | Zheng et al. (2019) |
| | – Anti-inflammatory | In vivo | Wu et al. (2016) |
| | – Antimicrobial | In vitro | Garcia et al. (2022) |
| | – Cytotoxicity against cancer cells | In vitro, in vivo | Bovi et al. (2013), Lemieszek et al. (2013, 2016), Meng et al. (2021), Valenti et al. (2020), Wang et al. (2014a), Zhang et al. (2021) |
| *Coprinus comatus* (O.F. Müll.) Pers. | – Antioxidant | In vitro, in vivo | Cao et al. (2019), Sihoglu Tepe (2021), Gao et al. (2021) |
| | – Antidiabetic | In vivo | Cao et al. (2019), Ding et al. (2010), Husen et al. (2021), Ratnaningtyas et al. (2022) |
| | – Anti-hepatotoxic | In vivo | Stilinović et al. (2020) |
| | – Antihyperlipidemic | In vivo | Gao et al. (2021) |
| | – Cytotoxicity against cancer cells | In vitro | Dotan et al. (2011), Nowakowski et al. (2021), Rouhana-Toubi et al. (2015) |
| *Coriolus versicolor* (L. ex Fr.) Quel. | – Antioxidant | In vitro | Hossen et al. (2021), Janjusevic et al. (2018), Kozarski et al. (2012), Raseta et al. (2020) |
| | – Acetylcholinesterase inhibitory | In vitro | Fang et al. (2015), Janjusević et al. (2017) |
| | – Cytotoxicity against cancer cells | In vitro, in vivo, clinical study | Habtemariam (2020), Sun et al. (2012) |
| *Flammulina velutipes* (Curtis) Singer | – Antioxidant | In vitro | Hu et al. (2016), Wang et al. (2016) |
| | – Anti-inflammatory | In vitro, in vivo | Su et al. (2018), Zhao et al. (2020) |
| | – Anti-Alzheimer | In vitro, in vivo | Zhang et al. (2018) |
| | – Cytotoxicity against cancer cells | In vitro, in vivo | Leung et al. (1997) |
| | – Immunomodulatory | In vitro, in vivo | Meng et al. (2018), Ye et al. (2020), Yin et al. (2010) |
| *Grifola frondosa* (Dicks.) | – Antioxidant | In vitro, in vivo | He et al. (2017), Wu et al. (2021) |
| | – Antidiabetic | In vivo, in vitro | Chen et al.( 2018), Guo et al. (2020b), Jiang et al. (2020), Ma et al. (2014), Shen et al. (2015), Su et al. (2013), Xiao et al. (2015) |

(continued)

**Table 1** (continued)

| Mushroom name | Biological activity | Application | References |
|---|---|---|---|
| | – Antihypertensive | In vivo | Preuss et al. (2010) |
| | – Antihyperlipidemic | In vivo | Kubo and Nanba (1997), Fukushima et al. (2001), Guo et al. (2020b) |
| | – Antiviral | In vitro | Gu and Sivam (2006), Mayell (2001) |
| | – Cytotoxicity against cancer cells | In vitro, in vivo | Chen et al. (2018), Cui et al. (2007), Wang et al. (2013a) |
| | – Gut microbiota regulating | In vivo | Guo et al. (2020b), Friedman (2016), Liu et al. (2019) |
| | – Immunomodulator | In vitro | Harada et al. (2003), Kodama et al. (2002), Masuda et al. (2009b), Wang et al. (2013c) |
| *Pleurotus ostreatus* (Jacq. Ex Fr) P. Kumm. | – Antioxidant | In vitro, in vivo | Golak-Siwulska et al. (2018a), Piska et al. (2017) |
| | – Antidiabetic | In vivo | Golak-Siwulska et al. (2018a), Piska et al. (2017) |
| | – Anti-atherosclerotic | In vivo | Golak-Siwulska et al. (2018a), Piska et al. (2017) |
| | – Anti-inflammatory | In vitro, in vivo | Golak-Siwulska et al. (2018a), Piska et al. (2017) |
| | – Cytotoxicity against cancer cell lines | In vitro, in vivo | Gu and Sivam (2006), Jedinak et al. (2010), Jedinak and Sliva (2008), Piska et al. (2017), Venkatakrishnan et al. (2010), Wiater et al. (2011), Wu et al. (2011) |

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