Food & Medicine Homology

ISSN 3006-6867 (print); 3006-4252 (online)
https://doi.org/10.26599/FMH.2025.9420042



Review Article

# Research progress on the mechanism of functional activity of edible fungi polysaccharides—focusing intestinal mucus as a key and entry point

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**Received:** 6 August 2024 / **Revised:** 27 August 2024 / **Accepted:** 2 September 2024

**Abstract:** Edible fungi polysaccharide is a naturally active substance with a complex structure, which has immunomodulatory activity, can regulate intestinal flora, and reduces the body's inflammatory response. Currently, studies on the immune activity of polysaccharides from edible fungi mainly focus on intestinal immunity. Based on the current research direction on the immune activity mechanism of polysaccharides, this paper summarized the direct effects of polysaccharides on intestinal immune cells and the indirect regulatory effects mediated by intestinal flora. At the same time, we found that the active function of polysaccharides needs to pass through the intestinal mucus layer first. The intestinal mucus layer is rich in mucins and special microorganisms with mucins as the carbon source, which act as the first line of defense of the intestinal barrier. The interaction between polysaccharides and intestinal mucins will affect the integrity of the intestinal barrier. And the interaction between polysaccharides and intestinal mucin, to provide a new strategy for the study of the activity mechanism of edible fungi polysaccharides.

**Keywords:** edible fungi polysaccharides; intestinal immunity; mucin; intestinal flora

**Citation:** Yu Y. Y., Duan Y. N., Ma S., et al. Research progress on the mechanism of functional activity of edible fungi polysaccharides—focusing intestinal mucus as a key and entry point. *Food & Medicine Homology*, 2025, 2: 9420042. https://doi.org/10.26599/FMH.2025.9420042

## 1 Introduction

Edible fungi is a term used to describe large fungi that are consumed as food or medicine, because of its delicious taste and rich nutritional value, it has a long tradition of edible and medicinal use in China[1].

Edible fungi play an important part in the dietary structure of consumers worldwide. In 2022, global production of edible fungi reached 56.299 million t, with a output value of $70.09 billion. China, as the largest producer of edible fungi in the world, whose total production of edible fungi in 2022 was 42.254 million t, with a total output value of RMB 388.722 billion (approximately $57,795 million).

The most common edible fungi include *Pleurotus eryngii*, *Flammulina velutipes*, *Lentinula edodes*, *Auricularia auricular*, *Ganoderma lucidum*, *Cordyceps sinensis*, etc. Edible fungi are rich in nutrients, including polysaccharides, proteins, cellulose, vitamins, minerals, etc. They are low in sugar and fat but high in protein[2]. Further researches indicate that edible fungi process a range of functions, including anti-oxidation, anti-inflammatory, anti-inflammatory, anti-tumor, hypoglycemic, immune regulation and so on[3,4].

Among these, edible fungi polysaccharides have been widely studied as the main active substances, and researches show that it has a variety of activities to regulate the health level of the organism, such as immune enhancement[5], antioxidant[6], regulation of intestinal flora[7] and the improvement of blood glucose and blood lipid levels[8]. Many researchers have focused on the immune-enhancing function and mechanism of edible fungi polysaccharides. Edible fungi polysaccharide, as an effective non-specific immune modulator, plays a significantly positive role in the promotion of the immune factors secretion, improvement of immune organs function, regulation of immune cell proliferation and activation of the complement system[9]. *In vitro* and *in vivo* experiments, Fang *et al.*[10] investigated that the polysaccharides derived from *Agaricus brasiliensis* significantly enhanced the indices of spleen and thymus and exhibited immunomodulatory properties in mice. Xing *et al.*[11] demonstrated that *G. lucidum* polysaccharide inhibits the proliferation of gastric cancer cells through *in vitro* experiments, promoting the expression of apoptotic gene *Bax* and inhibiting the expression of anti-apoptotic gene *Bcl-2*, thereby enhancing the susceptibility of cancer cells to



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death. The study of the mechanism of immune enhancement has revealed that edible fungi polysaccharides can regulate a range of health hazards, including abnormal glucose and lipid metabolism, oxidative stress disorder and imbalance of intestinal flora structure. This can indirectly enhance immune function[12-14]. Consequently, the related research idea has evolved from a focus on the direct effect of "polysaccharide-cell" to an emphasis on the indirect effect of "polysaccharide-intestinal flora-cell".

It has been demonstrated that polysaccharides derived from edible fungi are inherently challenging to be directly digested and absorbed by the gastrointestinal tract. However, they can be colonised in the colon and, under the influence of intestinal flora, undergo fermentation, affecting the secretion of relevant immune factors. The intestinal mucus layer, as the initial barrier, plays a significant role in "contacting" and "receiving" the products of the previous stage of digestion, while also influencing the generation of the products of the subsequent stage. Consequently, due to the complexity and individual variability of digestion, further studies on the mechanisms of immunomodulation at this stage is relatively limited and novel. This leaves considerable scope for controversy and exploration.

This review describes the immunomodulatory pathways of edible fungi polysaccharides in intestinal cells and action on the intestinal flora, resulting the indirect regulatory effects. It goes on to discuss the role of polysaccharide digestion products and intestinal mucus in the surface layer of intestinal cells. Finally, it presents a systematic elaboration of the action mechanism of edible fungi polysaccharide immunomodulation.

## 2 Studies on the mechanism of immune function of edible fungi polysaccharides

### 2.1 Direct action mechanism

In the preliminary stages of research, the focus is on the use of *in vitro* immune cell models to investigate the functions of edible fungi polysaccharides in enhancing cell phagocytosis and inducing the secretion of immune factors; It is also important to note that, as a food component, edible fungi polysaccharides have to be ingested in order to exert relevant activities. Consequently, intestinal cell models, such as small intestinal epithelial cells, have also been employed to investigate the immune-enhancing activities of edible fungi polysaccharides during digestion. These researches led to the identification of the mechanisms of action shown in Fig. 1.

The activation of immune response signaling pathways such as nuclear factor-kappa B (NF-κB) and mitogen-activated protein kinases (MAPK) in immune cells induce their secretion of immune factors, including interleukin-1α (IL-1α,) IL-6 and other immunoreactive factors. In an *in vitro* immune cell model, Xu *et al.*[15] demonstrated that the polysaccharide from the fruiting bodies of *P. eryngii* (EPA-1) could induce macrophages to release immunoreactive factors, including NO, tumor necrosis factor α (TNF-α), IL-1, IL-6, and other immunoreactive factors. This was achieved by activating the signaling proteins of p38 mitogen-activated protein kinase, extracellular regulated protein kinases and c-Jun N-terminal kinase (P38, EBK, and JNK), as well as the translocation of the transcription factor NF-κB in MAPKs. Wang *et al.*[16] demonstrated that *F. velutipes* fruiting body polysaccharide (FVPB1) could activate B cells in mice through the MAPK signaling pathway, promoting their proliferation, secretion of immunoglobulin G (IgG), immunoglobulin M (IgM) and production IL-10. Li *et al.*[17] demonstrated that the *Morchella* polysaccharide derivative (SFMP-1) inhibited the activation of the NF-κB pathway, and protected rat alveolar macrophage NR 8383 against PM2.5-induced inflammatory response. Yuan *et al.*[18] demonstrated that *Astragalus* polysaccharide (APS) could inhibit the expression of inflammatory factors TNF-α and IL-8 mRNA, reduce the protein activity of NF-κB, and exert intestinal immunoprotection using lipopolysaccharide (LPS)-injured small intestinal epithelial cells.

Regulation of the oxidative stress damage signaling pathway, such as Nrf2 exerting immune-enhancing functions. Li *et al.*[19] constructed doxorubicin-induced AC16 cardiomyocytes and found that increasing the dose of *Poria cocos* polysaccharides enhanced the proliferation ability of AC16 cells and activated the

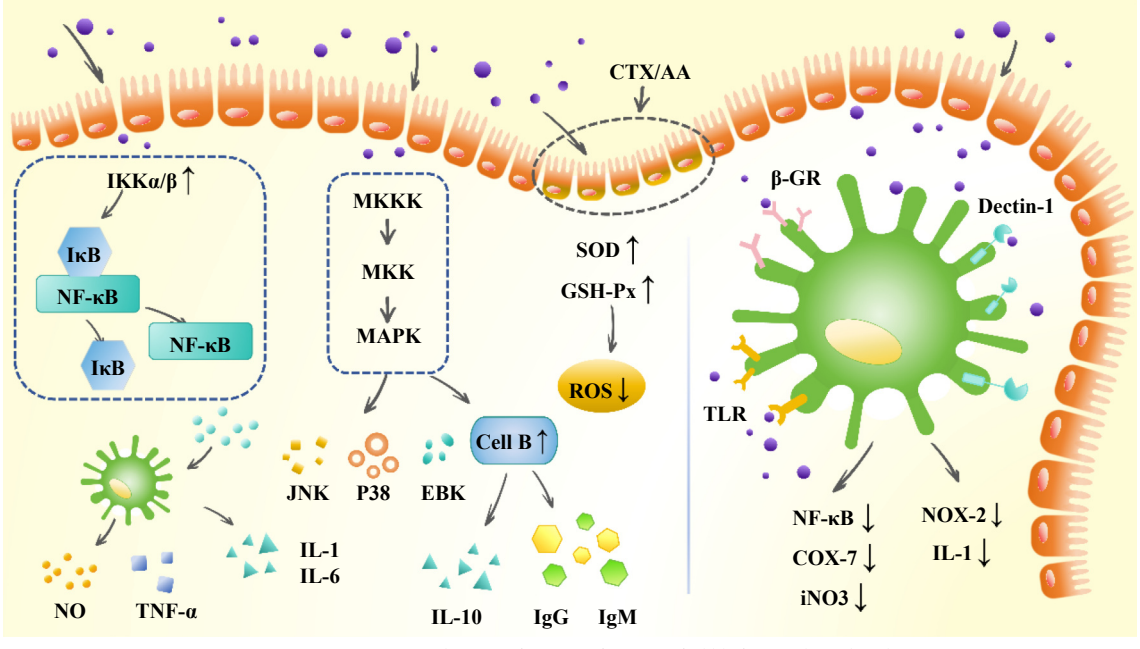


**Figure 1** Direct action mechanism of immune function of edible fungi polysaccharides.

nuclearrespiratoty factor 2/heme-oxygenase 1 (Nrf2/HO-1) signaling pathway. It demonstrated that the treatment could significantly up-regulate the superoxide dismutase (SOD) level, the expression of Nrf2 and HO-1 proteins, and down-regulate the expression of inflammatory factors, malondialdehyde (MDA) and the apoptosis rate[19]. Furthermore, it was observed that *Lentinus edodes* mycelium polysaccharides can reduce cellular oxidative stress damage of islet β cells damage induced by high glucose toxicity. It accelerated the nuclear translocation of Nrf2, promote the expression of detoxification enzymes[20]. Establishing a Caco-2-RAW 264.7 cell co-culture model and utilizing LPS for the induction of inflammation, Hu *et al.*[21] discovered that *Ganoderma atrum* polysaccharides regulated the phosphorylation levels of extracellular regulated protein kinases 1/2 (ERK1/2), JNK, and P38 in the MAPK pathway, activated the Nrf2/ kelch-like ECH-associated protein 1 (Keap1) pathway, significantly up-regulate the expression of Nrf2 and Keap1 protein, and inhibited the overproduction of reactive oxygen species (ROS), exerting an anti-inflammatory effect.

When combined with cell membrane-specific pattern recognition receptors (PRRs), such as *β*-glucan receptors, dectin-1 receptors, Toll-like receptors, etc., it stimulates immune cells to exert immune-enhancing effects. Ma *et al.*[22] extracted *β*-glucan from *Inonotus obliquus* and demonstrated through *in vitro* tests that it could inhibit NF-κB, cyclooxygenase-7 (COX-7) and inducible nitric oxide synthase (iNOS) signaling pathways in macrophage RAW 264.7. Furthermore, *in vitro* tests were conducted on THP-1 cells (human monocytic leukaemia macrophage), which demonstrated that *β*-glucan extracted from *Agaricus bisporus* could inhibit COX-2 protein and IL-1, while inhibiting the inflammatory response[22]. Duan *et al.*[23] cultured the extracellular polysaccharides of *G. lucidum* G0119, G0154, and the hybrid strain GZ36 of the two by liquid fermentation, and found that the extracellular polysaccharide 20E fractions of the three strains, despite being unable to stimulate the release of NO from macrophages to a significant extent, were all found to activate the dectin-1 receptor *in vitro*. The hybrid strain GZ36 exhibited a particularly strong activity in this regard (Table 1).

The above findings indicate that the immune-enhancing function of polysaccharide fractions derived from the same edible fungi source, prepared by different methods, can be significantly different due to structural changes[26]. Based on this, it can be considered that edible fungi polysaccharides need to be digested before they can exert their immune-enhancing function, even though it has been found that most edible fungi polysaccharidses are not completely hydrolysed after digestion in the oral cavity, stomach, and small intestine, but their fine structure is still slightly changed[27]. Consequently, only for the digestive process, as the basis of its activity, there is a paucity of reliable theoretical support for the premise of the immune-enhancing function and mechanism of action of edible fungi polysaccharides, i.e., particularly in relation to the structural and compositional characteristics they interact with intestinal immune cells in the intestinal tract. Consequently, there is an urgent need for a precise interpretation of the correspondence between the changes in the fine structure of edible fungi polysaccharides before and after digestion and their immune-enhancing functions The relevant scientific issues provide the basis for a systematic analysis of the immune-enhancing functions and mechanisms of edible fungi polysaccharides.

### 2.2 Indirect action mechanism

Based on the indigestible nature of edible fungi polysaccharides, the direct interaction of edible fungi polysaccharides with immune cells, recently, with the growing body of evidence linking intestinal flora to the health of the organism, researchers have gradually shifted their focus to the aspect of the intestinal immune-enhancing function of edible fungi polysaccharides through the regulation of intestinal flora in the colon. This is because the majority of edible fungi polysaccharides are fermented by the intestinal flora colonising the colon as a source of energy after ingestion and converted into other active components such as short-chain fatty acids (SCFAs), thus exerting the corresponding intestinal immune-enhancing functional activities[28, 29]. For example, the non-specific immune function of *Pleurotus ostreatus* polysaccharides on *Apostichopus japonicus* was demonstrated, and the diversity between the related functions and their effects on the diversity of intestinal flora was revealed[30]. Another reaearch utilising an acetic acid-induced ulcerative colitis model has elucidated the mechanism by which *H. erinaceus* polysaccharides (HEP) regulate the intestinal flora, thereby maintaining intestinal homeostasis and enhancing immune tolerance[31]. It was demonstrated that dietary *β*-glucan supplementation promoted the proliferation of *α*-amoebae and warty microorganisms in the gut of sea cucumbers, decreased the relative abundance of *Flavobacterium*, and regulated the gut microbial composition[32]. Using a mouse model of dextran sulfate sodium salt (DSS)-induced inflammation, Xie *et al.*[33] found that *Tremella fuciformis* polysaccharides significantly enhanced the diversity of intestinal communities, restored the relative abundance of beneficial *Lactobacillus*, *Odoribacter*, *Helicobacter*, Ruminococcaceae and Marinifilaceae flora, stimulated Foxp3+ T cells, and promoted the production of anti-inflammatory cytokines. It was found that *G. lucidum* polysaccharides (GLP) significantly reduced the abundance of harmful bacteria such as *Aerococcus* and *Ruminococcus*, increased the levels of *Blautia*, *Dehalobacterium*, *Parabacteroides*, and *Bacteroides*, and inhibited the metabolism of inflammatory factors in the intestinal tracts of type 2 diabetic mice[34]. Furthermore, Chen *et al.*[35] demonstrated that HEP could significantly enhance the expression of tight junction proteins, including Occludin, Claudin, and ZO-1 on LPS-induced oxidative stress porcine small intestinal epithelial cells (IPEC-J2). This resulted in the repair of damaged intestinal barriers, alteration of the diversity of intestinal microbiota, and protection of the intestinal microstructure[35]. A synthesis of the extant literature reveals that the current research agenda is focused on three key areas: 1) the impact of edible fungi polysaccharide intake on intestinal immune function, encompassing immune factors, intestinal mucosal barrier, etc.; 2) resolving the interaction between edible fungi polysaccharides and intestinal flora; 3) the correlation the results of the two (Table 2).

The preceding research findings have led to the formulation of further hypotheses regarding the immune-enhancing function and mechanism of action of edible fungi polysaccharides. One such hypothesis, based on the results of a subsequent study, suggests that the key role of intestinal characteristic strains in the function of edible fungi polysaccharides can be revealed through the use of aseptic animal models combined with fecal transplantation. This approach preliminarily revealed the immune-enhancing function of edible fungi polysaccharides through regulating the intestinal bacterial flora[37].

However, in the colon, due to the complexity of the structure of edible fungi polysaccharides and the composition of the related products, it has not yet been reported that the products of digestion through the oral cavity, stomach and small intestine

**Table 1** Direct action mechanism of immune function of edible fungi polysaccharides

| Function | Source | Name | Molecular weight (Da) | Monosaccharide composition | Model | Mechanism | Reference |
|---|---|---|---|---|---|---|---|
| The activation of immune response signaling pathways in immune cells, inducing their secretion of immune factors | *P. eryngii* | EPA-1 | $9.97 \times 10^4$ | Man, Glu and Gal (2.2:1.0:3.2) | RAW 264.7 cell | Release the immune activity factor of NO, TNF-α, IL-1 and IL-6 through activation of signal protein of P38, ERK, JNK in MAPKs and translocation of nuclear NF-κB | [15] |
| | *F. velutipes* | FVPB1 | $2.04 \times 10^4$ | Gal, Man, Fuc and Glu (1.8:1.2:1:15.4) | B cell | Stimulate B cells, promote B cell proliferation, and increase secretion of IgG, IgM and IL-10 by B cells, activating Breg to release IL-10 via JNK, P38 and ERK1/2 signaling pathways | [16] |
| | *Morchella esculenta* | SFMP-1, CFMP-1 | $7.0 \times 10^3$, $6.9 \times 10^3$ | Nm | NR8383 cell | Suppress nuclear translation of the NF-κB and inhibit the degradation and phosphorylation of NF-κB | [17] |
| | *Astragalus* | APS | Nm | Nm | IEC-6 cell | Inhibit the expression of TNF-α and IL-8 mRNA, and decrease the activity of NF-κB protein | [18] |
| | *Sarcodon imbricatus* | SIPS | 56 331.8–93 963.6 | Nm | BALB/c mice | Regulate the production of immunoglobulins including IgA, IgG and IgM in the serum and spleen, promote the secretion of IL-2, IL-6, IL-10, IL-12 and IFN-γ of serum and spleen in CTX-induced immunosuppressive mice | [19] |
| Regulation of the oxidative stress damage signaling pathway | *G. atrum* | PSG-1 | Nm | Man, Gal and Glu | CTX-induced immune dysfunction in mice | Increase the activities of the antioxidant enzymes (SOD, CAT and GPx) in spleen and thymus of the mice subjected to CTX | [20] |
| | *G. lucidum* | GAP | Nm | Nm | IEC-6 cell | Decrease LDH activity and MDA content, and increase SOD and GSH-Px activities | [21] |
| | *Dictyophora indusiata* | DIP | Nm | Nm | RAW 264.7 cell | Activate MAPK and NF-κB signaling pathway, and stimulate macrophages to secrete NO, IL-1β, IL-6, TNF-α and other inflammatory cytokines | [24] |
| Combined with cell membrane-specific pattern recognition receptors, such as *β*-glucan receptors, Dectin-1 receptors, Toll-like receptors, etc., stimulating immune cells to exert immune-enhancing effects | *I. obliquus* | EE (16.2%), PEF (0.24%), EAF (2%), *n*-BF (3.92%) and WF (9.6%) | Nm | Nm | RAW 264.7 cell | Inhibit effects on NO production and NF-κB luciferase activity in macrophage RAW 264.7 cells and cytotoxicity against human prostatic carcinoma cell PC3 and breast carcinoma cell MDA-MB-231 | [22] |
| | *G. lucidum* G0119, G0154 and their hybrid strain GZ36 | G0119-P1, G0119-P3 G0154-P1, G0154-P2, G0154-P3 GZ36-P1, GZ36-P3 | $5.193 \times 10^6$, $6.033 \times 10^4$, $8.957 \times 10^6$, $4.437 \times 10^6$, $6.184 \times 10^4$, $7.549 \times 10^6$, $8.148 \times 10^4$ | Gul, Xyl, Man, Gal and Fuc | RAW 264.7 cell HEK-Blue™ hDectin-1 a cell | The 20 E of the three strains (G0119, G0154 and GZ36) stimulates Dectin-1 | [23] |
| | *P. eryngii, L. edodes, Coprinus comatu, Hericium erinaceus, Ganoderma lingzhi* | PE, LE, CC, HE, GLLZ-2, GLHN-1 | $4.826 \times 10^6$, $3.538 \times 10^6$, $1.272 \times 10^7$, $3.213 \times 10^6$, $1.850 \times 10^6$, $3.240 \times 10^6$ | Fuc, Glu, Gal, Xyl, Man | HEK-Blue™ hDectin-1 a cell | Ganoderma lucidum and hericium 30E with higher *β*-glucan content had stronger activity to activate Dectin-1 receptor *in vitro* | [25] |

**Table 2** Indirect action mechanism of immune function of edible fungi polysaccharides

| Function | Source | Name | Molecular weight (Da) | Monosaccharide Composition | Model | Mechanism | Reference |
|---|---|---|---|---|---|---|---|
| Fermented by the intestinal flora colonising the colon as a source of energy after ingestion and converted into other active components such as SCFAs, thus exerting the corresponding intestinal immune-enhancing functional activities | *P. ostreatus* | POPS-1, POPS-2, POPS-3 | Nm | Nm | *A. japonicus* | The relative abundance of Proteobacteria was reduced, while the relative abundance of Chloroflexi was increased | [30] |
| | *H. erinaceus* | HECP | $8.667 \times 10^4$ | Nm | DSS-induced colitis in C57BL/6 mice | Modulate the distribution of the intestinal flora, restore the relative abundances of vital bacteria including *Clostridiales*, *Akkermansia* and *Desulfovibrio*, prevent the imbalance of gut microbiota | [31] |
| | *T. fuciformis* | HTP | Nm | Nm | DSS-induced colitis in mice | Increase gut community diversity, and restore the relative abundances of *Lactobacillus*, *Odoribacter*, *Helicobacter*, Ruminococcaceae, and Marinifilaceae | [33] |
| | *G. lucidum* | GLP | $1.37 \times 10^4$ | Man, Glu, Gal, Rha and Ara (3.16:16.17:3.74:1.65:1) | HFD and streptozotocin-induced type 2 diabetic rats | Inhibited inflammatory substances metabolism, reduce fasting blood glucose and insulin levels | [34] |
| | Wild morels | MP | Nm | Nm | Cyclophosphamide (Cy)-treated mice | Increase levels of SCFA-producing bacteria | [36] |
| | *Pleurotus geesteranus* | PGP | $4.87 \times 10^6$, $9.84 \times 10^6$ | Glu, Gal | ALD mice | Affect the α- and β- diversity of gut microbiota, alter the gut microbial community at the phylum and genus levels | [37] |

interact with colonic immune cells. It is therefore unclear which pathway and the subsequent mechanism of action is involved. The action of the products of digestion by the intestinal flora before and after fermentation by the intestinal flora represents a significant constraint to research on the immune-enhancing function and mechanism of action of edible fungi polysaccharides. The aforementioned scientific issues represent the principal constraints impeding research into the immune-enhancing function and mechanism of action of polysaccharides derived from edible fungi.

## 3 Interaction of glycolytic digestion with intestinal mucins

Edible fungi polysaccharides are natural polymer composed of a variety of monosaccharides, rich in *β*-glucan[38], which stimulates the body's immune system and has functional activities such as anticancer, anti-inflammatory and antioxidant. As a difficult-to-digest non-starch polysaccharide, edible fungi polysaccharides are not completely degraded by endogenous digestive enzymes in the oral cavity and gastrointestinal tract. Instead, it reaches the human gut through digestion and is then degraded by enzymes secreted by intestinal microorganisms into monosaccharides or oligosaccharides[39-41]. The microorganisms then use these carbon sources to produce SCFAs such as acetic acid, propionic acid and butyric acid, which act on the intestinal epithelial cells and regulate the immune function of the body[42]. For example, *Boletus auripes* polysaccharide, in the *in vitro* simulated digestion process, although the molecular weight and the composition of monosaccharides will change slightly, the overall amount of reducing sugars did not change significantly. This indicates that it is difficult to be degraded and absorbed in the gastrointestinal tract. In contrast, in the *in vitro* simulated fermentation experiment, the total carbohydrate content of polysaccharides and the pH of the fermentation broth kept decreasing within 24 h. It indicated that polysaccharide as a carbon source was continuously degraded and utilized by intestinal microorganisms and produced acidic chemicals-SCFAs, which promoted the growth of beneficial bacteria, such as *Phascolarctobacterium* and *Dialister*, while regulating pH[43]. In addition, it was also found that *Auricularia cornea* var. li. polysaccharides did not show significant changes in typical absorption peaks and functional groups in *in vitro* digestion experiments, but the breaking of some glycosidic bonds led to a decrease in the glyoxylate content of the polysaccharides, as well as changes in the microstructure[44]. It suggests that digestion has a certain effect on polysaccharides, and it is worth exploring whether this effect affects the immunological activity of polysaccharides.

At present, the immune regulation function of edible fungi polysaccharides is primarily investigated in relation to intestinal immunity. Conversely, the research on intestinal immune enhancement tends to focus on the second and third barriers of the intestinal immune system, namely intestinal epithelial cells and the lamina propria, which is rich in T cells and B cells in the lower layer of epithelial cells[45,46]. However, there exists a gelatinous network structure in the gut composed of mucins-the mucus layer, which is the first barrier of the intestinal immune system[47]. It has been found that the intestinal mucus layer, as a physical line of defense for intestinal immunity, not only resists exogenous pathogens, but also interacts with active small molecules to form mucin-bioactive complexes, which affects their absorption and diffusion in the intestine[48]. Before polysaccharides can be active in the gut, they need to first pass through the mucus layer and bind to mucin 2 (MUC2) with electrostatic interactions, which in turn exerts specific functional activities[49,50].

In conclusion, the immunological activity of edible fungi polysaccharides in the organism needs to go through digestion and fermentation in the gastrointestinal tract, which may affect the fine structure of polysaccharides and thus change the surface electrostatic force between mucins and polysaccharides. If the

immunological activity of edible fungi polysaccharides on intestinal epithelial cells is studied directly, the interaction between intestinal mucus and polysaccharides is ignored, which has some limitations in the study of nutrient activity mechanism. In the following section, the interaction between the intestinal mucus layer and polysaccharides from edible fungi will be briefly described to provide a new direction for the current research on the functional activity mechanism of edible fungi polysaccharides.

### 3.1 Intestinal mucus

The intestine is not only the main organ for digestion and absorption of nutrients in the human body but also the largest immune organ. The intestinal mucus is the first barrier of the body's immune system[51]. The average thickness can reach 700 microns, covering the surface of intestinal epithelial cells. The intestinal mucus layer is approximately 100 times thicker than respiratory mucus, which serves to protect epithelial cells and resist the majority of pathogens, maintaining human body health. The intestinal mucus layer is primarily composed of water, lipids[52], and multiple core protein compositions, including mucins, antimicrobial peptides, and secretory immunoglobulin A (sIgA), which inhibit the invasion of intestinal cells by exogenous pathogens[53,54]. The principal component is highly glycosylated gel-type mucin produced and released by goblet cells (GC), which is responsible for the elastic gel properties of the mucus layer[55]. The intestinal mucus layer is divided into an inner and an outer layer. The inner mucus layer is strong and lattice-like. It can separate intestinal microbiota from intestinal epithelial cells, selectively filter foreign substances, and prevent the invasion of pathogenic macromolecules and harmful bacteria[56]. It forms a kind of protection for the intestinal epithelial cells and acts as an immune defense. In contrast, the outer layer of mucus plays a role in the colonization of the intestinal flora, the maintenance of intestinal homeostasis, and the facilitation of microbial degradation of glycans. The thickness of intestinal mucus varies in different parts of the gut. In general, the more microbial colonization, the thicker the intestinal mucus layer, and the thickness of the mucus layer is greater in the colon than in the ileum[57,58]. In addition to lubrication, protection of intestinal epithelial cells, and reduction of mechanical damage in the gut, intestinal mucus can also affect the immune function of the body by regulating the composition of intestinal microbes. The absence of intestinal mucins affects the proportion of intestinal microbiota and triggers intestinal inflammation. In an experiment using the mouse model born in littermates but with different Muc2 content was observed that the proportion of Firmicutes and Bacteroidetes decreased in the gut of the Muc2 (−/−) group, and mice continued to develop colitis. But it will return to Muc2 (+/+) levels under the action of broad-spectrum antibiotics, reducing the inflammatory damage in mice[59]. In mice induced by a Western diet (WSD), the jejunum mucous layer thickness is reduced, leading to a specific depletion of the mucus barrier. As the number of commensal microorganisms dependent on Muc2 decreases, intestinal mucus resistance to the pathogen decreases. This can be expressed as microorganisms colonizing the jejunal mucus layer passively exerting pathogen resistance[60]. At the same time, intestinal mucins are glycosylated proteins with a specific *O*-glycan structure, which affects the abundance of host gut microbes. Hino *et al.*[61] found that when dietary intake of indigestible carbohydrates is limited, intestinal mucin-derived *O*-glycans can serve as an endogenous carbon source that is utilised by microbes in the rat cecum, increasing the abundance of *Marvinbryantia formatexigens*, *Hungatella hathewayi* and *Clostridium scindens*, among others, to promote host and gut microbial symbiosis. Furthermore, the intestinal mucus layer may be closely related to other components of the intestinal immune system, acting as the first line of defense of intestinal immunity. Purified human intestinal mucin and murine mucins MUC2/Muc2 have been shown to regulate intestinal dendritic cells (DCs), promote neutrophil migration, and drive the function of intestinal inflammation repair under the stimulation of IL-8 chemokines[62]. Meanwhile, Muc2 is also regulated by innate immunity. When worms are infected in mice, TLR2-mediated type 2 immunity stimulates GC to produce mucin, replenishing the mucous layer to expel the worms[63]. In addition, macromolecular plant polysaccharides can also affect the intestinal mucus layer, such as *Dendrobium hairy* polysaccharide has been demonstrated to promote intestinal goblet cell proliferation and increase the amount of mucin[64]. It has been demonstrated that sulfhydryl *Codonopsis pilosula* polysaccharide can enhance the adhesion of *Lactobacillus rhamnosus* (LGG) to the intestinal mucosa, increasing the number of beneficial bacteria in the gut and contributing to the maintenance of intestinal health[65] (Tables 3 and 4).

In conclusion, the current research on the intestinal mucus layer has focused on the interaction between the intestinal mucin MUC2 and the intestinal microbiota. Although the complex structure of macromolecular polysaccharides, and intestinal mucin interaction was reported less frequently, edible fungi polysaccharides, which can be considered a kind of intestinal prebiotics, will mediate intestinal flora and affect the secretion of mucin. The relationship between the two will be further elucidated in the following to provide more data for the mechanism of edible fungi polysaccharides research to improve intestinal immune activity.

### 3.2 Effect of mucins on polysaccharides and their glycolytic products

Mucins constitute a family of highly glycosylated proteins of high relative molecular mass, which are found in various mucosal tissues and organs of the body. The mucin family comprises proteins with a tandem repeat structure comprising proline (Pro), threonine (Thr) and serine (Ser) (PTS structural domain), which are highly glycosylated[84]. Additionally, a non-repetitive region is present at the carboxyl and amino terminals, exhibiting a low content of Ser/Thr and minimal *O*-glycosylation. A diverse range of mucins has been identified, with 22 having been named to date. These can be classified into two main groups according to their structure and function: membrane-bound mucins and secreted mucins. Membrane-bound mucins include MUC1, MUC3A, MUC3B, MUC4, and so forth. They possess special transmembrane structural domains that enable them to bind to epithelial cell membranes, thereby participating in epithelial cell signaling, regulation, and repair. Secreted mucins are classified as gel-type or non-gel-type. Gel-type mucins form a gel structure at the surface of epithelial cells, providing a physical barrier that lubricates and protects these cells[85,86]. Human intestinal mucus is composed of secreted MUC2, which is a gel-type mucin. In contrast, non-gel-forming mucins are associated with innate immunity[87].

As the main component of intestinal mucus, intestinal mucins first form oligomers in the rough endoplasmic reticulum (RER) through molecular disulfide bonds, and then the oligomers are

**Table 3** Effect of edible fungi polysaccharides on intestinal mucosal barrier

| Source | Name | Model | Dosages and time | Effect on mucin | Effect on intestinal flora | Protein/mRNA expression | Mechanism | Reference |
|---|---|---|---|---|---|---|---|---|
| *Hericium* | HFP | Forskolin, a cAMP agonist (FSK)-induced ICR mice model | 100, 200, 400 mg/(kg·day) for 14 days | Improve the coverage of mucus in both mouse ileum and colon<br>Not upregulate the expression of *MUC2* gene | Ruminococcaceae↑<br>Lachnospiraceae↑<br>Staphylococcus↓<br>Enterobacter↓ | ANO1↑ (activating chloride channel expression)<br>f5-HT and PGE2↑ | HFP modulates intestinal microbiota and gut fluid secretion through targeting chloride channels CFTR and CaCCs | [66] |
| *F. velutipes* | FVP | $CdCl_2$ induced intestinal -intestinal injury model. Pseudo-sterile mice treated with antibiotics. Fecal microbial transplantation | 100 mg/kg b.w., gavage for 4 weeks | Cannot form FVP-mucin layer, FVP moleculesmight enter and go through the intestinal mucin layer to reach and interact with intestinal epithelium to secrete mucus and provide additional | Bacteroides↑<br>Desulfovibrionales↓<br>Clostridium↓ | Occludin and Claudin-1↑<br>GPR43 and GPR109A↑ | As an effective therapeutic agent against $CdCl_2$-induced gut damage via SCFA-mediated regulation of intestinal inflammation and gut microbiota-related energy metabolism | [67] |
| *B. aereus ameliorates* | BAP | DSS-induced colitis C57BL mice model | 200, 400 mg/kg for 14 days | BAP1-1 intervention improved the defect in the number of MUC2-positive goblet cells in colitis mice and promoted the activation of MANF | Lachnospireaceae - NK4A136↑<br>Prevotellaceae↑<br>Bacteroidaceae↑ | Tff3, Muc2 and Klf4↑<br>key glycosyltransferase (Chst4, Fut2, and Gal3st2)↑<br>MANF↑<br>CHOP and BATF2↓<br>Downstream genes CXCL9 and CXCL10↓ | Involve the activation of MANF-MUC2 signaling pathway and the regulation of microbial homeostasis to promote the protection of damaged mucus barrier | [68] |
| *C. sinensis* | CSP | Cy-treated intestinal barrier injury female BALB/c mice model | 25, 50, and 100 mg/kg b.w. for 7 days | Increased the goblet cells and mucins area | Nm | IAP, DAO, EGF and EGFR↑<br>ZO-1 and Claudin-1↑<br>MLCK, p-MLC↓<br>p-ERK↑<br>p-JNK and pp38↓ | Attenuate Cy-induced intestinal barrier injury associated with mitogen-activated protein kinases (MAPKs) pathways | [69] |
| *C. sinensis* | CSP | Cy-treated intestinal barrier injury female BALB/c mice model | 25, 50, and 100 mg/kg b.w. for 8 days | | *Lactobacillus*↑<br>*Bifidobacterium*↑<br>*Bacteroides*↑<br>*Clostridium*↓<br>*Flexispira*↓ | TNF-α, IL-2 and IL-21↑ | Recover Cy-induced intestinal mucosal immunosuppression by regulating Th cells differentiation via stimulating cytokines secretion and transcription factors production may associated with TLRs and NF-κB pathway<br>Reversed the levels of SCFAs in colon and restored Cy-induced gut microbial dysbiosis by modulating microbial community structure and composition | [70] |
| *I. obliquus* | IN | STZ induced type 2 diabete (SPF)-grade Kunming mice model | 150, 300, and 600 mg/kg b.w. for 9 weeks | Increase the expression levels of the *Ki-67*, *ZO-1*, and *MUC2* genes | Firmicutes↑<br>Bacteroidetes↓ | Ki-67↑<br>ZO-1 and MUC2↑<br>IL-6 ↓ | Protected against diabetes mellitus by ameliorating intestinal barrier dysfunction. IN also suppressed the pro duction of proinflammatory cytokines, enhanced the function of the intestinal mucosal mechanical barrier, promoted the proliferation of beneficial bacteria and reduced the abundance of pathogenic bacteria, thereby ameliorating diabetes mellitus | [71] |

(Continued)

| Source | Name | Model | Dosages and time | Effect on mucin | Effect on intestinal flora | Protein/mRNA expression | Mechanism | Reference |
|---|---|---|---|---|---|---|---|---|
| *T. fuciformis* | TFP | 1. DSS-induced male BALB/c mice UC model | 50, 100, and 200 mg/kg b.w. for 7 days | Increase mucuslayer thickness in colitis mice Lead to higher expression levels of Muc-2 and Clca1 | Nm | TNF-α, IL-1β and IL-6↓ ZO-1 and OCLN (occludin)↑ | The clinical symptoms and histopathological changes of DSS induced UC mouse model were significantly improved, and inflammatory cell infiltration was inhibited. Its mechanism is closely related to the restoration of intestinal barrier integrity | [72] |
| | | 2. LPS-stimulated Caco-2 cells model | TFP dose at 25, 50 and 100 μg/mL | Upregulate the expression of TJP1, OCLN, Clca1 and Muc-2 | | IL-1β and IL-6↓ TNF-α↓ TER↑ FITC-dextran↓ (LPS-stimulated Caco-2 cells) | | |
| *A. auricula* | AAPs DAAPs (prepared from AAPs by alkaline treatment) | High-fat and high-cholesterol diet combined with carbon tetrachloride ($HFHCD/CCl_4$) induced nonalcoholic fatty liver disease (NAFLD) male C57BL mice model | 200 mg/kg b.w. for 8 weeks | AAPs and DAAPs recoverd the expression of Muc-2, ZO-1, Occludin and Claudin-1 | Firmicutes to Bacteroidetes ratio (F/B)↓ *Allobaculum*↓, *Olsenella*↓, *Ruminococcus* 2↓ *Clostridium*_XVIII↓ *Lactobacillus*↑ *Bifidobacterium*↑ *Dorea* and *Odoribacter*↑ | TNF-α, MCP-1, NF-κB and TLR4↑ Col1a1↓ | Protective effects were closely related to alleviating gut microbiota disturbance, keeping the intestinal barrier, altering the BAs profile and regulating the mRNA expression of BAs metabolism | [73] |

**Table 4** Effect of plants polysaccharides on intestinal mucosal barrier

| Source | Name | Model | Dosages and time | Effect on intestinal mucosal barrier | Effect on intestinal flora | Protein/mRNA expression | Mechanism | Reference |
|---|---|---|---|---|---|---|---|---|
| Safflower | SPS | DSS-induced colitis C57BL mice model | 60, 120, 180 mg/kg for 14 days | Improve mucosal barrier function and colon epithelial integrity in UC mice Increase the expression of ZO-1, Occludin, Claudin-1, and MUC2 | *Limosilactobacillus*↑ *Akkermansia*↑ *Bacteroides*↓ *Bifidobacterium*↑ unidentified_ Lachnospiraceae↑ | Reg-3β, Reg-3g, and Reg-3γ↑ | Achieved through inhibiting the activation of the STAT3/NF-κB signaling pathway related to the inflammatory factor CHI3L1, regulating the disorder of intestinal flora | [74] |
| Apple | MAP | 1, 2-DMH and DSS induced colorectal adenocarcinoma | Basal diets mixed with different doses of MAP (1.25%, 2.5% and 5%, *m*/*m*) for 7–20 weeks | Nm | Nm | MUC1↓ A lower $\beta$-catenin level in the nucleus, while a higher $\beta$-catenin level in the cytoplasm, compared with that of model group | Lie in that MAP affected the ex pression and function of MUC1 and promoted the translocation of $\beta$-catenin from nucleus to cytoplasm | [75] |
| *Gracilaria lemaneiformis* | SP | DSS-induced colitis BALB/c mice model | 200, 400, 600 mg/kg for 4 weeks | SP treatments, protective effects of high dose SP was confirmed by 21.82%, 43.65% and 97.11% Respectively increase positive region of Claudin-1, ZO-1 and MUC-2 | *Actinobacteria*↑ *Corynebacterium*_1↑ *Enterorhabdus*↑ *Bacteroides*↓ | TNF-α, IL-6, IL-1β↓ SCFA, GPR43, GPR109A and Olfr78↑ | Alleviate DSS-induced colitis via enhancing intestinal barrier, reducing inflammation, activating SCFA receptors and regulating gut microbiota | [76] |
| *Mesona chinensis* Benth | MBP | DSS-induced colitis C57BL/6 mice model | 12.5, 25, 37.5 mg/kg for 15 days | Significantly increase the level of occludin, ZO-1 and MUC-2 proteins | *Helicobacter*↓ *Prevotella*↓ *Lactobacillus*↑ *Coprococcus*↑ | MPO, TNF-α and IL-1β↓ IL-10↑ SOD, CAT and GSH-Px MDA↑ | Regulates the anti-inflammatory effect of intestinal cells by restoring the intestinal barrier, may be related to the MAPK/NF-κB signaling pathway | [77] |
| *Lycium barbarum* | LBP | DSS-induced colitis C57BL/6 mice model | 150, 300 mg/kg for 30 days | Significantly improve the colonic tissue structure by upregulating MUC-2, claudin-1, and ZO-1 protein expression | *Akkermansia*↑ *Bifidobacterium*↑ *Turicibacter*↓ *Clostridium_sensu_* stricto_1↓ *Escherichia-Shigella*↓ *Faecalibaculum*↓ | IL-1β, IL-6, and TNF-α↓ MPO↓ DCA↑ TGR5↑ | Boost the abundance of *Dubosiella* in intestinal microbiota, rincreasing LCA, DCA and the expression of TGR5, ultimately strengthening the intestinal barrier, influenced by the change in the abundance of *Dubosiella* | [78] |
| Sea cucumber body wall (*Thelenota ananas*) | Ta-FUC | Simulated saliva-gastrointestinal digestion | 4.0 mg/mL | FUC could facilitate interaction with the intestinal mucosa at pH 7.0, maintain the integrity of the intestinal mucosa, and be a potential material for designing colonic administration delivery systems | Proteobacteria↓ Bacteroidota/ Firmicutes↑ | Nm | Exhibit higher adhesive function in the intestinal environment than in the gastric environment. The main supramolecular interactions were identified as disulfide bonding, hydrogen bonding, and hydrophobic interactions for intensity, prolonging the retention of FUC in the intestinal mucosa and build a three-dimensional network, helping improve the MUC barrier properties against mucosal delivery of functional components in the intestinal tract | [79] |

(Continued)

| Source | Name | Model | Dosages and time | Effect on intestinal mucosal barrier | Effect on intestinal flora | Protein/mRNA expression | Mechanism | Reference |
|---|---|---|---|---|---|---|---|---|
| *Atractylodes macrocephalae* Koidz. | AMP | DSS-induced acute colitis C57BL/6 mice model | 100 mg/kg for 14 days | The mRNA expressions of Claudin-1, Occludin, and ZO-1 increased The expression of MUC-1 was higher (not remarkable); MUC-2 was significantly increased in DSS + AMP group | *Enterococcus*↓ *Lactobacillus*↑ | TNF-α, IL-1β, IL-6↓ | Suppress the generation of proinflammatory cytokines such as IL-1β, IL-6 and TNF-α as well as the infiltration of neutrophils in colon; strengthen chemistry barrier and intestinal TJ through boosting the expressions of MUC-2 and Claudin-1; promote the proliferation of beneficial bacteria, and inhibits harmful bacteria, thereby ameliorate colitis induced by DSS | [80] |
| Sea buckthorn | SBP | High-fat diet (HFD) induced mice cognitive dysfunctions C57BL/6 male mice model | HFD chow containing 0.1% SBP (*m/m*) for 12 weeks | SBP in diet significantly reversed the mucus layer impairments and improved MUC-2 expression. SBP in the diet significantly raised the expression of Claudin-1, ZO-1 and Occludin | *Ileibacterium*↑ *Lactobacillus*↓ *Dubosiella*↓ *Olsenella*↓ *Helicobacter*↓ *Ruminiclostridium_9*↓ | TNF-α/IL-1β/IL-6↓ NF-κB pathway↓ CREB/BDNF/TrkB pathway↑ | The reversal effects of SBP on gut dysbiosis might be the important reason for its positive effects on cognitive dysfunction induced by HFD in mice | [81] |
| *Momordica charantia* | MCP | 1. DSS-induced colitis C57BL/6 mice model 2. Pseudo-sterile mouse model (FMT experiment) 3. LPS-induced inflammation in RAW264.7 cells model | 200 and 500 mg/kg for 7 days _ _ | Significantly elevate mRNA and protein expression levels of MUC2 | *Parabacteroides*↑ *Allobaculum*↑ *Ruminococcus*↑ *Allobaculum*↓ *Dorea*↓ *Sutterella*↓ | Reg3b, Reg3g and Ki67↑ | Alleviate inflammation in colitis mice by alleviating DSS induced intestinal barrier damage, regulating intestinal flora and inflammatory pathways | [82] |
| Blackened jujube | BJP-4 | DSS-induced colitis C57BL/6 mice model | 100, 200 and 400 mg/kg for 7 days | After the administration with BJP-4, there was upregulation in the relative expression level of ZO-1 and MUC-2 | f_Muribaculaceae↑ *Lactobacillus*↑ Lachnospiraceae_NK4 A136_group↑ o_Clostridia_UCG-014↓ *Bacteroides*↓ *Escherichia-Shigella*↓ | IL-6 and TNF-α↓ IL-10↑ SOD and CAT restored, MDA↓ TLR4/MyD88/ NF-κB/NLRP3 signaling pathway↓ | BJP-4 dose-dependently alleviated DSS-induced colitic symptoms through altering gut micro biota structure, modulating TLR4/MyD88/ NF-κB/NLRP3 pathway, rebalancing pro/anti-inflammatory cytokines, improving oxidative sta tus, enhancing the integrity of the intestinal epithelial barrier and pro moting the production of SCFAs. The gut microbiota played a central role in anti-inflammatory activity | [83] |
| *Dendrobium fimbriatum* | cDFPW1 | 1. DSS-induced colitis C57BL/6 mouse model 2. Co-culture system consisting of intestinal organoids and LPLs from the colon of mice in Matrigel at a ratio | 200 mg/(kg·day) for 21 days | Directly promote the proliferation of intestinal epithelial cells to protect the integrity of intestinal mucosa and contribute to alleviate DSS-induced colitis | Nm | IL-1β, IL-6, IL-17, IL-23, CXCL1, McP-1, MIP-1α and MIP-1β↓ IL-10, IL-22 and IFN-γ↑ | Promote the regeneration of ISCs to protect the integrity of intestinal mucosa via LPLs secreted IL-22, thus playing an important role in ameliorating UC | [64] |
| *C. pilosula* | sC-CCP-2 | Intestinal adhesion experiment of composite membrane *in vitro* | 5 mg/mL | The sulfhydryl group on the surface of sC-CCP-2 forms a disulfide bond with the cysteine residue on the protein on the surface of LGG, forming a adhesion between LGG and the mucus, and increasing the viscosity of the mucus to LGGAdhesion | Nm | Nm | sC-CCP-2/LGG can form adhesion between sC-CCP-2 and mucus, and the adhesion force between SC-CCP-2 and mucus is the strongest. sC-CCP-2 can increase the intestinal adhesion of LGG, prolong the residence time of LGG in the intestine, and promote the intestinal adhesion and colonization of LGG | [62] |

*O*-glycosylated on the Golgi body. The main mucin type in the small intestine and colon is MUC2, which connects many oligosaccharides in the form of *O*-glycosylated junctions[88]. The structure of these glycans is complex, mainly divided into three regions, in which the core region corresponds to the first *N*-acetyl-glucosamine (GalNAc) singly or double substituted by *α*- or *β*-galactose (*β*-Gal), *β*-*N*-acetyl-galactose-glycosamine (*β*-GlcNAc) and *α*-*N*-acetyl-glucosamine (*α*-GalNAc). The skeleton and peripheral regions contain four monosaccharides: galactose (Gal), fucose (Fuc), GalNAc, and *N*-acetylneuraminic acid (NeuAc)[54]. These alternatively linked glycans wrap around the protein core to avoid its degradation by intestinal endogenous proteases, while simultaneously imparting a specific charge to the surface layer of mucin to maintain the antigenic properties of the mucin[80]. Covalent disulfide bonds link monomeric mucins to form a grid of gelatinous material, with the inner layer covering the host intestinal epithelial cells; the outer layer of *O*-glycans is the initial connection site between gut microbes and host cells.

It is first necessary for edible fungi polysaccharides to be digested in the gastrointestinal tract before they can come into contact with the intestinal mucosa. Only after selective filtration in the intestinal mucus layer can they interact with intestinal immune cells. The interaction between polysaccharides and mucins is primarily governed by hydrogen bonding and electrostatic forces between the two entities. The positively charged NH2 group of chitosan is capable of forming electrostatic interactions with negatively charged gastric mucins. These interactions, in conjunction with hydrogen bonding and water-transport interactions, serve to enhance the mucosal adhesion properties of chitosan, thereby facilitating wound healing[89]. Ma *et al.*[90] characterised the interaction of porcine mucins (MUC) with *P. eryngii* polysaccharides (PEPs) and its *in vitro* simulated digestion products (DPEPs). The researchers observed that both PEP and DPEPs exhibited a notable interaction with MUC. Furthermore, they discovered that DPEPs possess the capacity to disrupt hydrogen bonds within the complementary region of mucins, resulting in an electrostatic repulsion between the chains. This phenomenon has the potential to influence the viscosity and stability of polysaccharide-mucins complexes in solution. This interaction results in alterations to the structure of polysaccharide-mucin complexes, which may influence the indirect active function of polysaccharides within the organism[90]. The structure of intestinal mucin is more dense than that of gastric mucus and respiratory mucus. The mucin-glycan structure has the capacity to resist bacteria and to absorb small-molecule nutrients. Furthermore, microbial fermentation products of edible fungi polysaccharides, such as SCFAs, must traverse the mucus layer before exerting their effects on the second and third intestinal barriers. The passage of such small molecule fermentation products through the intestinal mucus is more facile than that of large molecule polysaccharides[91].

Additionally, this glycan-modified mucin structure exhibits a selective colonization of microorganisms[92]. Microorganisms degrade edible fungi polysaccharides by encoding a variety of polysaccharide-digesting enzymes that facilitate the conversion of polysaccharides into oligosaccharides/glucose or SCFAs. These intermediates are more effective at acting on intestinal cells than the original polysaccharides. *Bacteroides thetaiotaomicron* has been demonstrated to utilise mucins for growth. It possesses a region on its surface designated the polysaccharide utilisation loci (PUL), which encodes a diverse array of proteins that degrade polysaccharides, including surface glycan-binding proteins (SGBP), SusCH/SusDH transporter proteins, periplasmic and surface CAZymes, as well as regulator proteins, amongst others, facilitate the conversion of the polysaccharide into a smaller molecule that is better able to perform its active roles[93,94]. Bifidobacteria exhibit a high degree of adherence to the human gut, recognising extracellular polysaccharides and transporting them to the cytoplasm for digestion[95]. This process is primarily mediated by the ATP-binding cassette transporters (ABC) and the phosphotransferase system (PTS)[96]. In conclusion, mucins can interact with edible fungi polysaccharides in two ways: 1) Mucins can alter the viscosity and potential of food-borne polysaccharides through electrostatic interactions, which can modify the physical properties of polysaccharides. 2) Mucins can affect microbial colonisation and restrict polysaccharide degradation through microbes.

In order to gain further insight into the interactions between mucins and polysaccharides, it is essential to analyse the surface charge of polysaccharide and mucin particles. This will enable us to determine the interaction forces that underpin complex formation and to investigate whether alterations in the structure of the complex affect the active function of polysaccharides. Furthermore, microorganisms act as intermediaries in the interconnections between polysaccharides and mucins, exhibiting intricate physiological processes within the organism. Investigating the degradation mechanisms of diverse microorganisms for endogenous mucin *O*-glycans and exogenous polysaccharides represents a pivotal objective in maintaining equilibrium between intestinal microorganisms, mucins, and dietary polysaccharides.

### 3.3 The action of polysaccharides and their digested fermentation products on mucin

As previously stated, the intestinal mucin MUC2 exhibits a highly glycosylated *O*-glycan structure, with the degree of glycosylation influencing the biological function of mucins. A study has demonstrated that dietary polysaccharides can replenish total body *O*-glycans and alter mucin expression[97]. Zhao *et al.*[98] identified that the modulatory effects of dietary polysaccharides on *O*-glycans were associated with the heterogeneity of monosaccharides. The study also revealed that *α*-1, 4 glycosidic bonds may influence the glycosylated *O*-glycans of laminin on mucin. This was achieved by providing six distinct dietary polysaccharide and mixed polysaccharide structures to C57BL/6J mice. Furthermore, mixed polysaccharides comprising monosaccharide constituents with disparate glycosidic bonds demonstrated enhanced efficacy compared to single polysaccharides. It has been demonstrated to promote the production of fucosylated neutral glycans, reduce acidic glycans, and stimulate microbial abundance and diversity[98]. Polysaccharides with different structures can also exert an influence on mucin glycosylation by modulating the intestinal flora. Tuncil *et al.*[99] extracted polysaccharides with nuanced differences from three different wheats for the purpose of studying changes in the intestinal flora during *in vitro* fermentation. Furthermore, it was discovered that wheat polysaccharides with a higher arabinose abundance were capable of markedly increasing the abundance of *B. thetaiotaomicron* and *Faecalibacterium prausnitzii*, resulting in a notable elevation in propionate concentration. Additionally, *B. thetaiotaomicron* demonstrated the capacity to modify cuprocytes and mucin glycosylation, thereby regulating the intestinal mucus barrier *in vivo*[100].

Microorganisms acting as a bridge between polysaccharide and

mucin interactions can be modulated by edible fungi polysaccharides to influence mucin expression. The two main areas of expression are the ability of SCFAs, the microbial fermentation products of polysaccharides, to influence the production of intestinal mucins. The second is that polysaccharides can change the number of symbiotic flora that feed on intestinal mucus, thereby regulating mucin expression, maintaining the dynamic balance of intestinal mucus and improving the body's immunity. SCFAs not only affect the bile acid cycle to reduce inflammatory responses, but also regulate the expression of the intestinal mucin MUC2. Burger-van *et al.*[101] treated human colonic LS174T cells with SCFAs and found that a low concentration of butyric acid (1–2 mmol/L) was able to increase the expression of MUC2 through the binding of the promoter of MUC2 by the AP-1 transcription factor. SCFAs can also regulate the secretion of prostaglandin e2, stimulate the secretion of MUC2 from intestinal epithelial cup cells and improve the intestinal mucus barrier[102]. Edible fungi polysaccharides, as prebiotics, may improve mucin expression by increasing the body's short-chain fatty acid content. For example, straw mushroom polysaccharides can increase the levels of acetic acid, propionic acid, butyric acid and total SCFAs to increase intestinal mucin secretion[103]. As an immunomodulatory substance, mushroom $\beta$-glucan has been processed into various forms of nutritional supplements that can be fermented by intestinal microorganisms to produce SCFAs, lower intestinal pH, and alter the elasticity and motility of mucins after oral administration. It can also be taken up by M cells and small intestinal epithelial cells in the small intestine, altering the number of cuprocytes and stimulating mucin production by intestinal mucus[104]. *In vitro* fermentation experiments with porcini polysaccharides, elevated levels of butyric acid were able to mediate methylation of the MUC2 promoter, increase mucin expression and attenuate the body's ulcerative colitis response[105].

Secondly, polysaccharides have the potential to alter the diversity of the intestinal flora by increasing the number of intestinal mucus-feeding microorganisms that are capable of modulating mucin secretion. In addition to the existing studies on the effects of different sources of active polysaccharides on the structure of the intestinal flora, the abundance of a species colonising the intestinal mucus layer, *Akkermansia muciniphila*, has been found to be closely related to polysaccharide intake[63]. *A. muciniphila*, which primarily utilises MUC2 as a growth and metabolic substrate, has the potential to weaken the intestinal mucus layer by degrading MUC2, thereby indirectly influencing intestinal immune function[106]. Additionally, *A. muciniphila* regulates intestinal immune function through the deployment of ligands characteristic of intestinal epithelial cells[107]. Furthermore, non-digestible polysaccharides, including *Fructus Mori* polysaccharide and APS, were identified as substrates for *B. thetaiotaomicron*[108,109]. The sulfate esterase expressed by *B. thetaiotaomicron* was shown to degrade human colonic mucin *O*-glycans, enhance mucin colonization, and stimulate mucin secretion[110]. Zong *et al.*[111] observed that *A. auricular* polysaccharides restored the relative abundance of *Bifidobacterium bifidum* in the body of obese mice. Furthermore, they noted that *Bifidobacterium bifidum* encoded protein (bbhII) expression, which could be expressed by the microorganism, could regulate the immune function of the intestines. This protein expression promotes the utilisation of mucin-sulphated glycans by other bacteria[112].

Other studies have characterized mucin-degrading microorganisms in humans, in addition to *A. muciniphila* mentioned above, there are also *Victavallales bacterium*, *B. bifidum*, *Streptomyces lividans*, *Blautia coccoides*, etc. These bacteria groups also have great potential in mucin degradation ability. It may be screened as a mediator of polysaccharide and mucin interaction These bacteria groups also have great potential in mucin degradation ability. It may be screened as a mediator of polysaccharide and mucin interaction[113]. The diverse range of edible fungi polysaccharides and their fermentation products have been demonstrated to significantly contribute to the enhancement of intestinal health. As shown in Fig. 2, the interplay between polysaccharides, microorganisms, and mucins exerts a multifaceted influence on the immune system, prompting a spectrum of responses.

In conclusion, in the process of exerting the immune enhancement function of edible fungi polysaccharides in the

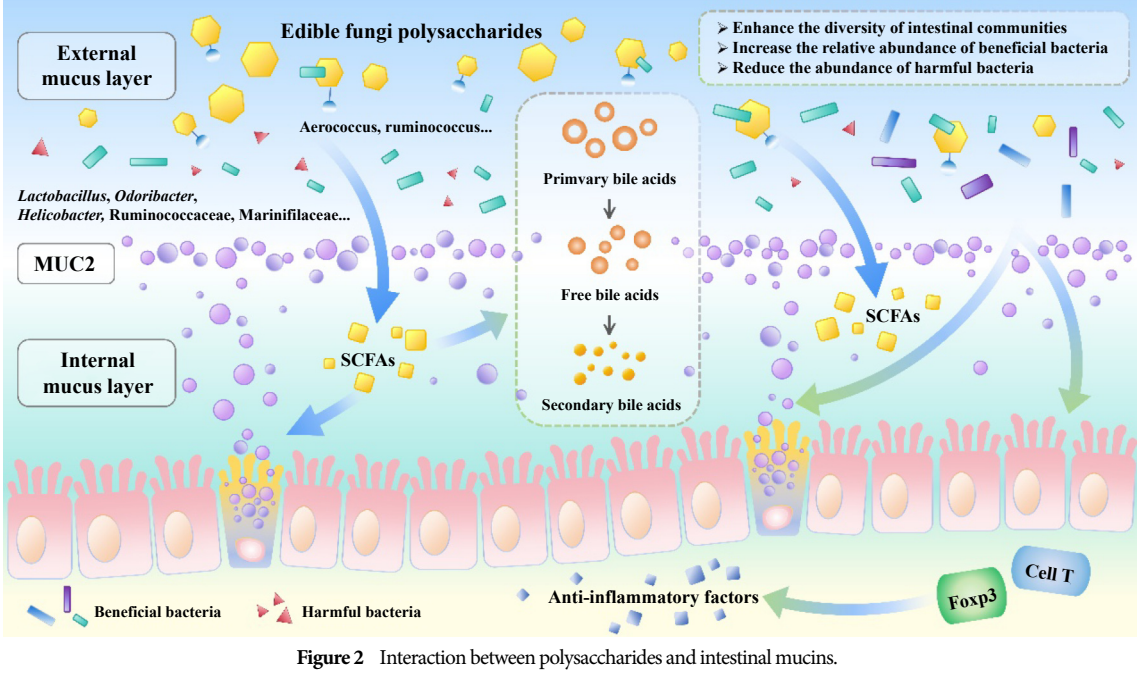


**Figure 2** Interaction between polysaccharides and intestinal mucins.

intestinal tract: 1) the influence of mucins on the structure of polysaccharide digestion products and the activity of immune enhancement function; 2) the filtration effect of mucins on the enhancement function of polysaccharides fermentation products; 3) the influence of mucins caused by polysaccharides by regulating the structure of intestinal flora. These three points are new ideas and key entry points for research into the immune enhancement function and mechanism of edible fungi polysaccharides.

## 4 Discussion and outlook

Edible fungi contain a variety of natural active ingredients, are rich in nutrients, have a wide range of species, and have high nutritional and medicinal value. Polysaccharide is one of the most important active ingredients in edible fungi, which can regulate intestinal immunity and interact with intestinal commensal bacteria to exert anti-inflammatory, anti-cancer and other immune functions after ingestion by the human body. Current research on the mechanism of action of polysaccharides focuses mainly on the protective effects of polysaccharides on immune cells and inflammation in mice. One of these is to reduce the inflammatory response by stimulating the proliferation of immune cells and the secretion of immune factors through direct action on intestinal immune cells. Another is the degradation of edible fungi polysaccharides to produce SCFAs with the help of the gut flora. As the main source of energy for intestinal cells, SCFAs can maintain the integrity of the intestinal barrier and prevent the entry of harmful substances. However, due to the complexity of the intestinal environment, edible fungi polysaccharides must pass through the oral cavity, digestion in the gastrointestinal tract, microbial fermentation, and filtration by the mucus tissue in the upper layer of intestinal cells before they can act on the cells after entering the intestinal tract. The intestinal mucosa is the physical barrier of the intestinal tract and the first line of intestinal immunity. The intestinal mucus layer consists of highly glycosylated mucin (MUC2) secreted by cup cells. The outer layer of this mucus tissue is colonised by a large number of commensal microorganisms, and the dense, sterile environment of the inner layer blocks the contact of exogenous substances with the intestinal epithelial cells, thus ensuring the health of the host. Polysaccharides can come into direct contact with mucins and alter the physical properties of the complex through electrostatic interactions. This change may be related to the fine structure of the polysaccharide, but it is difficult to discuss specifically at this time due to the complexity of the polysaccharide structure in edible fungi.

Furthermore, it is important to acknowledge the role of the intestinal flora, which has been likened to the 'second brain' of the organism, in the study of the relationship between polysaccharides and mucins. A particular subset of the intestinal flora is capable of utilizing both exogenous polysaccharides and endogenous mucin *O*-glycans. Firstly, the mucin MUC2 provides sites for the gut flora to adhere within the mucus layer, enabling the ingestion of nutrients. Additionally, they are capable of converting exogenous polysaccharides into SCFAs. Consequently, the production of SCFAs can stimulate the expression of mucins. Secondly, the ingestion of polysaccharides can alter the relative abundance of this class of microorganisms, prompting them to degrade mucins and alter the thickness of the mucus layer. Both modes of action are inextricably linked to the intermediate role of the gut flora. Consequently, studying the interactions among polysaccharides, gut flora, and mucins represents a novel avenue for investigating the mechanistic basis of polysaccharide immunoreactivity. At present, there is a paucity of systematic and comprehensive insight into the mechanisms through which polysaccharides derived from edible fungi exert their detrimental effects on the intestinal flora and mucus layer. It is imperative to investigate the specific effects of polysaccharides on intestinal flora and intestinal mucus in the context of the physicochemical changes that occur in the organism with edible fungi polysaccharides. Furthermore, special flora that utilise intestinal mucus as a food source, such as *Ackermannia*, *Polymorphobacterium*, *Bifidobacterium*, and so forth, can be employed as a point of departure for mechanistic studies to investigate the specific effects of polysaccharides with varying structures on these flora. This can then be linked with mucins to specifically analyse the role of polysaccharides in repairing damage to the intestinal mucus layer. Polysaccharides derived from edible fungi may serve as immunomodulators, targeting mucins and associated microorganisms, and linking them to specific intestinal diseases. This research avenue could also provide a scientific foundation for the future development of high-quality nutritional and health foods.

## Conflicts of interest

The authors declare that there are no conflicts of interest in this work.

## Acknowledgements

This work was supported by the National Natural Science Foundation of China (No. 32372324).

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