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# Structure, function and mechanism of edible fungus polysaccharides in human beings chronic diseases

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**Abstract**

The feasibility of human nutritional supplementation is imperative. As a part of daily diet, edible fungus polysaccharides have a variety of health promoting effects, especially for the prevention of chronic diseases. Based on the extensive collection and collation of relevant research datas, the beneficial effects of edible fungus polysaccharides on various chronic diseases were analyzed, and the structure and functional mechanism of edible fungus polysaccharides with anti-chronic disease properties were summarized in this current review. Based on a comprehensive analysis of the current researchs on edible fungus polysaccharides, it was considered that edible fungus polysaccharides can be used as the material basis of anti-chronic disease drugs. In addition, the relevant contents can also provide some reference for the selection and development of anti-chronic disease drugs.

**Keywords:** edible fungus polysaccharides; chronic diseases; mechanism and pathway; active structure.

**Practical Application:** The relevant contents not only contribute to the further development of the edible fungus polysaccharide industry, but also provide references for the selection and development of anti-chronic disease drugs.

## 1 Introduction

Chronic non-communicable diseases, known as chronic diseases, are usually a group of diseases with complex etiology, insidious, long course and can not be cured for a long time, and some diseases that cannot be determined so far. At present, chronic diseases seriously endanger human health and quality of life, and have become one of the diseases that attract much attention in the world today (Raghupathi & Raghupathi, 2018). The types of chronic diseases that may occur in different parts of the human body were shown in Figure 1. Available datas showed that the number of deaths caused by chronic diseases accounted for a large proportion of the global death each year (Ghosh et al., 2016). The main cause of this consequence was the chronically neglected, mild or unnoticed symptoms of the human body. Currently, clinical drugs (especially biological agents) are generally used to treat chronic diseases, but these drugs generally have the disadvantages of side effects and high cost (Gautam & Jachak, 2009). Studies have shown that many natural compounds can provide better options for the treatment of chronic diseases (Roy et al., 2016), and a large number of studies have confirmed that compounds derived from a variety of natural products can be used as active drugs against different chronic diseases (Yang et al., 2013; Tang et al., 2014; Yarla et al., 2016; Harsha et al., 2017; Hasanpourghadi et al., 2017; Banik et al., 2018; Tewari et al., 2018). These plant-derived compounds provide additional and prominent options for existing drug systems. So far, more than 10000 plant chemicals including polysaccharides, flavonoids, triterpenoids and alkaloids have been identified. These phytochemicals have shown long-term and significant pharmacological properties, and available datas showed that nearly 80% of the global population used phytomedicines to treat various chronic diseases (Shanmugam et al., 2011; Parikh et al., 2014; Kanchi et al., 2017; Ko et al., 2017; Sethi et al., 2018; Ong et al., 2019; Varughese et al., 2019).

Edible fungi are a general term of edible species in higher fungi, which have large fleshy or colloidal fruiting bodies. Interestingly, Edible fungi are widespread on the earth, and nearly 22,000 species of edible fungi have been found and reported, of which about 10% have been studied in depth (Tsubone et al., 2014). Edible fungi are favored by people all over the world because of their delicious taste and unique flavor, which has also driven the rapid development of the global edible mushroom industry. As of 2019, China's edible fungi production accounted for about 70% of the world's total production (Hu et al., 2020). At present, the edible fungus industry has become the fifth largest agricultural industry in China (Ba et al., 2021). It can be seen that the edible fungus industry has broad market prospects. Studies have confirmed that edible fungi contain a variety of bioactive substances, such as polysaccharides (Li et al., 2022), proteins (González et al., 2020), terpenoids (Zhao et al., 2020; Guofeng et al., 2020), vitamins (Mingqing et al., 2020), minerals (Liu, 2018), etc., and these active substances can play a vital role in the human body (Zhang et al., 2020b; Nhi et al., 2022). Among them, edible fungus polysaccharide is undoubtedly a research hotspot in recent years. As early as 1970s, Japanese researchers

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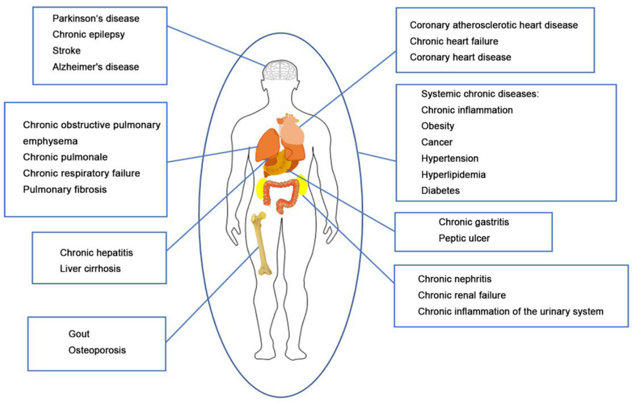


**Figure 1.** Chronic diseases in different parts of the human body.

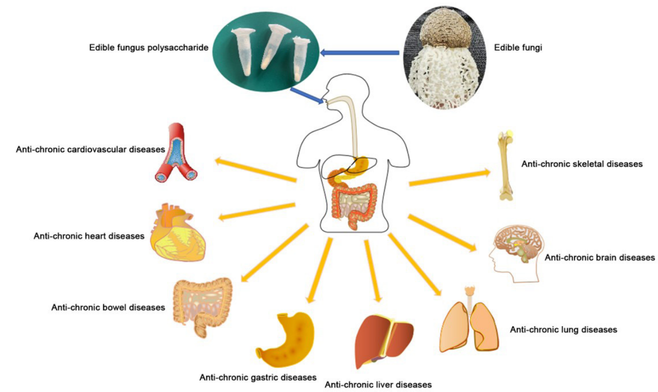


**Figure 2.** Edible fungus polysaccharides can resist a variety of chronic diseases.

were the first to prove that lentinan had a certain anti-tumor activity (Qing, 2011). Since then, edible fungus polysaccharides have attracted extensive attention from researchers in many fields such as medicine, biology, pharmacology and food science. With the in-depth excavation of researchers, it was found that edible fungus polysaccharides can regulate the function of the body at multiple levels through a variety of pathways and mechanisms (Liu et al., 2022; Zhao et al., 2020), thereby inhibiting the occurrence and development of human diseases.

It is worth mentioning that in recent years, a large number of studies have shown that edible fungus polysaccharides can be used to treat or delay the development of chronic diseases. For example, Li et al. ( 2019b) have confirmed that *Poriacocos* mushroom polysaccharides can be used as an anti-tumor drug. In addition, Ma et al. (2022) suggested that the consumption of edible fungus polysaccharides had certain beneficial effects on chronic diseases such as obesity, inflammation and cancer. Edible fungus polysaccharides can be helpful for a variety of chronic diseases, as shown in Figure 2.

There are various mechanisms of action of edible fungus polysaccharides against chronic diseases. Zhang et al. (2022) found that *Ganoderma lucidum* polysaccharides can improve the levels of transforming growth factor-β1 (TGF-β1) and interleukin-10 (IL-10), increase the level of Foxp3 Treg cells, and regulate abnormal energy metabolism, thereby alleviate the cognitive impairment in a mouse model of chronic cerebral hypoperfusion. In addition, *Ganoderma lucidum* polysaccharides can induce apoptosis and autophagy of MCF-7 cells through the MAPK signaling pathway, thereby showing its strong anti-tumor activity (Hanyu et al., 2020). In addition, Wang et al. (2021b) intervened tumor-bearing mice with *Leucocalocybe mongolica* polysaccharides, and found that the polysaccharides could inhibit tumor growth by reducing tumor angiogenesis and tumor cell apoptosis. In terms of anti-inflammatory, Sheng et al. (2021) found that *Lentinus edodes* polysaccharides have anti-inflammatory effects. Additionally, *Craterellus cornucopioides* polysaccharides showed anti-inflammatory effect by reducing the production of inflammatory mediators (iNOS) and the expression of pro-inflammatory factors (TNF-α, IL-1β and IL-18), which may be related to the inhibition of NF-κB signaling pathway (Xu et al., 2021a). For hyperlipidemia, Yu et al. (2021) confirmed that *Cordyceps militaris* polysaccharides can alleviate hyperlipidemia by blocking preadipocyte differentiation.

It can be seen that edible fungus polysaccharides have certain beneficial effects on the occurrence and development of many chronic diseases. Next, this article will comprehensively review the effects and mechanisms of edible fungus polysaccharides on chronic diseases, in order to provide some reference for the development of related health food or medicine.

## 2 Effects of edible fungus polysaccharides on chronic diseases

### *2.1 Anti-cancer*

Cancer is one of the chronic diseases with extremely high morbidity and mortality. It was estimated that as early as 2012, about 8.2 million people died of cancer in the world, and by 2018, the number of deaths from cancer was as high as 9.8 million (Torre et al., 2015; Shabnam et al., 2018). It is worth noting that edible fungus polysaccharide is a kind of anti-tumor substance, which is currently considered to have good clinical application value. The anti-cancer research of edible fungus polysaccharides first started in 1969 (Qing, 2011). Since then, a series of studies have further proved that edible fungus polysaccharides have anti-cancer effects, and the relevant pathways were shown in Figure 3. Among them, Cui et al. (2020) proved that *Grifola frondosa* polysaccharides may be a possible drug for the treatment of cancer. Similarly, Roca-Lema et al. (2019) demonstrated that *Grifola frondosa* polysaccharides can significantly inhibit the proliferation, oncogenic potential, cell migration and invasion ability of colon cancer cells, and induce cytotoxicity. In addition, *Phellinus sensu lato* polysaccharides were expected to become an alternative anticancer agent or synergist for existing anticancer drugs (Yan et al., 2017). Zhang et al. (2019) reviewed 9474 reported lentinan-associated cancer treatment cases, and the results showed that lentinan can be used to treat common cancers such as gastric cancer, ovarian cancer, cervical cancer, colorectal cancer, lung cancer, heart cancer, and nasopharyngeal cancer.

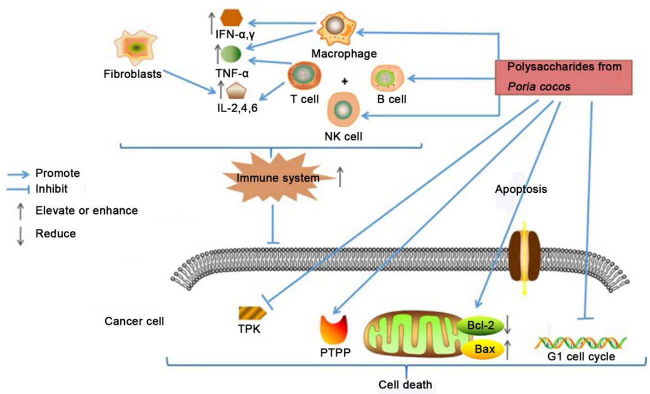


**Figure 3.** Anti-cancer pathways of edible fungus polysaccharides (Li et al., 2019a).

### *2.2 Anti-obesity*

Obesity is a very important public health problem in the whole world, and it is closely related to other diseases (Ganesan & Xu, 2018). According to the World Health Organization (WHO), the global obesity rate had doubled since 1980. In 2014, 39% (over 1.9 billion) of adults worldwide were overweight, of which over 13% (about 600 million) were obese, and 42 million children were overweight or obese. The WHO predicted that by 2025, approximately 25% of adults worldwide will be obese (Mohammed et al., 2018). Currently, numerous studies on various edible fungi have confirmed the anti-obesity effect of edible fungus polysaccharides from different perspectives (*in vivo* and *in vitro*). Mao et al. found that *Coriolus versicolor* polysaccharides can prevent the mutation of 3T3-L1 adipocytes, suggesting that it can be used as a prebiotic against obesity (Mao et al., 2015). Some researchers treated adipocytes with *Ganoderma lucidum* polysaccharides and found that *Ganoderma lucidum* polysaccharides reduced the expression of adipogenic transcription factors, suggesting that *Ganoderma lucidum* polysaccharides can be used as potential anti-obesity drugs (Thyagarajan-Sahu et al., 2011). In addition, Wang et al. (2015) proved that *Cordyceps militaris* polysaccharides can reduce the blood and liver lipid levels of mice through *in vivo* experiments, suggesting that *Cordyceps militaris* polysaccharides were a kind of phytochemicals that can resist obesity.

### *2.3 Anti-inflammatory*

Inflammation is one of the important processes to prevent cells from being damaged, and it is the body's defense response to stimulation (Isailovic et al., 2015). Inflammation is divided into acute inflammation (Serhan et al., 2015) and chronic inflammation (Isailovic et al., 2015). Usually, inflammation is beneficial and is the body's automatic defense response (Kuprash & Nedospasov, 2016; Shen et al., 2017; Soehnlein & Libby, 2021). However, in some cases, the presence of inflammation will cause a series of adverse effects on the body. For example, inflammation may underlie the pathogenesis of certain diseases, and when the body has a severe inflammatory reaction, the patient's life will be threatened (Pichler et al., 2017; Hsu et al., 2021). In addition, inflammation of vital parts or organs of the body can also cause irreversible consequences. For example, brain inflammation can lead to cognitive impairment, cerebral palsy, schizophrenia, etc. (Jiang et al., 2018), while vocal cord inflammation can block the trachea, leading to suffocation (Corry et al., 2021). Therefore, when a severe inflammatory response occurs in the body, timely intervention is required to reverse or reduce the body damage.

Numerous studies have shown that edible fungus polysaccharides have significant anti-inflammatory effects. Xu et al. (2021b) found that *Tremella fuciformis* polysaccharides can stimulate $Foxp3^+$ T cells, increase the production of anti-inflammatory factors, and reduce the production of pro-inflammatory factors and immunoglobulin A (IgA). Studies have confirmed that edible fungus glucan can prevent colitis by regulating mucosal inflammation (Schwartz & Hadar, 2014). Kanagasabapathy et al. (2012) demonstrated that *Pleurotus sajor-caju (Fr.) Singer* polysaccharides can significantly down-regulate the activity of the pro-inflammatory marker NF-κB, suggesting that it may be a kind of potential anti-inflammatory candidates. The anti-inflammatory activity of edible fungus polysaccharides was shown in Figure 4.

### *2.4 Anti-chronic liver diseases*

The liver is an important hub for many important physiological processes, including the support of immune system, the metabolism of major nutrients and the maintenance of lipid homeostasis, etc. Therefore, whatever the reason, liver function impairment is a serious health problem (Trefts et al., 2017). Studies have shown that polysaccharide-peptide extracted from *Grifola frondosa* can promote the elimination of mercury burden in the liver and kidneys (Zhang et al., 2018a). Liu et al. (2017) found that in the acute liver injury model induced by carbon tetrachloride, both the two polysaccharides extracted from the edible mushroom *Oudemansiella radicata* can inhibit the formation of hepatic malondialdehyde, and improve the activities of hepatic superoxide dismutase and glutathione peroxidase, which suggested that *Oudemansiella radicata* polysaccharides can protect the liver through an antioxidant mechanisms. In addition, Liu et al. (2018b) studied the protective effect of *Agaricus bisporus* polysaccharides on the liver, the results showed that *Agaricus bisporus* polysaccharides can significantly reduce the expression levels of TGF-β1 and Smad3 in the liver, suggesting that it had a certain protective effect on liver injury. In addition, *Agaricus bisporus* polysaccharides can also downregulate the TGF-β1/Smad signaling pathway, and related research provided an important reference for the development of hepatoprotective drugs or functional foods.

### *2.5 Anti-diabetes*

Diabetes mellitus is a kind of metabolic diseases characterized by hyperglycemia due to defective insulin secretion, impaired biological action, or both. Long term hyperglycemia will cause damage to various organs and tissues of the body (Afolayan & Sunmonu, 2011; Szkudelski & Szkudelska, 2015; Facchinello et al., 2017; Sahlan et al., 2020; Reilly et al., 2022). According the American Diabetes Association (2016), in 2012, 9.3% of Americans (29.1 million) with diabetes had type 2 diabetes,

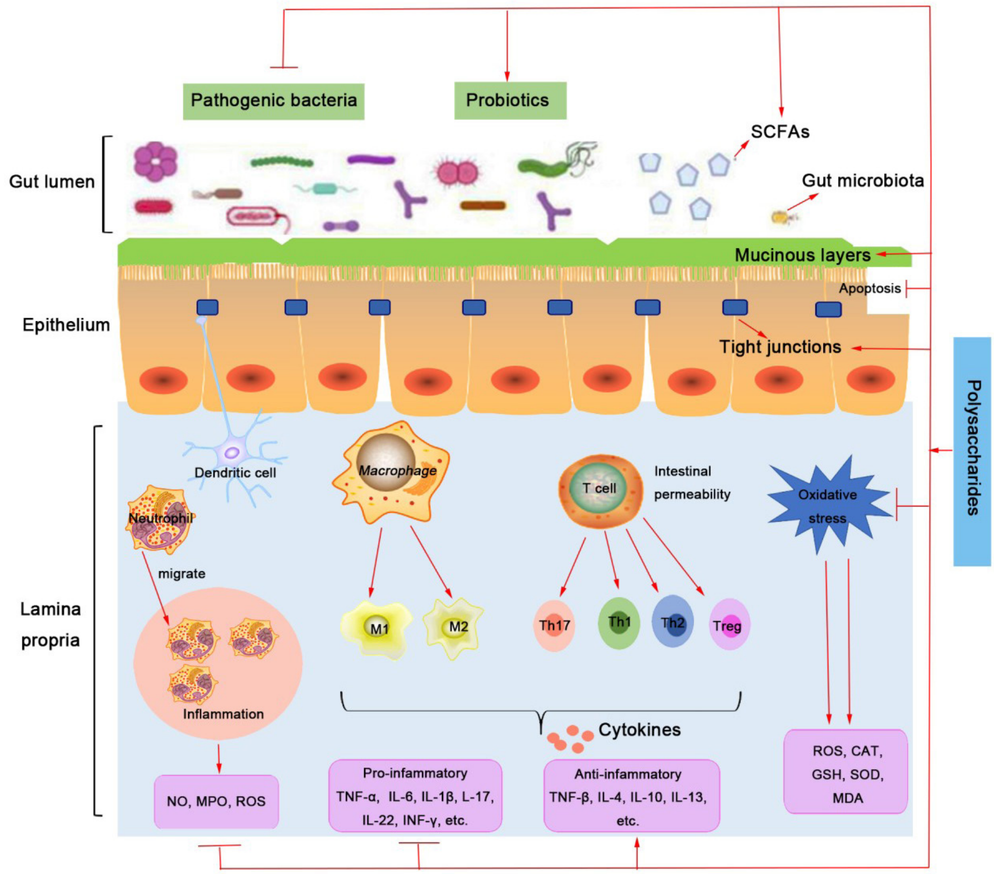


**Figure 4.** Anti-inflammatory effects of edible fungus polysaccharides (Li et al., 2021a).

and about 1 million had type 1 diabetes. It was estimated that by 2025, the number of people with type 2 diabetes in the world will increase to 300 million (Liu et al., 2013). Therefore, it is very important to find ways to fight diabetes. It has been reported that edible fungus polysaccharides can be used to intervene in the treatment of diabetes. Huang et al. (2012, 2014) found that the addition of *Pleurotus tuber-regium* polysaccharides significantly reduced the fasting blood glucose and glycosylated hemoglobin levels in diabetic rats. In addition, studies have shown that when the concentrations of *Astragalus* polysaccharides and *Oyster mushroom* polysaccharides were 0.4 mg/ml, the inhibition percentages of α-glucosidase were above 40%, indicating the both polysaccharides can treat diabetes by inhibiting glycosidase (Zhu et al., 2014). The results of Chou et al. (2016) showed that low molecular weight of *Inonotus obliquus* polysaccharides fraction (LIOP) treatment can ameliorate glucolipotoxicity-induced renal fibrosis by inhibiting the NF-κB/TGF-β1 signaling pathway in diabetic nephropathy mice.

### *2.6 Anti-chronic brain diseases*

Chronic brain diseases include Parkinson's disease (Rocha et al., 2018), chronic epilepsy (Hermann et al., 2008), stroke (Iadecola et al., 2020), Alzheimer's disease (Sliwinska & Jeziorek, 2021), etc. Currently, these chronic encephalopathy are difficult to cure, and seriously affect people's life safety and quality of life (Ehrenreich et al., 2004; Nazem et al., 2015; Lotankar et al., 2017; Weller & Budson, 2018; Cerri et al., 2019). Existing studies have shown that edible fungus polysaccharides can provide the possibility for the treatment of chronic brain diseases. The results of Hu et al. (2021) showed that *Amanita caesarea* polysaccharides can treat Alzheimer's disease by regulating oxidative stress-mediated endoplasmic reticulum stress. Similarly, Li et al. (2019b) confirmed that *Amanita caesare*a polysaccharides can exert protective effects against Alzheimer's disease through the Nrf2 pathway. Another study found that *Ganoderma lucidum* polysaccharides can treat cognitive decline associated with neurodegenerative diseases by promoting the proliferation of neural progenitor cell and the activation of the downstream cascades (Huang et al., 2017).

### *2.7 Anti-chronic lung diseases*

Common chronic lung diseases include chronic obstructive pulmonary disease, asthma, etc. and most of them are associated with oxidative stress. Studies have found that *Ganoderma lucidum* polysaccharide-loaded porous yolk shell particles suitable for pulmonary delivery displayed good inhalation therapy potential to treat chronic lung diseases by delivering to deep lung tissue and maintaining deposition (Xing et al., 2018). In addition, Chen et al. (2016) found that *Ganoderma lucidum* polysaccharides had positive effects on pulmonary fibrosis in rats, including reducing inflammatory cell infiltration, inhibiting lung index and collagen deposition, which further improved the level of oxidative stress in lung tissue. Furthermore, *Cordyceps sinensis* polysaccharides can increase the level of IL-1RA, reduce the content of hydroxyproline and the area of fibrosis in pingyangmycin-induced mice (Hu et al., 2019).

### *2.8 Anti-chronic skeletal diseases*

The incidences of chronic bone diseases in middle-aged and elderly people were relatively high (Lorentzon & Cummings, 2015; Management of Osteoporosis in Postmenopausal Women: the 2021 Position Statement of "The North American Menopause Society" Editorial Panel, 2021). There have been studies on chronic bone diseases, including osteomyelitis, joint tuberculosis, osteoporosis and arthritis (McCarthy, 2011; Signorelli et al., 2019). Chronic bone diseases have a longer onset and are often not detected until the later stages of the diseases. Therefore, it is extremely important to find effective ways to prevent/treat chronic bone diseases. A large number of studies have found that edible fungus polysaccharides have this function. For example, studies have shown that polysaccharides isolated from *Pleurotus rhinocerus* have immunomodulatory effects on bone marrow dendritic cells, which indicated that the polysaccharides can be used as medicines to prevent chronic bone diseases (Liu et al., 2019, 2022). Shibata et al. (2011) found that edible fungus polysaccharides can reduce FOFOX4-induced myelosuppression in patients with colorectal cancer.

### *2.9 Anti-cognitive dysfunction*

Cognition is the process by which the human brain accepts external information and acquires knowledge or applies knowledge after a series of processing (Khan et al., 2020), including memory, visual space, language, understanding and judgment (Pei et al., 2020). Cognitive dysfunction refers to the impairment of the above-mentioned cognitive functions, which seriously affects people's daily or social skills. Common cognitive dysfunction diseases include neurasthenia, mania, reactive psychosis (Mekori-Domachevsky et al., 2017; Anderson, 2019; Nemkova et al., 2019; Chumakov et al., 2021), etc. These diseases will seriously affect people's life safety and quality of life. Studies have shown that *Pleurotus ostreatus* polysaccharides can alleviate D-galactose and $AlCl_3$-induced cognitive impairments by increasing the expression of protein phosphatase, reducing the expressions of amyloid precursor protein, β-site scavenging enzyme and glycogen synthase kinase 3β, and enhancing the free radical scavenging ability (Zhang et al., 2016). In addition, the study found that *Flammulina velutipes* polysaccharides can change the intestinal flora of mice, which in turn was effective in improving learning and memory impairment in mice (Su et al., 2018). Zhang et al. (2018b) obtained the polysaccharides from *Flammulina velutipes* and found that the obtained *Flammulina velutipes* polysaccharides can be used as a kind of safe and effective drugs for the prevention and treatment of Alzheimer's disease by compatibilizing with ginsenosides.

### *2.10 Anti-other chronic diseases*

In addition to the above functional properties, edible fungus polysaccharides also have the functions of enhancing immunity, anti-hypertension, anti-hyperlipidemia, etc. The hypotensive process of edible fungus polysaccharides was shown in Figure 5. Some studies have shown that, as an immune stimulator, mushroom polysaccharides can inhibit tumor growth by activating macrophage and NK cytotoxicity (Akramiene et al., 2007). Fu et al. (2013) showed that *Morchella esculenta* polysaccharides can enhance the phagocytosis of mouse macrophages induced by D-galactose, and then significantly enhance the body's immune system. In addition, Yue et al. (2012) reviewed the physiological functions of *Antrodia camphorata* polysaccharides and proposed that the polysaccharides had the effects of anti-hypertension and anti-hyperlipidemia. Polysaccharides have complex structures, and many special biological activities are closely related to their complex spatial structures. In general, due to the repeated arrangement of the primary structure of the polysaccharide chain, the non-covalent interactions between the hydroxyl, amino, carboxyl and sulfate groups on the sugar chain cause the ordered polysaccharide secondary structure to form a regular coarse conformation, which is the tertiary structure of polysaccharide chains. The quaternary structure of polysaccharides refers to the aggregates formed by non-covalent bonds between two polymer chains (Ren et al., 2019).

## 3 Active structure of edible fungus polysaccharides

Edible fungi are important raw materials of natural polysaccharides, and the structural characteristics determine the functional properties of edible fungus polysaccharides. Therefore, it is crucial to analyze the structural characteristics of polysaccharides for their functional development. The primary structure of polysaccharides is mainly composed of monosaccharides, glycosidic bonds and branched chains, and the degree and number of branched chains of polysaccharides are related to the

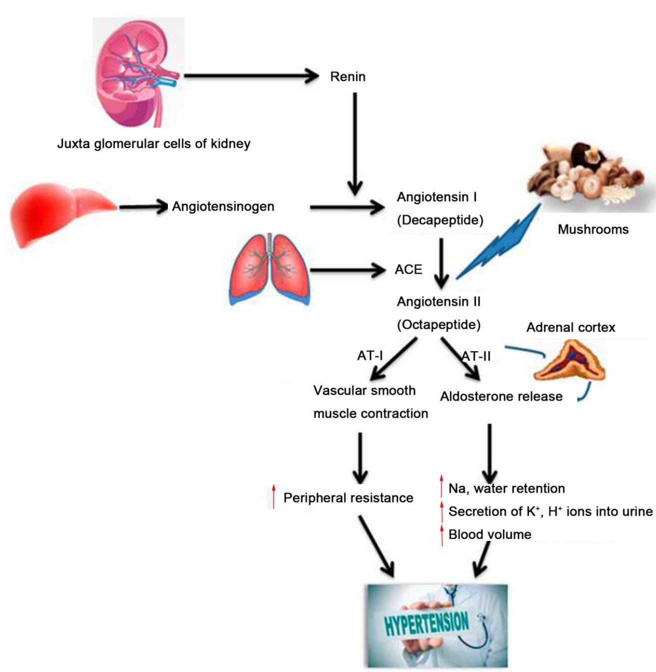


**Figure 5.** The antihypertensive process of edible fungi active substances (Ganesan & Xu, 2018).

connection mode and number of glycosidic bonds (Ding et al., 2022a). Existing studies have shown that monosaccharide configuration (α-configuration or β-configuration) can determine the orientation of glycosidic bonds and the primary structure of polysaccharides (Diener et al., 2019; Wu et al., 2019). Due to the non-covalent interactions between the hydroxyl, carboxyl, amino and sulfate groups of the sugar unit, the ordered secondary structure space becomes regular and thick, which is the tertiary structure of the polysaccharide chain. The quaternary structure of polysaccharides refers to the aggregates formed by non-covalent interactions between polymer chains (Wu et al., 2019).

Studies also have shown that there are certain differences in the amount and structural characteristics of polysaccharides contained in different edible fungi (Jing et al., 2021). For example, *Craterellus cornucopioide* polysaccharides and *Dictyophora indusiata* (Vent.ex Pers) Fisch polysaccharides with similar monosaccharide composition had proliferative activity on specific immune cells such as B cells, T cells and RAW264.7 cells, but *Craterellus cornucopioide* polysaccharides had a better effect on immune cell proliferation than *Dictyophora indusiata* (Vent.ex Pers) Fisch polysaccharides (Ding et al., 2022b). The molecular weight of polysaccharides affects the biological activity of polysaccharides. Yan et al. (2019) extracted polysaccharides from *Pleurotus eryngii*, *Flammulina velutipes*, *Pleurotus ostreatus* and white *Hypsizygus marmoreus*, and found that the molecular weights of the other three edible fungus polysaccharides were all about 20 kDa except for the *Pleurotus ostreatus* acid polysaccharides, which was about 5 kDa. In addition, the structural characteristics and functional activities of different polysaccharides derived from the same edible fungi were also different. Wang et al. (2021a) isolated three main polysaccharides (wHEP-1, wHEP-2 and wHEP-3) from the mycelium of *Hericium erinaceus*, and their average molecular weights were 5010, 1812 and 1118 Da, respectively. wHEP-1 was composed of mannose, galactose and glucose, while both wHEP-2 and wHEP-3 were composed of galactose and glucose with different molar ratios. The above polysaccharides were used to intervene cells and rats to compare the anti-inflammatory activity, and the results showed that the anti-inflammatory activity of wHEP-1 was the best. Gong et al. (2020) extracted and obtained two kinds of polysaccharides (TZP1-1 and TZP2-1) from the fruiting bodies of *Thelephora ganbajun*, and found that the relative molecular weights of TZP1-1 and TZP2-1 were 207000 and 4886 Da, respectively. Among them, TZP1-1 was composed of mannose, rhamnose, galactose and xylose, while TZP2-1 was composed of mannose, glucose, galactose and xylose, and the cytotoxicity of TZP1-1 was superior to that of TZP2-1 *in vitro*. The structures of different edible fungus polysaccharides were shown in Figure 6.

## 4 Intervention mechanism of edible fungus polysaccharides on chronic diseases

As mentioned above, edible fungus polysaccharide is a special kind of biologically active substance, and also a kind of biological

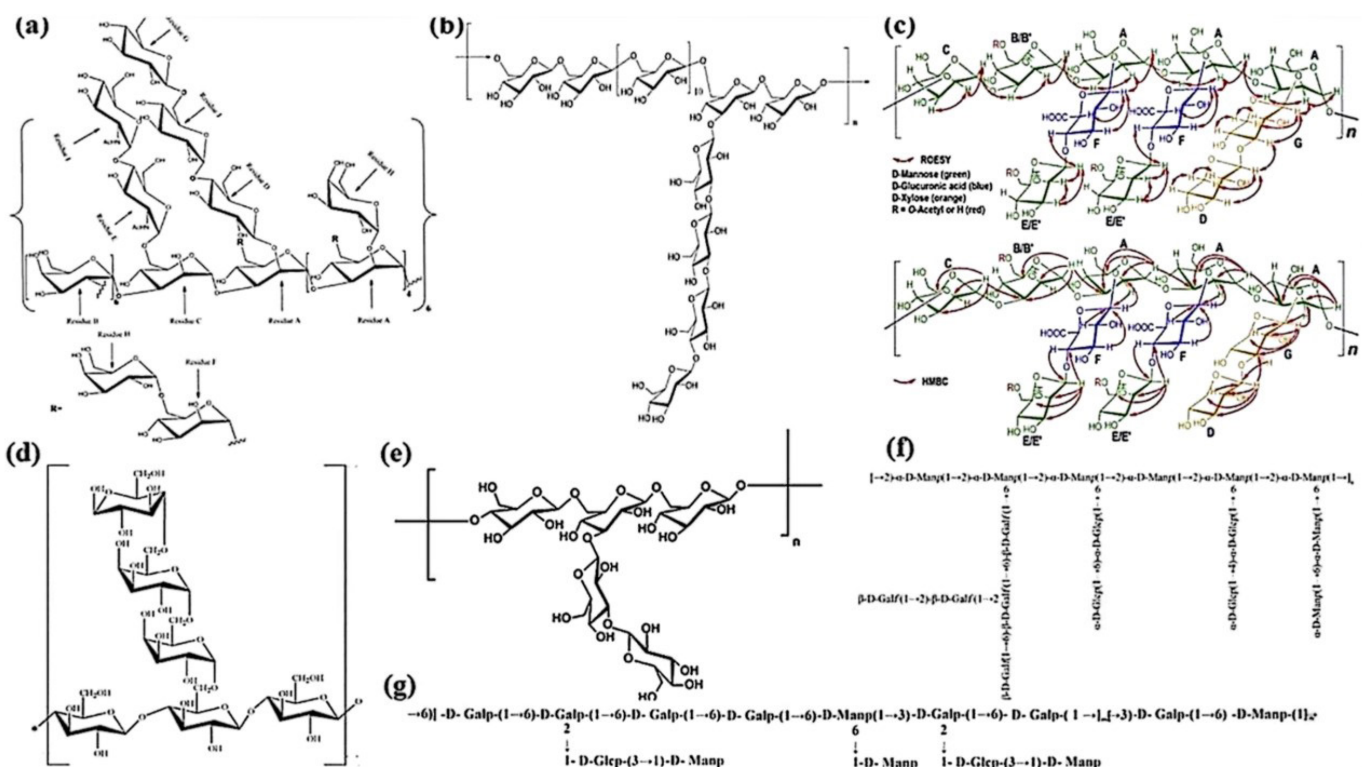


**Figure 6.** Structural characteristics of different edible fungus polysaccharides with specific biological activities (Guo et al., 2021). (a) MIPW50–1 (*Morchella importuna* polysaccharide); (b) HBP (S*arcodon aspratus* (Berk.) polysaccharide); (c) TAP-3 (*Tremella aurantialba Bandoni et Zang* glucuronoxylomannan); (d) BSF-X (*Boletus speciosus Frost* polysaccharide); (e) The polysaccharides from the fruiting bodies of *G. sinense*; (f) SB1–1 (*Shiraia bambusicola* polysaccharide); (g) EPA-1 *(Pleurotus eryngii* polysaccharide).

response enhancer and regulator, which is not only helpful for the treatment of various diseases, but also can enhance the immunity of the body. Nowadays, researchers have studied the effects of edible fungus polysaccharides on chronic diseases at the molecular level. The molecular mechanisms and signal pathways that have been discovered were summarized as follows (Table 1).

Studies have found that edible fungus polysaccharides can improve chronic diseases by regulating oxidative stress and affecting signaling pathways such as NF-κB, KEGG, MAPK and PI3K/AKT, etc. For example, *F. velutipes* mushroom polysaccharides can reduce the level of plasma DAO and increase the activity of SOD in the intestine of mice with colitis to exert its antioxidant effect. In addition, *F. velutipes* mushroom polysaccharides can also exert anti-inflammatory effect by down-regulating the expressions of TLR4, NF-κB and p-p65, thereby inhibiting the TLR4/NF-κB signaling pathway (Zhang et al., 2020a). Simultaneously, *F. velutipes*

**Table 1.** The mechanisms of action of edible fungus polysaccharides on chronic diseases.

| Polysaccharide source | Type of chronic diseases | Model | Mechanism | References |
|---|---|---|---|---|
| *Ganoderma lucidum* | Enteritis | Dextransulfate sodium salt-induced Wistar rats | Up-regulating the expressions of Ruminococcus 1, CCL5, Cd3e, Cd8a, Il-21r, Lck and Trbv; down-regulating the expressions of *E. coli*-Shigella, CCL3, Gro, IL-11, MHC-2 and Ptgs | (Xie et al., 2019) |
| *Hericium erinaceus* | Enteritis | Dextransulfate sodium salt-induced C57BL/6 mice | Up-regulating the expressions of T-SOD and Bacteroides; down-regulating the expressions of NO, MDA, MPO, IL-6, IL-1β, TNF-α, COX-2, iNOS, p-p65/p65, p-IκBα/IκBα, pAkt/Akt, p-p38/p38, p-ERK/ERK and p-JNK/JNK; reducing the numbers of Verrucobacterium, Actinomyces, Arthrobacter, Methylobacter, Succinyl Vibrio, Desulfovibrio . | (Ren et al., 2018) |
| *Pleurotus djamor* | Chronic renal failure | Chronic renal failure mouse model | Clearing DPPH and superoxide anion free radicals; enhancing the activities of SOD, GSH-Px and CAT; reducing the level of MDA; increasing the expression of HO-1 protein; reducing the levels of CREA, UA and UREA; inhibiting the up-regulation of IL-6 and TNF-α; reducing the levels of TGFβ1 and Smad3 | (Li et al., 2021b) |
| *Armillariella tabescens mycelia* | Type 2 diabetes mellitus (T2DM) | A mouse model of insulin resistance in T2DM induced by high-fat diet combined with streptozotocin | Inhibiting the TXNIP/NLRP3 inflammasome pathway and activating the AMPK pathway | (Yang et al., 2020) |
| *Hericium erinaceus* | Enteritis | HOAc-induced SD rats; $H_2O_2$-induced Caco-2 cells | Up-regulating the levels of MMP, SOD, ATP, Bcl-2, IBA, GPR41, GPR43 and IgM; down-regulating the levels of MDA, TNF-α, IL-1, IL-6, ROS, p-p65, p65, caspase-3 and C3 | (Shao et al., 2019; Wang et al., 2019a) |
| *Poria cocos* | Enteritis | TNBS-induced Kunming mice | Increasing the levels of IL-4, IL-10 and DHT; decreasing the levels of MPO, MDA, TNF-α, IL-6, L-1β, IL-12, IFN-γ, IL-2, IL-17, Hmgcs2, Fabp2, Hp, B4galnt2, B3gnt6, Sap and Ca1 | (Liu et al., 2018a) |
| *Poria cocos* | Breast cancer | Human breast cancer MCF-7 cells | Inducing G1 cell cycle arrest and increasing Bax/Bcl-2 ratio | (Zhang et al., 2006) |
| *Inonotus obliquus* | Enteritis | Dextransulfate sodium salt-induced BALB/c mice | Up-regulating the levels of ZO-1, occludin, IL-4, IL-10, GATA-3, Foxp3 and p-STAT6; down-regulating the levels of p-STAT1, p-STAT3, IFN-γ, IL-17, T-bet and ROR-γt | (Chen et al., 2019) |
| *Dictyophora indusiata* | Enteritis | Dextransulfate sodium salt-induced C57BL/6 mice | Up-regulating the levels of GSH, $HO^-$, IL-10, Bcl-2, TJP1 and IRF4; down-regulating the levels of MDA, MPO, TNF-α, IL-6, IL-1β, IL-18, NLRP3, p-IκBα, p-STAT3, Bax, IRF5 and CD86 | (Wang et al., 2019b) |
| *Flammuliana velutipes* | Enteritis | Dextransulfate sodium salt-induced SD rats | Up-regulating the levels of SOD and IVA; down-regulating the levels of MPO, NO, DAO, TLR4, NF-κB and p-p65 | (Zhang et al., 2020a) |
| *Antrodia cinnamomea* | Lung cancer | Lung cancer cells | Inducing the proteasome-dependent degradation pathway; reducing TGFR protein level | (Lu et al., 2017) |
| *Poria polysaccharide* | Boost the immune system | Immunodeficient mice | Increasing the levels of serum IgA, IgG and IgM; Increasing the levels of IFN-γ and IL-4 | (Zhang et al., 2014) |

mushroom polysaccharides can also regulate the intestinal flora and enhance the production of short-chain fatty acids. The above contents all indicated the potential application value of *F. velutipes* mushroom polysaccharides as functional food ingredients (Dong et al., 2020; Zhang et al., 2020a). Ren et al. (2018) found that *H. erinaceus* polysaccharides can inhibit the occurrence and development of inflammation responses by inhibiting NF-κB, MAPK and PI3K/AKT signaling pathways and phosphorylation levels. *H. erinaceus* polysaccharides can regulate oxidative stress, inflammatory factors, and dysbiosis of gut microbes, suggesting that *H. erinaceus* polysaccharides may serve as a kind of potential dietary nutrients against chronic diseases in the future. Xie et al. (2019) pointed out that *Ganoderma lucidum* polysaccharides can affect the expressions of inflammation-related KEGG signal pathway genes, and relevant studies showed that *Ganoderma lucidum* polysaccharides can increase the expression levels of Ccl5, Cd8a, Cd3e, Lck, Il21r and Trbv, and reduce the expression levels of Ccl3, Il11, Gro, Ptgs2 and MHC2, thereby improving the body's immunity and reducing the risk of inflammation and cancer. Edible fungus polysaccharides can also regulate the body's immunity by regulating cytokines, thereby preventing/treating chronic diseases. Hsu et al. (2014) found that *Tremella mesenterica* polysaccharides can improve hyperglycemia and modulate T cell-mediated splenocyte innate immunity in rats with impaired glucose tolerance. In addition, *Tremella mesenterica* polysaccharides can also promote the production of IL-6 in splenocytes, thereby improving innate immunity and T-cell mediated immunity in the process of preventing or treating type 2 diabetes. Edible fungus polysaccharides can also interfere with chronic diseases in other way. Zhao et al. (2021) found that *Ganoderma lucidum* spore polysaccharide-peptide can significantly improve the levels of brain serotonin and norepinephrine, decrease the level of serum corticosterone, and improve the expression levels of BDNF, synapsin I and PSD95, indicating that *Ganoderma lucidum* spore polysaccharide-peptide can increase synaptic proteins in a BDNF-dependent manner, which in turn protected PC12 nerve cells from the toxicity of corticosterone.

## 5 Prospect

Edible fungus polysaccharides have diverse structural characteristics and biological activities, which provides important references for the development of new drugs and functional foods. It is worth noting that edible fungus polysaccharides can be used to prevent/treat various chronic diseases. However, the application of edible fungus polysaccharides in the treatment of chronic diseases still has some problems needed to be solved urgently.

(1) The composition and content of edible fungus polysaccharides obtained by different extraction methods are different, which seriously affects their functional activity. Therefore, in order to improve the effective components and functional activities of edible fungus polysaccharides, it is necessary to further optimize the extraction process;

(2) At present, the researchs on various edible fungus polysaccharides with physiological activity are still in the initial stage, and a large number of *in vitro* and *in vivo* experiments are still needed to verify their functional activities;

(3) Although the application potential of edible fungus polysaccharides in the treatment of chronic diseases has been reported, the specific mechanism of action is still lacking further exploration, which will seriously affect the clinical application of edible fungus polysaccharides.

## 6 Conclusion

Edible fungus polysaccharides have a place in the treatment/prevention of chronic diseases due to their powerful biological activity. This paper reviewed (1) Different edible fungus polysaccharides have different structural characteristics and functional activities; (2) The various beneficial effects of edible fungus polysaccharides on the body, including anti-cancer, anti-obesity, anti-inflammatory, anti-chronic liver diseases, anti-diabetes, anti-chronic brain diseases, anti-chronic lung diseases, anti-chronic skeletal diseases, anti-cognitive dysfunction and anti-other chronic diseases; (3) Edible fungus polysaccharides can improve chronic diseases by regulating oxidative stress or/and affecting NF-κB, KEGG, MAPK, PI3K/AKT and other signaling pathways.

Edible fungi contain a variety of components that are beneficial to the body, among which polysaccharide is one of the main active component. With the rapid development of research on the active ingredients and biological activities of edible fungus polysaccharides, people have increasingly recognized the health care function and potential medicinal value of edible fungus polysaccharides, especially their application value in the treatment of chronic diseases. The mechanisms of action of edible fungus polysaccharides in the treatment of chronic diseases are extremely complex, and the structures of polysaccharides affect their biological activity. The specific mechanism of action and structure-activity relationship need to be studied in depth for a long time. This review summarized the beneficial effects and possible mechanisms of edible fungus polysaccharides on chronic diseases, the relevant contents can provide references for the functional development of edible fungus polysaccharides, and also provide ideas for the development and utilization of drugs used for chronic diseases.

## Abbreviations

SOD, Superoxide dismutase; CCL5, Chemokine (C-C motif) ligand 5; Cd8a, Recombinant cluster of differentiation 8a; Cd3e, CD3 epsilon; Il21r, Recombinant human IL-21 receptor; Lck, Lymphocyte-specific protein tyrosine kinase; Trbv, T-cell receptor beta variables; CCL3, Chemokine (C-C motif) ligand 3; Gro, Growth-regulated oncogene; IL-11, Interleukin 11; MHC-2, Major histocompatibility complex; Ptgs, Post-transcriptional gene silencing; NO, Nitrous oxide; MDA, Malonaldehyde; MPO, Myeloperoxidase; IL-6, Interleukin 6; IL-1β, Interleukin 1β; TNF-α, Tumor necrosis factor-α; COX-2, Cyclooxygenase 2; iNOS, Inducible nitric oxide synthase; GSH-Px, Glutathione peroxidase; CAT, Catalase; DPPH, 1,1-diphenyl-2-picrylhydrazyl; CREA, Creatinine; UA, Uric acid; TGF-β1, Transforming growth factor-β1; ATP, Adenosine-triphosphate; IBA, Indolebutyric acid; GPR41, G-protein-coupled receptor 41; GPR43, G-protein-coupled receptor 43; IgM, Immunoglobulin M; ROS, Reactive oxygen species; IgG, Immunoglobulin G; IFN-γ, Interferon γ; IL-4, Interleukin 4; Hmgcs2, 3-hydroxy-3-methylglutaryl-coenzyme A synthase 2; Fabp2, Fatty acid-binding protein 2; B4galnt2, β-1,4-Nacetyl- galactosaminyl transferase 2; TJP1, Tight junction protein 1; IRFs, The interferon (IFN) regulatory factors; STAT3, Signal transducer and activator of transcription 3; IVA, Isovaleric acid; GATA-3, GATA binding protein 3; Foxp3, Forkhead box P3 transcription factor; RORγt, A member of the retinoic acid-related orphan receptor (ROR) family of transcription factors.

## Conflict of interest

The authors declare that there are no competing interests associated with the manuscript.

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## Author contributions

Conceptualization and funding acquisition, literature collection, writing - review & editing, drawing, **H.L.;** Project administration, resources, **X.L.;** Literature collection, writing - review & editing, **J.X.;** Literature collection, **S.C.**. All authors have read and agreed to the published version of the manuscript.

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