Carbohydrate Polymers 333 (2024) 121978

Contents lists available at ScienceDirect

Carbohydrate Polymers

journal homepage: www.elsevier.com/locate/carbpol

An Overview on Mushroom Polysaccharides: Health-promoting Properties, Prebiotic and Gut Microbiota Modulation Effects and Structure-function Correlation

Helena Araújo-Rodrigues [a,b], Ana Sofia Sousa [a], João Bettencourt Relvas [b,c], Freni K. Tavaria [a], Manuela Pintado [a,*]

[a] Universidade Católica Portuguesa, CBQF - Centro de Biotecnologia e Química Fina, Laboratório Associado, Escola Superior de Biotecnologia, Rua Diogo Botelho 1327, 4169-005 Porto, Portugal
[b] Program of Neurobiology and Neurological Disease, Glial Cell Biology Laboratory, Instituto de Investigação e Inovação em Saúde (i3S), Universidade do Porto, 4200-135 Porto, Portugal
[c] Faculdade de Medicina da Universidade do Porto (FMUP), Porto, Portugal

ARTICLE INFO

Keywords:
Mushroom polysaccharides
Health benefits
Gut microbiota modulation
Structure-function correlation
Underlying mechanisms
2018–2024 data overview

ABSTRACT

Mushroom polysaccharides are recognized as "biological response modifiers". Besides several bioactivities, a growing interest in their prebiotic potential has been raised due to the gut microbiota modulation potential. This review comprehensively summarizes mushroom polysaccharides' biological properties, structure-function relationship, and underlying mechanisms. It provides a recent overview of the key findings in the field (2018–2024). Key findings and limitations on structure-function correlation are discussed. Although most studies focus on β-glucans or extracts, α-glucans and chitin have gained interest. Prebiotic capacity has been associated with α-glucans and chitin, while antimicrobial and wound healing potential is attributed to chitin. However, further research is of utmost importance. Human fecal fermentation is the most reported approach to assess prebiotic potential, indicating impacts on intestinal biological, mechanical, chemical and immunological barriers. Gut microbiota dysbiosis has been directly connected with intestinal, cardiovascular, metabolic, and neurological diseases. Concerning gut microbiota modulation, animal experiments have suggested proinflammatory cytokines reduction and redox balance re-establishment. Most literature focused on the anticancer and immunomodulatory potential. However, anti-inflammatory, antimicrobial, antiviral, antidiabetic, hypocholesterolemic, anti-lipidemic, antioxidant, and neuroprotective properties are discussed. A significant overview of the gaps and research directions in synergistic effects, underlying mechanisms, structure-function correlation, clinical trials and scientific data is also given.

1. Introduction

1.1. Mushroom distribution and nutritional composition

Mushrooms are macrofungi with distinctive fruiting bodies and mycelia belonging to the Basidiomycetes and Ascomycetes classes (Cerletti et al., 2021; Lu et al., 2020). These classes have high molecular diversity and worldwide distribution, estimated between 15000 and 16000 mushroom species (Cerletti et al., 2021; Gong et al., 2020). About 2000 mushroom species globally have been characterized (Lu et al., 2020). Approximately 700 mushroom species are considered safe for human consumption (edible species) and possess positive health-related benefits (Cerletti et al., 2021).

Despite their great diversity, only 60 mushroom species are commercially cultivated, 10 of them being produced on a larger industrial scale in several countries (Gong et al., 2020). *Agaricus bisporus*, *Lentinula edodes*, *Pleurotus* spp., *Hypsizygus tessellatus,* and *Flammulina velutipes* are some of the most cultivated mushroom species worldwide (Marçal et al., 2021; Niego et al., 2021). Approximately 95 % of the global mushroom output corresponds to the Asia market (93 % to the China market), and a gradual increase in mushroom production in other countries has been registered. Nowadays, Europe is responsible for

* Corresponding author.
E-mail addresses: hrodrigues@ucp.pt (H. Araújo-Rodrigues), assousa@ucp.pt (A.S. Sousa), jrelvas@i3s.up.pt (J.B. Relvas), ftavaria@ucp.pt (F.K. Tavaria), mpintado@ucp.pt (M. Pintado).

https://doi.org/10.1016/j.carbpol.2024.121978
Received 29 November 2023; Received in revised form 20 February 2024; Accepted 21 February 2024
Available online 24 February 2024
0144-8617/© 2024 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC license (http://creativecommons.org/licenses/by-nc/4.0/).

approximately 3 % of worldwide production while the American continent for 1 %. China, Japan, and Poland have been the higher mushroom producers, with approximately 41, 0.47, and 0.38 million tons in 2021 (Bijla & Sharma, 2023). In 2021, about 44 million tons of mushrooms were globally produced, increasing yearly by about 8–9 % in the last decades (Knoema, 2022).

The organoleptic properties and rich nutritional value of these macrofungi contribute to their increasing trend. Edible mushrooms possess an excellent composition of carbohydrates (50–65 % on dry matter) and proteins (19–35 % on dry matter). They are a good source of high-quality dietary fiber and have a significant fraction of digestible proteins. At the same time, mushrooms possess lower fat content (2–6 % on a dry matter), being hypocaloric (Araújo-Rodrigues et al., 2022; Lu et al., 2020). Additionally, mushrooms are a good source of essential amino acids (e.g., tryptophan, phenylalanine, leucine, and valine), vitamins (e.g., thiamin, tocopherols, cobalamin, and ascorbate) and minerals (e.g., potassium, phosphorus, magnesium, and calcium). This nutritional profile is valuable and suitable for the dietary requirements of various age groups (children, adults and elderly), which are often deficient in plant nutrients (Araújo-Rodrigues et al., 2022; Bell et al., 2022; Sousa et al., 2023).

Numerous biological and functional properties have also been reported, contributing to these macrofungi's growing popularity (Marçal et al., 2021; Yadav & Negi, 2021). For centuries, natural products have been used for pharmaceutical purposes in several cultures based on empirical knowledge (Marçal et al., 2021). Mushrooms gained medicinal status in ancient times in traditional oriental medicine and were extensively used in the form of extracts, powders, concentrates, and others (Niego et al., 2021). Later, researchers began to characterize their biological mechanisms and started to find evidence of their pharmaceutical potential (Araújo-Rodrigues et al., 2022; Sousa et al., 2023).

1.2. Mushroom bioactive molecules as functional foods, nutraceuticals, and pharmaceuticals

Nowadays, numerous mushroom species, their groups of macromolecules, or specific isolated and purified compounds can also be used to formulate functional foods, nutraceuticals, and pharmaceuticals (Lu et al., 2020; Niego et al., 2021). "Functional foods" can be defined as normal food with enriched or enhanced nutritional properties that provide nutrients and energy, positively affecting human health. On the other hand, "nutraceuticals" correspond to a specific natural compound or nutrient as well as a food extract, generally marked as a supplement in the pharmaceutical format. Both functional foods and nutraceuticals possess demonstrated biological and functional benefits or protective effects against diseases (Araújo-Rodrigues et al., 2022; Damián et al., 2022).

Towards the development of novel functional foods, nutraceuticals, or health-protecting drugs, numerous research studies have focused on the biological and functional mushroom properties (Ma et al., 2018). Immunomodulating, antioxidant, antitumor, anti-inflammatory, antimicrobial, prebiotic, neuroprotective, antidiabetic, and other therapeutic effects have been attributed to different macrofungi species (Lu et al., 2020; Niego et al., 2021; Yadav & Negi, 2021; Yin et al., 2020).

Most health-promoting research studies involving mushrooms focus on testing extracts (a specific macromolecule or groups of macromolecules) (Lu et al., 2020). However, in several matrixes, the interaction between compounds has been suggested to enhance their bioactive properties compared to individual fractions. The hypothesis of a positive synergistic effect between several macromolecules present in mushrooms has also been proposed (Araújo-Rodrigues et al., 2022; Sousa et al., 2023; Venturella et al., 2021). Thus, the positive benefit can be associated with the whole mushroom diet, individual fractions, or macromolecules extracted from specific species (Yadav & Negi, 2021).

The bioactivities of some of the most cultivated and consumed mushroom species, such as *Pleurotus* spp., *A. bisporus*, and L. *edodes*, have been extensively described (Marçal et al., 2021; Niego et al., 2021; Sharma et al., 2021). Other extensively explored macrofungi species worldwide include *Trametes versicolor, Cordyceps sinensis,* and *Antrodia cinnaomea* species, which also demonstrate health-promoting properties (Lu et al., 2020; Yadav & Negi, 2021). Specific bioactive molecules with associated health properties were isolated and characterized from around 270 of the 700 mushroom species identified as safe (Yadav & Negi, 2021).

Some mushrooms' bioactive macromolecules include polysaccharides (e.g., α-glucans, β-glucans, and chitin), polysaccharide-protein complexes (e.g., lectins), proteins (e.g., fungal immunomodulatory proteins and ubiquitin-like proteins), unsaturated fatty acids (e.g., oleic and linoleic acids), ergosterol, terpenes (e.g., monoterpenoids and sesquiterpenoids) and phenolic compounds (e.g., caffeic, syringic and chlorogenic acids) (Araújo-Rodrigues et al., 2022; Gong et al., 2020; Lu et al., 2020; Niego et al., 2021; Yadav & Negi, 2021; Yin et al., 2020).

However, polysaccharides are the most prevalent and extensively studied macromolecules in mushrooms (Araújo-Rodrigues et al., 2022; Marçal et al., 2021; Yadav & Negi, 2021). These are typically described as "biological response modifiers" (Lu et al., 2020; Mirończuk-Chodakowska et al., 2021; Niego et al., 2021). In this context, the present review comprehensively summarizes the health-promoting impacts of mushrooms, focusing on polysaccharides as the most relevant and prevalent macromolecule group. Thus, the main direct bioactive properties of mushroom polysaccharides (especially β-glucans) and health effects mediated by their gut microbiota will be reviewed. This work also provides an overview of recent advances in polysaccharides' structure-function relationship and their underlying mechanisms, supported by in vitro and in vivo studies performed between 2018 and 2024, coupled with clinical trials.

2. Data resources utilized for mushroom polysaccharide studies and clinical trials overview

2.1. Research methodology

The search for mushroom polysaccharide studies published in the last years was carried out on the Web of Science and Google Scholar. The words search/keywords were "mushroom" and "polysaccharides", while selection options were "all databases", "topic", and studies published between 2018 and 2024. Only English-written papers published were selected. The titles and abstracts of papers were analyzed to select only studies focusing on mushroom polysaccharide structural properties, their biological and health potential and function-structure correlation. In the present review, about 160 studies were selected to discuss the most recent and key findings on mushroom polysaccharide bioactive properties and underlying mechanisms.

Regarding the clinical trials search, the ClinicalTrials.gov database was used. As expected, a low number of clinical trials were found and a lower number of clinical trials data in the 2018–2024 period were available. In this case, clinical trials targeting the mushroom diet and mushroom-derived supplements or drugs were searched beyond mushroom polysaccharide extracts. An overview of ongoing and completed clinical trials will be given in the next topic.

2.1.1. Clinical trials

Six active and 51 complete clinical trials were found that target mushroom supplementation, mushroom-isolated molecules, or mushroom-based drugs.

Generally, most clinical trials target immunomodulatory and cancer treatment. Together, these areas represent about 30 % of total clinical trials in the mushroom field. In clinical trials, β-glucans are the most studied bioactive polysaccharides. *L. edodes* is the most studied mushroom species, corresponding to approximately 20 % of the total clinical trials developed with these kinds of macromolecules. Besides L. *edodes*, *A. bisporus*, *A. blazei*, *G. lucidum*, *P. ostreatus*, *G. frondosa* and *Agaricus*

sylvaticus, were the most studied species. Following the impact of mushroom polysaccharides on cancer and immunomodulation, clinical trials also explored the general health benefits of mushroom food intake or food supplements in the immune system (National Library of Medicine, 2023; Panda & Luyten, 2022).

Probably, these results are due to the several proven benefits of lentinan, mainly in cancer therapy, and the pharma legal approval in Asia (including Japan and China) (Rao et al., 2021; Wang et al., 2017; Zhang, Zhang, et al., 2018) for approximately four decades. In Japan, lentinan was approved in 1985 for stomach cancer therapy by Food for Specific Health Use (FoSHU). In China, it was approved in the 1980s by the Chinese Food and Drug Administration (SFDA), and used in the treatment of different cancers (e.g., lung, gastric and colorectal cancer). Beyond cancer, this macromolecule was approved for hepatitis, malignant pleural effusion and human immunodeficiency virus (HIV) in China (Yang et al., 2019; Zhang, Zhang, et al., 2018).

Polysaccharide-protein (PSK) and polysaccharide-peptide (PSP) complexes are also used as adjuvants in cancer therapy in China and Japan. In Japan, PSK was commercially approved in 1977 by the Japanese Ministry (Bains et al., 2021; He et al., 2022), while PSP was in the 1990s (He et al., 2022). PSP has also been extensively used for the treatment of other diseases, for example, chronic bronchitis, hyperlipidemia and hepatitis in China (He et al., 2022). Although PSK and PSP are widely commercially available as food supplements, the European Medicines Agency (EMA) and the Food and Drug Administration (FDA) have not approved PSK and PSP use, since only few ongoing or completed clinical trials do exist (Jędrzejewski et al., 2023).

Since 2018, two clinical trials have been developed and completed. Dietary supplementation with three β-glucan sources (including *Ganoderma lucidum* and L. *edodes*) in protective QI deficiency was evaluated (Levy et al., 2021). Although the results suggested a positive impact of this supplementation, the study was not controlled by placebo (deceptive blinding). It would be important to design a complementary randomized and placebo-controlled study. During this period, a randomized and double-blind study was also carried out, analyzing the impact of L. *edodes*-based bars on levels of cholesterolemia and oxidative stress in participants with borderline cholesterol. The results suggested significant differences in triglyceride levels and some oxidative stress markers (catalase and reduced glutathione) between the placebo and intervention groups (NCT04186780, 2018).

Regarding active clinical trials, two studies were focused on mushroom application in COVID-19 disease (NCT04667247, 2020; NCT04951336, 2021). Both clinical trials were randomized, double-blind, placebo-controlled and combined *T. versicolor* and *Laricifomes officinalis* mushroom species, due to their immunomodulatory potential. The first study aimed to evaluate the effect of these species on the treatment of mild-to-moderate COVID-19 symptoms (as a drug) (NCT04667247, 2020), while the other was tested as an adjunct to vaccination for COVID-19 (as a dietary supplement) (NCT04951336, 2021). Another active clinical trial evaluated the potential of a single intra-articular injection of a chitosan-based drug on patients with advanced symptomatic knee osteoarthritis. This corresponded to a single-blind, randomized, controlled clinical trial that tested chitosan isolated from *A. bisporus,* corresponding to a linear glucosamine (GlcN) polysaccharide. Two other ongoing studies targeted the drug psilocybin isolated from the Psilocybe genus (magic mushrooms). The clinical trials evaluated the impact of this drug on obsessive-compulsive disorder and its mechanism of action through neuroimaging (NCT03300947, 2019; NCT04501653, 2021). The last study aimed at assessing the administration of a combination of a mushroom amino acid (ergothioneine) with taxifolin for immune system improvement (NCT05190432, 2021).

Despite the recent advances, clinical trials in the mushroom field are still scarce and limited. Clinical trials have not followed the advances and the large number of scientific studies in the last decade. Several gaps and shortcomings were identified in some of these clinical trials. For example, some of them are not well structured, randomized, double-blinded, or included a placebo control, which makes it difficult to compare the findings between different clinical trials and obtain effective and realistic conclusions. This could be a big step towards approving multiple drugs, some of which are already clinically used in Asia (e.g., lentinan, PSP and PSK).

2.1.2. Literature data

More than 130 biological properties are associated with mushrooms. Regarding mushroom polysaccharide studies in the period established, the overall results are presented in Table 1. About 2000 reviews and research papers were found. Approximately 17 % of the literature corresponded to review articles. To establish the main topics of the present review and try to cover some literature gaps, an analysis of the last years' reviews was performed. The main topics included in this review and the approximate number of studies involved are also presented in Table 1.

In these review studies, approximately half focused on mushrooms' general biological properties, mainly targeting specific mushroom genera and species. Basidiomycota was the most explored phylum in these studies, while *Ganoderma* spp. and *Pleurotus* spp. were the most reviewed genera. *Ganoderma lucidium* was the most revised species, followed by *Pleurotus ostreatus*. Beyond bioactive potential, some of these reviews focus on the extraction, chemical characterization and properties of mushroom polysaccharides. However, in most cases, the main focus was on their biological properties. Some of these studies also

Table 1
Overview of inclusion criteria and resultant outputs, main topics of published reviews (2018–2024) and key topics covered in this study.

Inclusion criteria for literature data selection	Databases	▪ Web of Science ▪ Google Scholar
	Words search/Keywords	▪ Mushroom ▪ Polysaccharides
	Selection options	▪ All databases ▪ Topic ▪ English-written papers
	Selection period	▪ 2018–2023
Overall results	Total number of studies	▪ ~2000
	Number of reviews	▪ 17 % (~300)
	Number of experimental studies	▪ 83 % (~1700)
Topics of review studies (~300 studies)	General biological properties, polysaccharides extraction, chemical characterization and properties	▪ ~140
	Antitumor	▪ ~40
	Anti-inflammatory, immune and antitumor	▪ ~20
	Diabetes	▪ ~15
	Neuroprotective	▪ ~10
	Selected studies	▪ 158
Selected studies	Topics covered in this review	▪ Chemical and structural composition ▪ Structure-function relationship ▪ Main properties and applications ▪ Health and other biological properties: prebiotic, gut microbiota modulation and their mediated effects, immunomodulatory, antitumor and antiproliferative, anti-inflammatory, neuroprotective, antidiabetic, hypocholesterolemia and antilipidemic, antioxidant, antimicrobial, antiviral, other health benefits (less explored health properties)

try to correlate mushroom polysaccharide structure and chemical properties with their biological properties. Molecular weight (MW) is the most widely recognized chemical characteristic that impacts biological properties. Other properties, such as chemical modifications and branching have been extensively described. However, specific structure-function relationships of mushroom polysaccharides are generally poorly discussed, and conclusions are limited due to incomplete and reduced structural data. In this context, the authors identified this as a literature gap.

Regarding reviews that focus on specific topics, the antitumor potential was the most explored area. As related mechanisms, anti-inflammatory, immune and antitumor studies, were also extensively combined topics. Between 2018 and 2024, the potential of these bioactive macromolecules in diabetes has also been extensively revised. Furthermore, an increasing interest in the neuroprotective properties of mushroom polysaccharides was registered. Other reviews focused on other applications of these biomolecules, namely, cosmetics, food biotechnology, feed and aquaculture fields, as well as extraction approaches, chemical analysis, cultivation techniques, postharvest processing strategies and by-products valorization. Additionally, there are reviews on the mushroom polysaccharides' antioxidant, antimicrobial, prebiotic, and gut microbiota modulation potential; and their therapeutical effect on health reinforcement, wound healing, and metabolic and chronic diseases (e.g., non-alcoholic fatty disease, cardiovascular, inflammatory bowel disease).

The available research studies during this period also extensively covered other biological properties of mushrooms. Some less explored biological properties in research studies were: the protective effect on DNA damage, anticoagulant, antiallergic, analgesic, wound and bone healing, improvement of cognitive capacity and immune system, hepatoprotective, antiaging, radioprotective and chemoprotective. Furthermore, an increase in the number of studies focusing on the gut microbiota potential of mushroom polysaccharides (mainly from 2021 onwards) was also verified, which aligns with the increasing trend in gut microbiota research in the last years.

Accordingly, in this review, despite the limited structural data of mushroom polysaccharides', the authors try to overview advances in the structure-function relationship and give a critical perspective on the limitations and gaps in this topic. At the same time, the authors propose some future research directions. Besides, according to the importance of gut microbiota and their axis, this work will give a special focus on gut microbiota-mediated effects. At the same time, an overview of other bioactive properties of mushrooms is also given. Despite data limitations, the authors tried to survey the structural data in the various studies focusing on the bioactive properties of mushroom polysaccharides. The health studies explored in the present review were subdivided into prebiotic, gut microbiota modulation and their mediated effects, immunomodulatory, antitumor and antiproliferative, anti-inflammatory, neuroprotective, antidiabetic, hypocholesterolemia and antilipidemic, antioxidant, antimicrobial, antiviral and other health benefits (Table 1). The last topic includes the least explored biological properties of mushroom polysaccharides. Among the 158 studies selected, 17 are previous to 2018 to attempt a more complete and robust discussion of some topics (mainly structure-function). By adopting this approach, this study will be able to offer significant insights and reach well-informed conclusions.

3. Mushroom polysaccharides

The composition of carbohydrates and other groups of macromolecules depends on the mushroom species, growing conditions (e.g., type of substratum and environmental conditions), and developmental stage (Lu et al., 2020; Yadav & Negi, 2021). The storage conditions and extraction methodologies similarly impact the concentration and bioactivity of mushroom macromolecules (Lu et al., 2020; Sousa et al., 2023; Wang, 2020). Also, different bioactive macromolecules can be found in the fruiting bodies and mycelia of the same mushroom species (Araújo-Rodrigues et al., 2022; Niego et al., 2021).

The carbohydrate group includes monosaccharides, disaccharides, and polysaccharides (Araújo-Rodrigues et al., 2022; Marçal et al., 2021). Biologically active polysaccharides are large MW compounds linked through glycosidic bonds by at least ten monosaccharides (Gong et al., 2020). Typically, mushroom polysaccharides have in common a backbone of β-linked glucose (Glc) (Chakraborty et al., 2020). However, other polysaccharides with galactose (Gal) or mannose (Man) backbone were also reported in these macrofungi. Polysaccharides can be classified as homoglycans or homopolysaccharides (containing only one type of monosaccharides) and heteroglycans or heteropolysaccharides (containing at least two different types of monosaccharides). These can be combined with peptides and proteins, forming peptide/protein-polysaccharides complexes (Chakraborty et al., 2020; Lu et al., 2020). These complexes are denominated proteoglycans, glycoproteins, and glycopeptides (Gong et al., 2020).

3.1. Structures and classifications

The most prevalent polysaccharides in edible mushrooms are α-, β- or mixed glucans (Gong et al., 2020; Maity et al., 2021). β-glucan is the most important and abundant therapeutic mushroom polysaccharide (3.1–46.5 %) (Cerletti et al., 2021; Chakraborty et al., 2020; Lu et al., 2020; Mirończuk-Chodakowska et al., 2021; Niego et al., 2021). In mushrooms, this macromolecule consists of D-Glc monomers linked through (1 → 3)-β and (1 → 6)-β glycosidic linkages (Cerletti et al., 2021; Chakraborty et al., 2020; Lu et al., 2020). Pleuran, lentinan, grifolan, ganoderan, and other β-glucan macromolecules were isolated from different mushroom species, namely, *P. ostreatus*, *L. edodes*, *G. frondosa* and *Ganoderna lucidum*, respectively (Chakraborty et al., 2020; Niego et al., 2021).

β-glucans generally possess triple helical conformation and differ in the glycosidic linkages' location, high MW, and branching patterns (Chakraborty et al., 2020; Du et al., 2019). The MW of β-glucan typically ranges between ten to thousands of kDa (Du et al., 2019; Gong et al., 2020). Some important characteristics of the main β-glucans and mushroom polysaccharides are described in Table 2.

Although β-glucans are the most reported bioactive polysaccharides, other macromolecules from this group also possess crucial health promotion properties. Beyond β-glucans, mushroom cell walls are also rich in chitin (Cerletti et al., 2021; Lu et al., 2020; Yadav & Negi, 2021), which is typically covalently connected to β-glucan (Jones et al., 2020). Chitin consists of an *N*-acetylglucosamine polymer with (1 → 4)-β linkages ((1 → 4)-2-acetamido-2-deoxy-β-D-glucan; Table 2), a component of a complex biopolymer network (protein-glucan-chitin). This macromolecule may be converted into chitosan through a deacetylation reaction (Bell et al., 2022; Jones et al., 2020; Martinez-Medina et al., 2021).

Even though less explored, linear and branched α-glucans are structurally available in mushrooms (Table 2). Specifically, linear α-glucans may possess exclusively (1 → 3)-α-D, (1 → 4)-α-D or (1 → 6)-α-D bonds or mixed bonds (Table 2). This group is designated as pseudorigeran and amylose when possessing (1 → 3)-α-D and (1 → 4)-α-D, respectively. Pseudorigeran is reported as the most prevalent in the cell wall of mushrooms (Reddy et al., 2021; Synytsya & Novák, 2013). Concerning the mixed group, combined (1 → 3)-α-D and (1 → 4)-α-D are designated as nigeran, while (1 → 4)-α-D and (1 → 6)-α-D bonds as pullulan. Alternatively, glycogen is the most typical branched α-glucan, possessing the linear chain of (1 → 4)-α-D and branches of (1 → 6)-α-D (Reddy et al., 2021). However, there is limited scientific data available on α-glucans, making further research on this subject mandatory to decipher in more detail their chemical structures.

Another interesting natural polysaccharide polymers are exopolysaccharides (EPS). These may be synthetized for some mushroom species (e.g., *P. ostreatus*) and secreted to the extracellular environment.

Table 2
Structural and biological properties of main polysaccharides (α-, β-glucans, and chitin) extracted from different mushroom species.

Polysaccharide	Mushroom species	Structure (basic unit)	Conformation	MW (kDa)	Main bioactivities	References
Ganoderan A, B and C (β-glucan)	*Ganoderma lucidum* (reishi)	(1 → 3)-β backbone, branched at C-6 with (1 → 6)-β Glc units (e.g., β-D-glucopyranosyl with β-(1 → 3) backbone and β-(1 → 6) side chains).	Branched Helical or coiled	5.8–4400	Prebiotic Immunomodulatory Antitumor Antiviral Antiangiogenic Hypoglycemic	(Cateni et al., 2022; Giavasis, 2014; Niego et al., 2021; Tomoda et al., 1986; Wu et al., 2024; Zheng et al., 2022)
Grifolan (β-glucan)	*Grifola frondosa* (maitake)	Three Glc units in the primary chain and one side chain linked through (1 → 6)-β glycosidic bonds.	Branched Triple-helix	300–1000	Prebiotic Immunomodulatory Antitumour Antidiabetes	(Chakraborty et al., 2020; Martinez-Medina et al., 2021; Mirończuk-Chodakowska et al., 2021; Nidhi, 2018; Niego et al., 2021; Yadav & Negi, 2021)
Hericium erinaceus polysaccharide (HEP)	*Hericium erinaceus* (lion's mane)	(1 → 6)-α-D-galactopyranosyl backbone generally composed of α-L-fucopyranose branches at the O-2 position.	Branched Triple-helix	19–1000	Immunomodulatory Antitumor Antioxidant Neuroprotective Hepatoprotective Antihyperglycaemic Hypolipidemic	(Su, Cheng, et al., 2023; Wang, Zhang, et al., 2019)
Krestin (β-glucan)	*Trametes versicolor* (*Coriolus versicolor*; turkey tail)	Heteroglycan: main chain of (1 → 4)-β and side chains of (1 → 3)-β and (1 → 6)-β, being the protein linked to the (1 → 6)-β chain.	Branched Triple-helix	100	Prebiotic Immunomodulatory Antitumor Antioxidant Neuroprotective Immune system reinforcement	(Ferreiro et al., 2018; Mirończuk-Chodakowska et al., 2021)
Lentinan[1] (β-glucan)	*Lentinula edodes* (shitake)	(1 → 3)-β backbone possessing two (1 → 6)-β branches at each five Glc.	Branched Triple-helix	300–800	Prebiotic Immunomodulatory Antitumor Antimicrobial Anti-inflammatory Antiallergic	(Mirończuk-Chodakowska et al., 2021; Nidhi, 2018; Niego et al., 2021; Wang et al., 2020; Wang, Xie, et al., 2019; Zhang, Su, et al., 2019; Zi et al., 2020)
Pleuran (β-glucan)	*Pleurotus ostreatus* (oyster)	Four Glc linked by (1 → 3)-β glycosidic bonds, possessing every Glc unit a side chain attached by (1 → 6)-β glycosidic bonds.	Branched Helical or coiled	600–700	Prebiotic Immunomodulatory Anti-inflammatory Antimicrobial/ Antiviral Antiallergic Immune system reinforce	(Cerletti et al., 2021; Chakraborty et al., 2020; Martinez-Medina et al., 2021; Mirończuk-Chodakowska et al., 2021; Niego et al., 2021; Yadav & Negi, 2021)
Schizophyllan[2] (sizofiran; β-glucan)	*Schizophyllum commune* (split gill)	Three Glc molecules linked by (1 → 3)-β glycosidic bonds, possessing one Glc side chain connected with the main chain by (1 → 6)-β glycosidic bonds.	Branched Triple-helix	100–200	Prebiotic Immunomodulatory Anti-inflammatory Antimicrobial/ Antiviral Antitumor	(Chakraborty et al., 2020; Mirończuk-Chodakowska et al., 2021; Niego et al., 2021; Thongsiri et al., 2021)
Pseudonigeran (α-glucan)	*Agrocybe cylindracea* *Cryptococcus* spp. *Ganoderma* spp. *Lentinus edodes* *Pleurotus* spp.	Basic units of (1 → 3)-α-D.	Linear	9–560	Prebiotic	(Reddy et al., 2021)
Amylose[3] (α-glucan)	*Agaricus blazei* *Pleurotus ostreatus*	Basic units of (1 → 4)-α-D.	Linear	10–400	Energy source	(Reddy et al., 2021)
Pullulan[4] (α-glucan)	*Tremella mesenterica*	Basic units of (1 → 4)-α-D, alternating with (1 → 6)-α-D.	Linear	100–5000	Drug delivery Wound healing	(Reddy et al., 2021)
Glycogen[5] (α-glucan)	*Agaricus bisporus* *Cordyceps sinensis* *Flammulina velutipes*	Linear chain with (1 → 4)-α-D and branches with (1 → 6)-α-D.	Branched Helical	200–400	Antioxidant Immunomodulatory Antiviral	(Reddy et al., 2021)
Chitin[6] (β-glucan)	Several species	(1 → 4)-β linked *N*-acetyl-glucosamine (protein-glucan-chitin complex).	Linear	10–1000	Prebiotic Antimicrobial Wound healing	(Bell et al., 2022; Cerletti et al., 2021; Jones et al., 2020; Lu et al., 2020; Martinez-Medina et al., 2021; Yadav & Negi, 2021)

Glc – glucose; [1]IUPAC nomenclature: (2*R*,3*R*,4*S*,5*S*,6*R*)-2-[[(2*R*,3*R*,4*S*,5*R*,6*R*)-4-[(2*S*,3*R*,4*S*,5*R*,6*R*)-4-[(2*S*,3*R*,4*S*,5*R*,6*R*)-4-[(2*S*,3*R*,4*S*,5*R*,6*R*)-3,5-Dihydroxy-4-[(2*R*,3*R*,4*S*,5*S*,6*R*)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy-6-[[(2*R*,3*R*,4*S*,5*S*,6*R*)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxymethyl]oxan-2-yl]oxy-3,5-dihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy-3,5-dihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy-3,5,6-trihydroxyoxan-2-yl]methoxy]-6-(hydroxymethyl)oxane-3,4,5-triol; [2]IUPAC nomenclature: [3)-β-D-glucopyranosyl-(1 → 3)-[β-D-glucopyranosyl-(1 → 6)]-β-D-glucopyranosyl-(1 → 3)-β-D-glucopyranosyl-(1→]n; [3]IUPAC nomenclature: (1 → 4)-α-D-Glucopyranan; [4]IUPAC nomenclature: 5-[[3,4-dihydroxy-6-(hydroxymethyl)-5-[[3,4,5-trihydroxy-6-(methoxymethyl)oxan-2-yl]methoxymethyl]oxan-2-yl]methoxymethyl]-6-(hydroxymethyl)oxane-2,3,4-triol; [5]alpha-D-gluco-hexopyranosyl-(1 → 4)-[alpha-D-gluco-hexopyranosyl-(1 → 6)]-alpha-D-gluco-hexopyranosyl-(1 → 4)-alpha-D-gluco-hexopyranose; [6](1 → 4)-2-acetamido-2-deoxy-β-D-glucan.

Concerning chemical structure, EPS can be constituted by simple sugars (e.g., Glc, xylose- Xyl) or sugar derivatives (e.g., sugar-protein complex) with different linkage patterns (Choudhary, 2020).

3.2. Structure-function relationship

Polysaccharides can differ in the basic structure, number, and type of bonds as well as in the nature and number of side chains (Du et al., 2019; Gong et al., 2020; Lu et al., 2020; Mirończuk-Chodakowska et al., 2021). Depending on their structural characteristics, polysaccharides exhibit different biological properties (structure-function relationship) (Gong et al., 2020; Maity et al., 2021; Niego et al., 2021; Wang, Han, et al., 2022). This dependence has been mainly associated with the MW, chemical composition, glycosidic bond, tridimensional conformation (e.g., single, double, or triple helix), branching configuration, and resultant solubility (Du et al., 2019; Gong et al., 2020; Lu et al., 2020; Maity et al., 2021; Wang, Han, et al., 2022). Polysaccharides' biological attributes depend highly on their solubility (Araújo-Rodrigues et al., 2022; Li et al., 2019; Reddy et al., 2021). MW, α or β configuration, glycosidic linkage pattern, degree of branching, and surface ionic properties also strongly impact glucans' solubility (Araújo-Rodrigues et al., 2022; Reddy et al., 2021).

The extraction conditions (e.g., solvents, extraction time and temperature) used also play crucial roles in several parameters, such as extraction yield and quality, chemical structure and resultant biological properties (Du et al., 2019; Gong et al., 2020). Chen et al. (2020) compared polysaccharides extracted by hot water (HW), high-pressure (HP), microwave (MA) and ultrasound-assisted (UA) extractions from *Schizophyllum commune*. These approaches impacted mushroom polysaccharide yield, MW, monosaccharide composition, and bioactive profile. The study suggested that UA resulted in lower yield and lower MW polysaccharides but higher antioxidant and hypoglycemic potential. The highest MW polysaccharide fractions present in UA extraction was 11 kDa, which was lower than the extracted with other approaches. Some studies have suggested that UA and MA may extract lower MW polysaccharides than HW (Shang et al., 2018). Regarding monosaccharide composition, HP, MA and UA extractions exhibited similar monosaccharide constitutions: Man, glucose (Glc), rhamnose (Rha), galacturonic (GalA) and glucuronic (GlcA) acids. UA also possess ribose (Rib) and MA fucose (Fuc). On the other hand, HW extraction exhibited a significantly different monosaccharide composition, containing besides Glc, Rha, GalA and GlcA, Rib and Fuc, and also Rha, arabinose (Ara) and Xyl. Although in all cases Man, Glc, Rha, GalA and GlcA were the most prevalent monosaccharides, the results indicated differences in molecular ratios, suggesting different chemical compositions. However, the Fourier transform infrared spectrum (FTIR) did not show differences in the chemical structure of the polysaccharides. This may indicate that the different extraction approaches do not affect polysaccharide structures. In parallel, scanning electron microscopy (SEM) showed variations in the microstructure of polysaccharide extracts (Chen et al., 2020). Although the key findings of the study were significant, no conclusions concerning polysaccharide structure, linkage types and branching patterns of different extraction methods were available.

Similarly, Shang et al. (2018) evaluated the impact of different extraction methods on the yield, MW, and monosaccharide composition of extracted polysaccharides. Their work compared four different methods: HW, UA, enzyme-assisted, and enzyme-ultrasonic-assisted. The study found that the enzyme-assisted approach resulted in polysaccharides with higher antioxidant properties. Although in this study the triple-helix conformation of extracted polysaccharides was demonstrated, this study also lacks the analysis of linkage types and branching degree and how extraction approaches can affect these parameters.

Moreover, Tepsongkroh et al. (2023) extracted polysaccharides from *Volvariella volvacea* using different temperatures and pressures in HW and HP extraction methods. Combining both methods, resulted in the highest β-glucan content, yield and antioxidant properties. This study used nuclear magnetic resonance (NMR) spectroscopy to analyze the structural properties of polysaccharide extracts. The results indicated that the predominant polysaccharides present in the extracts were β-glucans with a combination of both (1 → 3)-β and (1 → 6)-β linkages. While several studies focus on polysaccharide MW analysis, extraction yield, monosaccharide identification and quantification, and how different extraction methods impact bioactive properties, it may be crucial to include the analysis of polysaccharide conformation, linkage types and branching patterns in these types of studies to establish more robust correlations between their structure and function.

3.2.1. Molecular weight (MW)

Strong bioactivities have been typically associated with polysaccharides with higher MW. MW is the most reported and established chemical characteristic that impacts biological properties. This fact may be explained by the better affinity of higher MW polysaccharides to bind to the immune cell's receptors (Gong et al., 2020; Wang, Han, et al., 2022; Zhang, Lei, et al., 2022). However, low MW polysaccharides have been associated with higher antioxidant properties. This can be explained by their enhanced intramolecular hydrogen bonding effects of O—H and the presence of electron-donating substituents. Plus, the degradation of low MW polysaccharides may contribute to their increased antioxidant potential. Some hydrolysis approaches involve enzymatic (cellulase), acid or alkali hydrolysis, MA and UA application (Wang, Han, et al., 2022). Furthermore, scientific data suggested that too small or too large MW are not effectively utilized by gut microbiota (Zhao et al., 2023). This was supported by the study of Tian et al. (2022), which showed that higher MW polysaccharides isolated from *Hericium erinaceus* exhibited lower solubility and were difficult to hydrolyze by gut microbiota. However, other high MW polysaccharides (39.1×10^8 Da) showed an opposite tendency, such as *Helvella leucopus* polysaccharide, exhibiting a significant prebiotic effect.

Accordingly, although a greater MW appears to enhance the immunological effects of mushroom polysaccharides by improving their affinity to the immune cell's receptors, low MW polysaccharides may exhibit higher antioxidant properties. Establishing a correlation between MW and prebiotic potential seems to be challenging due to differences in literature reports.

3.2.2. Chemical modifications and association with other molecules

Some chemical modifications in β-glucans namely, methylation, hydroxymethylation, hydroxypropylation, sulfation and carboxymethylation plus sulfation have also been associated with higher biological properties (Du et al., 2019; Ferreira et al., 2015). For example, these alterations increase water solubility and resultant bioactive properties than corresponding native forms, in *Poria cocos* (Du et al., 2019; Li et al., 2019). Acetylation of a polysaccharide extracted from *Inonotus obliquus* resulted in increased antioxidant potential (Li et al., 2023), while that from *Hypsizygus ulmarius* improved antitumor, antioxidant, and anticoagulant activities (Thimmaraju et al., 2023). Rizkyana et al. (2022) extracted and characterized *P. ostreatus* polysaccharides: the results suggested that its sulfation improved anticoagulant properties.

Therefore, chemical modifications are generally recognized to favor the biological properties of β-glucans and other mushroom polysaccharides. Moreover, the association of polysaccharides with other macromolecules may also be positive in terms of biological potential. For example, the association between mushroom polysaccharides and some groups (e.g., glycoproteins; proteoglycans, polysaccharide sulfates or selenides) is generally recognized to have a positive impact on antitumor activity (Gong et al., 2020; Zhang, Lei, et al., 2022).

3.2.3. Monosaccharide composition

The correlation between monosaccharide composition and bioactive properties of mushroom polysaccharides is not straightforward. A recent study did not find a correlation between their specific monosaccharide

composition and gut microbiota modulation potential. Nevertheless, some studies have suggested that a higher complexity of monosaccharide may positively impact gut microbiota modulation (Zhao et al., 2023). In other words, although a correlation between specific monosaccharides and gut microbiota modulation was not established, a high diversity of monosaccharide types (heteropolysaccharides with high variability of monosaccharides) may have a positive impact.

Similarly, according to studies conducted by Zhang, Lei, et al. (2022) and Chakraborty et al. (2020) heteropolysaccharides or a high diversity of monosaccharides, respectively, may be associated with antitumor properties. Through a literature review, Maity et al. (2021) suggested that a stronger immunomodulatory potential may also be connected to heteroglycans. Alternatively, the presence of specific monosaccharides (Gal, Man, and Fuc, with different molar ratios) may also be positive in terms of immunomodulatory, antitumor and antiproliferative effect (Chakraborty et al., 2020; Deveci et al., 2019; Maity et al., 2021). Deveci et al. (2019) studied the structural and biological activities of polysaccharides extracted from different mushroom species (*Fomes fomentarius*, *Fuscoporia torulosa*, *Ganoderma adspersum*, *Ganoderma applanatum*, *G. lucidum*, *Phellinus igniarius*, *P. ostreatus*, and *Porodaedalea pini*) and, beyond monosaccharide composition, the structural characterization indicated the presence of α- and β- bonds in the main chain. Furthermore, other work directly correlated the polysaccharides' monosaccharide composition with antioxidant activity. In this study, a higher Gal content was linked to stronger 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging, ferrous ion reducing power (FRAP) and metal chelating activities (Zhang, Hu, et al., 2018).

Even though the primary findings suggest that a high diversity of monosaccharide composition may have positive implications in terms of bioactive potential, it is challenging to establish a connection between the function of polysaccharides and their monosaccharide composition. This probably results from the high diversity of monosaccharide constitution and variation in molecular ratios. Additionally, most studies involve a mixture of polysaccharides, making it difficult to determine the monosaccharide composition of each polysaccharide separately.

3.2.4. Branching patterns

Some authors have compared the linear and branching structures of mushroom β-glucans and tried to correlate them with their biological activity. It has been found that β-glucans with linear (1 → 3)-β (de Jesus et al., 2018) and (1 → 6)-β (Sarkar et al., 2012) may have a strong immunomodulatory potential, as well as non-linear structures with (1 → 3)-β and (1 → 6)-β backbones branched at O-6 and O-3, respectively (Maity et al., 2021). This correlation was established in a water-insoluble isolated β-glucan with a triple helical structure. This polysaccharide contains a backbone of (1 → 3)-β-D-glucopyranosyl, with one branching unit of β-D-glucopyranosyl substituted at O-6 in each three-backbone unit (Rout et al., 2008). Besides, other authors have isolated and studied two polysaccharides from *T. versicolor* (29.8 and 50.9 kDa), which suggests that higher MW and fewer branches resulted in strong and better immunomodulatory properties. The structure of these polysaccharides corresponded to a backbone of (1 → 4)-β−/(1 → 3)-β-D-glucopyranosyl group, with branches linked to O-6 (Zhang et al., 2021).

Regarding anticancer properties, several works have shown that β-glucans with a higher branching degree may exhibit antitumor activities, as reported by Bae et al. (2013). Other studies also associated the strong antitumor properties with a branched structure (Zhang, Lei, et al., 2022). For example, (1 → 3)-β linkages in the main chain of β-glucans and additional (1 → 6)-β branching may result in high antitumor potential (Chen et al., 2019; Maity et al., 2021; Surenjav et al., 2006). Typically, (1 → 6) branching increases solubility due to the favorable solution entropy, while high MW glucans with linear chains may be insoluble and possess a microfibrillar nature. The increased hydrophobicity seems to result in higher glucan solubility (Reddy et al., 2021).

Several authors have suggested that a branching structure could enhance the health properties of mushroom β-glucans. However, the exact relationship between branching and functionality is not yet well understood. Therefore, comprehensive research is required to fully grasp the correlation between the branching and function of polysaccharides. It is essential to collect and analyze detailed structural information to unlock the complete therapeutic potential of these compounds. By doing so, a deeper understanding of the complex underlying mechanisms of mushroom β-glucans and their health-promoting effects can be achieved.

3.2.5. Conformation

Several works have highlighted the significant role of triple helical conformation in biological activities (e.g., antitumor) (Ferreira et al., 2015; Maity et al., 2021; Meng et al., 2020; Surenjav et al., 2006; Zhang, Lei, et al., 2022). However, other conformations such as random coil (Zhang, Lei, et al., 2022) and helical conformation (Ferreira et al., 2015) may possess significant antitumor and immunomodulatory activities. Scientific data is generally lacking in understanding the impact of chain conformation alteration on biological properties (Du et al., 2022).

3.2.6. Limitations on structure-function correlations

According to the literature survey, most of the experimental studies lack comprehensive and detailed information on the chemical structure (e.g., conformation, type and linkages, branching pattern) of mushroom polysaccharides. Most studies that include general structure-function correlations failed to evaluate or specify some key characteristics of mushroom polysaccharides that could also play a significant role in their functional properties. Moreover, testing whole extracts instead of specific polysaccharides makes it difficult to establish a clear relationship between the chemical structure and its corresponding functions or activities. Most of the studies included crude extracts, with several structures and uncertainties. In some cases, the application of additional isolation and purification strategies would overcome these issues.

It is important to know the chemical structure to gain mechanistic insights into how mushroom polysaccharides interact with biological systems and to ensure consistency in the composition of the extracts used in research. Additionally, understanding the chemical structure is also vital to optimize extraction methods, while preserving the integrity of the polysaccharides, helping researchers choose the most suitable methods for preserving bioactivity. This review has identified a gap in the literature, which presents an area for further research. Although some techniques that provide information about the type of linkages, branching degree and conformations are expensive and time-consuming (e.g., NMR), standard approaches are of utmost relevance to establishing more robust structure and function correlations.

3.3. Main applications and biological properties

The wide range of polysaccharide applications results from their biodegradability, non-toxicity, biocompatibility, high availability, and numerous biological properties (Maity et al., 2021). Although the insolubility of some α-glucans may limit their application in the food and health fields, the literature in this area is very scarce and limited. The available literature on α-glucan is essentially based on isolation and structural characterization (Reddy et al., 2021). Accordingly, increasing research on α-glucans is imperative to identify possible uncovered bioactive properties. However, the prebiotic potential (Table 2) is the main bioactive property associated with α-glucans (Reddy et al., 2021). Additionally, EPS, which possess several crucial roles in communication, defense against predation and pathogenicity in mushrooms, have also been considered high-value macromolecules for medical, pharmaceutical, and other areas (Choudhary, 2020; Reddy et al., 2021). Some health benefits of EPS include antimicrobial, antiviral, anticancer, and antidiabetic effects (Choudhary, 2020).

Chitin and chitosan also possess numerous applications due to their antimicrobial potential and biocompatible and biodegradable nature.

Thus, mushrooms are an alternative source of chitin and chitosan (Bell et al., 2022; Cerletti et al., 2021; Jones et al., 2020). Although there is a high prevalence of chitin in the mushroom cell wall, scarce studies focusing on this mushroom macromolecule are still available. An increasing interest in chitin and chitosan was registered in recent years due to their wound healing and reducing scarring potential (Table 2), verified in clinical trials (Jones et al., 2020).

Concerning β-glucans, the immunological modulation, metabolic and gastrointestinal impacts are the most reported bioactivities. However, several health properties have been associated with this macromolecule (Araújo-Rodrigues et al., 2022;Cerletti et al., 2021 ; Niego et al., 2021). The several biological and physiological functions of β-glucans are described in Table 2: prebiotic, immunomodulatory, anti-inflammatory, anticancer, antioxidant, antimicrobial, antiviral, antidiabetic, antilipidemic, and hypoglycemic (Lu et al., 2020; Niego et al., 2021; Yadav & Negi, 2021; Yin et al., 2020). The biological properties of mushroom polysaccharides, mainly β-glucans, are discussed in the following sections.

4. Prebiotic potential

The intestinal barrier can be divided into mechanical, chemical, immunological, and biological. The biological barrier corresponds to the intestinal resident bacteria (Hao et al., 2022; Ma, Xu, et al., 2022). The human gut harbors a complex and dynamic microbial community, mainly composed of bacteria (most obligate anaerobes), fungi, and viruses. *Firmicutes*, *Bacteriodetes*, *Actinobacteria*, and *Proteobacteria* are the most incident phyla, playing a crucial role in gut homeostasis (Bonfili et al., 2021; Yin et al., 2020). Multiple parameters impact their composition (e.g., lifestyle, genetics, and age), but diet is one of the most crucial factors (Ghezzi et al., 2022; Lu et al., 2020; Yin et al., 2020). Gut microbiota is involved in the undigestible polysaccharides fermentation and the consequent production of short-chain fatty acids (SCFAs) and other essential metabolites. They are also involved in the metabolism of some important compounds (e.g., drugs, bile acids, and sterols), as well as in the synthesis of some vitamins (e.g., vitamin K and components of vitamin B) (Bonfili et al., 2021; Yin et al., 2020).

In 1995, prebiotics were defined as ingredients indigestible by the gastric and upper gut tract, selectively fermented by probiotic bacteria present in the colon (e.g., lactobacilli and bifidobacteria) (Gibson et al., 2017; Gong et al., 2020; Nidhi, 2018). The most prevalent non-digestible polysaccharides present in mushrooms are α-glucan, β-glucan, chitin, hemicellulose, galactans, mannans, xylans, and peptide/protein-polysaccharides complexes (Mirończuk-Chodakowska et al., 2021; Yadav & Negi, 2021). Their β-glycosidic bonds are non-digestible by human gastrointestinal enzymes (Cerletti et al., 2021; Niego et al., 2021), generally resisting gastric acidity, hydrolysis by digestive enzymes, and gastrointestinal absorption. Depending on the structural composition of mushroom polysaccharides and possible interactions with other compounds, they may reach the colon without any gastric and upper gut tract digestion (Gong et al., 2020).

However, in the colon, gut microbiota can metabolize polysaccharides (Lu et al., 2020; Yadav & Negi, 2021). Through the resultant prebiotic effect, mushroom polysaccharides may increase the proliferation of probiotic bacteria, enhancing positive modifications in the gastrointestinal dynamics (Gong et al., 2020; Lu et al., 2020; Yadav & Negi, 2021). At the same time, by regulating gut microbiota dynamics, the bacterial endotoxin levels are reduced (Lu et al., 2020). Several beneficial genera, such as *Bacteroides*, *Bifidobacterium*, *Akkermansia*, and *Parabacteroides*, are typically promoted (Bonfili et al., 2021; Zheng et al., 2022). For instance, lentinan and polysaccharides extracted from *Morchella* spp., *I. obliquus*, and *F. velutipes* positively impact *Bacteroidetes*, while *Firmicutes* are negatively affected (Zhao et al., 2023). Additionally, they have been associated with an increase in several intestinal fermenting genera, such as *Lactobacillus* and *Enterococcus*. About 50 mushroom polysaccharides (water and UA extracts with a polysaccharide yield between 6 and 11 %) promoted the growth of *Lactobacillus acidophilus* and *Lacticaseibacillus rhamnosus* strains (Nowak et al., 2018).

Several studies have attested the prebiotic potential of entire mushroom or polysaccharide fractions of *Pleurotus* spp., *L. edodes*, *A. bisporus*, *G. lucidum*, *Coprinus comatus*, *T. versicolor, Auricularia auricula-judae, Schizophylum commune* Fr, *P. cocos* and *Tremella fuciformis* (Sharma et al., 2021). Similarly, mushroom chitin (Martinez-Medina et al., 2021; Yadav & Negi, 2021) and α-glucans (Reddy et al., 2021) also possess prebiotic potential. In Table 3, some recent examples of these studies are described. These studies can be divided into *in vitro* fermentation with single strains (Inyod et al., 2022; Moumita & Das, 2022; Zhang, Zhao, et al., 2022), *in vitro* human fecal fermentation (Fu et al., 2023; W. Hu et al., 2023; Ma, Piao, et al., 2022; Wu et al., 2022; Zhang, Zhao, et al., 2022), animal studies (Khan et al., 2018; Lai et al., 2022; Wang, Lu, et al., 2019), and clinical trials. Some studies also include gastrointestinal simulation, but no significant impact is typically described in the polysaccharide fraction. Generally, the mushroom polysaccharides fractions tested promoted the growth of probiotic strains or showed the capacity to modulate human intestinal microbiota and stimulate the production of SCFAs.

In vitro human fecal fermentation is the most used technique to assess prebiotic potential, being a widely used approach to understanding the potential of dietary fiber in modulating the microbiota. This approach allows the evaluation of fermentative rate, SCFAs production, and impact on different bacteria groups present in human gut microbiota (Fu et al., 2023; Wang, Wichienchot, et al., 2019). Moreover, several mushroom studies also focus on the prebiotic research of the mushroom diet (entire mushroom) (Balakrishnan et al., 2021; Chaudhary et al., 2018; Kulshreshtha, 2023; Lu et al., 2020; Moumita & Das, 2022; Sharma et al., 2021). These studies were not discussed in the present review since the main focus is polysaccharides. Polysaccharides are typically the most prevalent group and, consequently, they may be the main responsible portion for mushroom prebiotic potential (Araújo-Rodrigues et al., 2022; Sousa et al., 2023).

The progress in microbiome research projects resulted in the expansion of the "Prebiotics" concept. This has allowed the recognition of other molecules that positively impact microbial colonization. Nowadays, prebiotics are classified as "a substrate that is selectively utilized by host microorganisms conferring a health benefit" (Gibson et al., 2017). In this context, the prebiotic potential can be extended to other mushroom macromolecules, such as peptides, phenolics, polyunsaturated fatty acids, and linoleic acid (Farias et al., 2019). Probiotics, prebiotics, or synbiotics may balance the gut microbiota ecosystem, promoting microbial proliferation and health-stimulating metabolite production (Lu et al., 2020).

4.1. Gut microbiota modulation impacts

Besides the direct impact on the intestinal biological barrier, several other mediated effects result from gut microbiota modulation. Intestinal microbiota interacts with the host through immune, neuroendocrine, and neuronal pathways (Bonfili et al., 2021; Ghezzi et al., 2022). Thus, gut microbiome dysbiosis has been directly connected with the development of several clinical conditions. This dysbiosis may impact immunity, inflammation, glucose and lipid metabolism, ongoing cancer, neurological function, and other physiological processes (Bonfili et al., 2021; Gong et al., 2020; Yadav & Negi, 2021). Due to the correlation between gut microbiota and host health, the exploration of the therapeutic potential of mushroom-derived prebiotics is a recent research trend (Yadav & Negi, 2021). Some of the main health-promoted effects mediated by gut microbiota modulation are illustrated in Fig. 1.

Numerous studies have shown the potential of mushroom consumption on gut microbiota modulation and the consequent impact on body homeostasis and specific disorders. Animal models with induced target diseases are the most used in studies assessing the gut microbiota-

Table 3
Examples of recent studies focusing on the prebiotic potential of mushrooms polysaccharides.

Mushroom species	Polysaccharide fraction	Type of study	Main results	References
Agaricus bisporus	Polysaccharides extract (MW: 3.62 × 10^6 Da; composed by Glc 62 %, Gal 20 %, Man 8 %, Xyl 3 %, Fuc 3 %, and Ara 2 %)	In vitro GIT simulation and in vitro human fecal fermentation	↑ SCFAs (e.g., acetic) ↑ *Prevotella, Phascolarctobacterium and Parabacteroides* ↓ *Fusobacterium*, *Escherichia, Sutterella*, and *Desulfovibrio*	(Fu et al., 2023)
Coprinus comatus	Chitin-glucan complex (β-chitin; Glc and GlcN; *N*-acetylation degree: 62 %; and crystallinity index: 25 %)	In vitro human fecal fermentation	↑ *Bacteroides* and *Bifidobacterium* ↑ SCFAs (e.g., propionic and butyric)	(Zhang, Zhao, et al., 2022)
Dictyophora indusiata	Water-soluble (WS) and -insoluble (WI) polysaccharide extracts (composed by WS: Xyl, Gal, Glc, and Man; and WI: Glc)	Animal (young mice) Gavage administration Fecal microbiota analyses	↑ Intestinal microbial diversity ↑ *Lactobacillus* ↑ SCFAs (e.g., acetic and butyric)	(Lai et al., 2022)
Ganoderma lucidum and *Poria cocos*	Polysaccharide commercial preparation (both species mycelia and fruiting bodies polysaccharides; 30 % purity from Zhi-Quing-Tang Biotech Company Ltd., China)	Animal (6 weeks old rats) Gavage administration Fecal microbiota analyses	↑ Beneficial bacteria (e.g., *Bifidobacterium choerinum and Eubacterium rectale)* ↓ Pathogenic bacteria ↑ SCFAs and lactic acid	(Khan et al., 2018)
Lentinula edodes	Commercial lentinan (not specified) combined with *Lycium barbarum* and *Poria cocos* polysaccharides	Animal (young rats) Intragastric administration Fecal microbiota analyses	↑ SCFAs-related bacteria (e.g., *Lactobacillus* and *Bifidobacterium)* and their primary metabolism ↓ *Enterococcus*	(Wang, Lu, et al., 2019)
Macrocybe crassa	Extracts with a mixture of polysaccharide (4.1–4.5 %), protein (0.35–0.37 %) and phenolic (3.05–6.40 %) compounds	In vitro GIT simulation and in vitro fermentation with single strains	↑ LAB (e.g., *L. sakei* and *L. plantarum*) ↓ Pathogenic bacteria (e.g., *Salmonella* spp., *Staphylococcus aureus* and *Escherichia coli*)	(Inyod et al., 2022)
Pleurotus eryngii	*Pleurotus eryngii* polysaccharide (PEP; composed by Glc 78 %, Man 9 %, Gal 8 %, Rib 0.4 %, Ara 3 % and Fuc 0.3 %)	In vitro GIT simulation and in vitro human fecal fermentation	↑ *Firmicutes* ↓ *Bacteroidetes* and *Proteobacteria* ↑ SCFAs (e.g., acetic and propionic)	(Ma, Piao, et al., 2022)
Pleurotus florida	Polysaccharide extract (68 % of β-glucans)	In vitro fermentation with single strains	↑ Probiotic strains grow (*Lactiplantibacillus plantarum*) ↑ SCFAs (e.g., acetic and propionic)	(Moumita & Das, 2022)
Tremella fuciformis	Four polysaccharide extracts (88–91 % of polysaccharides; MW: 18.6 × 10^5 Da; molecular ratios: Man 1, GlcA 0.07–0.09, Glc 0.02–0.03, Xyl 0.30–0.32 and Fuc 0.19–0.20)	In vitro GIT simulation and in vitro human fecal fermentation	↑ *Phascolarctobacterium*, *Lachnoclostridium* ↑ SCFAs (e.g., acetic, propionic and butyric)	(Wu et al., 2022)
Volvariella volvacea	Four polysaccharide extracts (88–93 % of polysaccharides; MW: 123.6–135.8 kDa; molecular ratios: Gal 1.73–1.86, Glc 0.71–0.75, Man 0.71–0.72, GlcA 0.71–0.73)	In vitro GIT simulation and in vitro human fecal fermentation	↑ Bacteroidetes/ Firmicutes ratio ↑ *Bacteroides* and *Phascolarctobacterium* ↓ Escherichia-shigella ↑ SCFAs (e.g., acetic, propionic and butyric)	(Hu et al., 2023)

MW – molecular weight; SCFA: Short-chain fatty acid; GIT: gastrointestinal tract; Ara – arabinose; Fuc – fucose; Gal – galactose; Glc – glucose; GlcA – glucuronic acid; GlcN – glucosamine; Man – Mannose; Rib – ribose; Xyl – xylose.

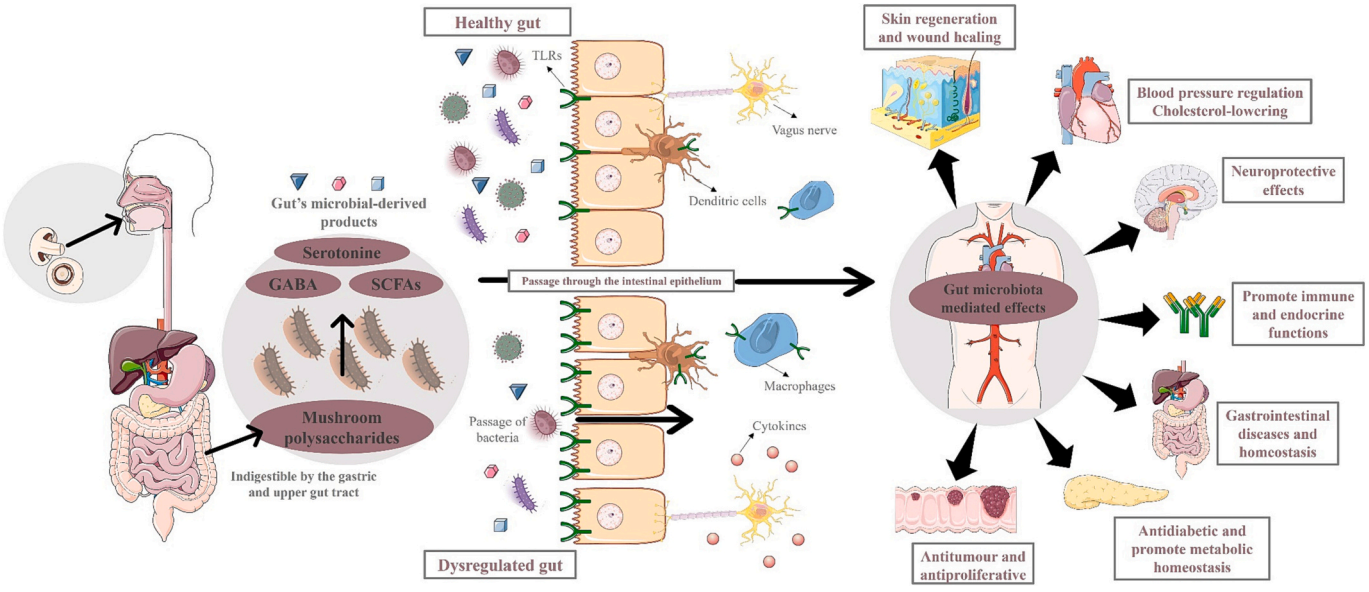

Fig. 1. Some health effects mediated by gut microbiota modulation through mushroom consumption.

mediated effects. Table 4 presents some recent research studies in the field. In parallel, in sections 4.1.1, 4.1.2, 4.1.3 and 4.1.4, some of the most reported gut microbiota-mediated effects are also described, and recent research studies are reviewed.

4.1.1. Effects on the gastrointestinal tract

Gut microbiota modulation mediated by mushroom consumption has several health-related benefits for the gastrointestinal system (Cerletti et al., 2021; Lu et al., 2020; Yadav & Negi, 2021). Also, gut microbiota transplantation after mushroom polysaccharides diet (MW:

Table 4
Examples of recent studies focusing on the gut microbiota-mediated effects of mushroom polysaccharides.

Mushroom species	Polysaccharides fraction	Type of study	Target	Gut microbiota-mediated effect	Reference
Flammulina velutipes	Polysaccharide extract (containing uronic acid residues, (1 → 4)-β linkages, pyranose rings and/or sulfated aromatic ring; molecular ratio: Glc 72, Man 7, Gal 14, Ara 4, Xyl 1.4, Fuc 0.59, Rib 0.59)	Animal (4-weeks-old mice) $CdCl_2$-induced intestinal injury Gavage administration Gut microbial transplantation Fecal microbiota analyses Gut biochemical assays	Intestinal inflammation and barrier dysregulation	↑ *Bacteroides*, ↓ *Desulfovibrionales* and *Clostridium* ↑ SCFAs (e.g., propionic and butyric) ↑ Tight junction genes (occludin and claudin-1) and G-protein-coupled receptor genes (GPR43 and GPR109A) ↓ Proinflammatory cytokines (TNF-, IL-1, and IL-1β) ↓ Intestinal inflammation, modulate intestinal permeability and barrier Gut microbial transplantation promote similar effects	(Hao et al., 2023)
Grifola frondose, Hypsizygus marmoreus and *Pleurotus eryngii*	Commercial polysaccharide extract (Nutrient composition: 20 % of dietary fiber; Glc 33.5 %)	Human (18 healthy volunteers) Oral administration Fecal microbiota analyses Intestinal IgA levels and metabolomics	Intestinal homeostasis and immune system	↑ *[Eubacterium] ventriosum* group ↑ SCFAs (e.g., propionic and butyric) No significant effects on metabolomics ↑ Intestinal IgA levels	(Nishimoto et al., 2023)
Hericium erinaceus	HEP (→4)-α-D-Glcp(1→, →3)-β-D-Glcp (1→, →6)-α-D-Glcp(1→, and α-D-Glcp (1 → residues; MW: 7.5×10^7 Da; molecular ratio: Glc 56.7, Gal 24.2, Fuc 7.9, Man 5.9, Xyl 2.3, GlcA 1.27, Rib 1, ManA 0.5, Ara 0.3)	Cellular (acrylamide-induced injury in IEC-6 cell) and animal (6-weeks-old male mice) with normal and decreased intestinal barrier Gavage administration Test of HEP and fermented HEP (FHEP) Fecal microbiota analyses Biochemical assays	Intestinal barrier homeostasis	Cellular: FHEP ↑TEER and paracellular permeability HEP and FHEP ↑Tight junction and mucin expression Animal: Enhance the intestinal barrier function ↑*Bacteriodetes*, *Firmicutes* ↓*Klebsiella*, *Shigella* ↑ SCFAs (e.g., acetic, propionic and butyric acid) ↓ Proinflammatory cytokines (TNF-, IL-1, and IL-6) FHEP ↑Immune molecules (IgA, IgG, and IgM) ↑ Occludin, ZO-1/ -2, claudin-3/ -4, MUC2 ↓ claudin-2	(Su, Cheng, et al., 2023; Su, Li, et al., 2023)
Huangshan Floral Mushroom	Polysaccharide extract ((1 → 3)-β-glucan; MW: 7.2×10^5 Da)	Animal (6-weeks-old mice) Induced ulcerative colitis Gavage administration Fecal microbiota analyses Gut biochemical assays	Intestinal diseases (ulcerative colitis)	↑ Microbiota diversity ↓ Harmful bacteria ↑ SCFAs (e.g., acetic and butyric) Regulating immune balance of Th17/Treg and inflammatory factor secretion ↓ Intestinal mucosal barrier injury ↓ Ulcerative colitis	(Zou et al., 2022)
Armillariella tabescens	Water-soluble polysaccharide extract ((1 → 4)-α-D-Glcp with branches at O-6 and terminated with T-α-D-Glcp; composed by Glc 89 % and Ara 7 %)	Animal (5/6-week-old mice) Diabetes induced Gavage administration Fecal microbiota analyses Kidney and gut biochemical assays	Gut-kidney axis (diabetes kidney disease)	↑ Verrucomicrobiawas ↓ Proteobacteria ↑ Tight junction protein, intestinal barrier function ↓ Systemic inflammation ↓ LPS content and NLRP3 inflammasome activation ↓ Renal oxidative stress injury	(Yang et al., 2020; Zhang, Zhang, et al., 2019)
Grifola frondosa	Polysaccharide (38.2 %) and protein (37.8 %) extract (GF500; MW > 5000 Da; composed by Glc 47 %, Ara 30 %, Man 19 %, Rib 1.9 %, Rha 1.7 %, Xyl 0.3 % and Gal 0.16 %)	Animal (6-week-old rats) Diabetes induced Gavage administration Fecal microbiota analyses Serum, liver and gut biochemical assays	Gut-liver axis (diabetes)	↑ *Firmicutes/ Bacteroidetes* ratio, *Turicibacter* ↓ Fasting serum glucose, insulin resistance, serum lipids ↓ Inflammatory markers mRNA levels ↓ Insulin resistance related to metabolic abnormalities	(Xiao et al., 2021)
Lentinula edodes	Commercial lentinan (>98 % purity; Yuanye Biological Technology Co., Ltd., China)	Animal (9-week-old mice) Nonalcoholic steatohepatitis induced Oral administration Fecal microbiota analyses Gut and liver biochemical assays	Gut-liver axis (Nonalcoholic steatohepatitis)	↑ *Bifidobacterium* ↓ Proteobacteria and Epsilonbacteraeota ↑ Intestinal barrier integrity and redox balance ↓ Steatohepatitis and NF-κB-PTP1B-Akt-GSK3β (inflammation–insulin) ↑ Insulin sensitivity	(Yang et al., 2022)
Pleurotus eryngii	Soluble polysaccharide extract (69.6 %; MW: 740 kDa; composed by Glc 83 %, Gal 9.2 % and Man 8 %)	Animal (6-week-old mice) Obese induced Oral administration Fecal lipid and microbiota	Gut-liver axis (obesity)	↑ *Firmicutes* ↑ SCFAs bacteria (e.g., Anaerostipes) ↑ Feces' lipid and total bile acids ↑ LDLR liver and GPR43 adipose tissue genes expression	(Nakahara et al., 2020)

(*continued on next page*)

Table 4 (*continued*)

Mushroom species	Polysaccharides fraction	Type of study	Target	Gut microbiota-mediated effect	Reference
		analyses Lipid and cholesterol metabolism		↓ Total serum cholesterol and LDL cholesterol levels ↓Weight gain and fat accumulation ↑ Energy and SCFAs metabolism bacteria	
Poria cocos	Water-soluble extract (polysaccharides and polyphenols)	Animal (7-week-old mice) Ultraviolet B-induced skin lesions Oral administration Fecal microbiota analyses Skin biochemical assays	Gut-skin axis (skin lesions)	↑ Villus length and mucin content ↑ mucin barrier balance ↓ Oxidative stress and proinflammatory cytokines ↓ Systemic and skin inflammation ↑ CD206 positive cells (immune homeostasis)	(Zhang, Huang, et al., 2022)
Lentinula edodes	Commercial β-glucan extract (1 → 3)-β/(1 → 6)-β-glucans, (1 → 3)-β-glucan or (1 → 3)-β/(1 → 4)-β-glucan; Yuanye Biotechnology Co., China)	Animal (9-week-old healthy mice) Oral administration Fecal microbiota analyses Gut and brain tissue biochemical assays	Gut-brain axis (cognition)	↓ Proinflammatory cytokines (IL-6, TNF-α) ↑ IL-10 ↓ Microgliosis in the prefrontal cortex and hippocampus ↑ Synaptic proteins levels and ultrastructure ↑ Temporal order recognition memory	(Hu et al., 2022)
Sparassis crispa	Polysaccharide extract (MW: 1.4×10^4 Da; molecular ratio: Glc 52, Gal 31, Fuc 15, and Man 1.8)	Animal (10-week-old mice) Alzheimer's disease induced Gavage administration Fecal microbiota analyses Gut and brain tissue biochemical assays	Gut-brain axis (Alzheimer's disease)	Reshape gut microbiota ↑ SCFAs (e.g., acetic and butyric) ↑ Colon tight junction proteins expression ↓ LPS level ↓ Proinflammatory cytokines (IL-6, TNF-α, IL-1β) ↓ Glial activation, TLR4 and NF-κB ↑ Neurotransmitters level ↓ neuropathological changes	(Zhang, Guo, et al., 2022)

SCFAs – short-chain fatty acids; MW – molecular weight; Th17 - T helper 17 cells; Treg - regulatory T cells; IgA - immunoglobulin A; IgG - immunoglobulin G; IgM - immunoglobulin M; Zo-1 - Zonula occludens-1; Zo-2 - Zonula occludens-2; MUC2 - mucine 2; TEER - Trans-epithelial electrical resistance assay; PTP1B - protein tyrosine phosphatase 1B; Akt - protein kinase B; GSK3β - Glycogen synthase kinase-3 beta; LDLR - low-density lipoprotein receptor; GPR43 - G-protein-coupled receptor 43; LDL – low-density lipoprotein; mRNA - messenger ribonucleic acid; LPS – lipopolysaccharides; NLRP3 - nucleotide-binding domain leucine-rich repeat family pyrin domain containing 3; CD206 - mannose receptor; TNF-α - tumor necrosis factor-α; IL – interleukin; TLR – toll-like receptor; NF-κB - nuclear factor kappa-light-chain-enhancer of activated B cell; Ara – arabinose; Fuc – fucose; Gal – galactose; GalA - galacturonic acid; Glc – glucose; Man – mannose; ManA - mannuronic acid; Rha – Rhamnose; Xyl – xylose.

24,670–663,792 Da; methylation degree: 41.24 %; and monosaccharide composition: Man, Rib, Glc, Gal, Xyl, Ara, Fuc, and GlcA) for 4 weeks partially alleviated gut-induced damage (Hao et al., 2023). Animal experiments are the most used to assess the modulation of intestinal microbiota for gastrointestinal diseases, mainly using mouse models with induced diseases. Generally, these works demonstrated a reshaping of gut microbiota diversity through mushroom polysaccharide ingestion (Table 3) due to an increased SCFAs and SCFAs-producing species (Dalile et al., 2019). The most abundant SCFAs are butyric, propionic, and acetic acids, and several studies have reported an increase in these acids through gut microbiota modulation by consuming mushroom polysaccharides (mainly β-glucans) (Fu et al., 2023; Nishimoto et al., 2023; Zhang, Guo, et al., 2022; Zou et al., 2022). They are key drivers of human body homeostasis and decrease the risk of various diseases, possessing several important roles, for example, in the intestines, liver, and brain (Bonfili et al., 2021; Lu et al., 2020; Niego et al., 2021; Yadav & Negi, 2021; Yin et al., 2020).

Consuming mushrooms has a positive impact on the intestinal biological barrier as it promotes the production of SCFAs, which decreases the luminal pH. This decrease in pH inhibits the growth of pathogenic microorganisms such as *Listeria monocytogenes* and *Escherichia coli*, while promoting the growth of probiotic bacteria. Therefore, SCFAs play a vital role in strengthening the intestinal microbial barrier (Li et al., 2020; Ma, Xu, et al., 2022). Alternatively, this acidification process can also improve the absorption of essential nutrients and minerals (e.g., calcium, phosphorus, and magnesium) (Yin et al., 2020), which may be compromised in several gastrointestinal diseases (Khan et al., 2018).

Additionally, SCFAs are absorbed by the colon through monocarboxylate transporters and used by the mitochondria in the citric acid cycle to provide energy to intestinal epithelium cells (Brial et al., 2018; Dalile et al., 2019; Yin et al., 2020). The non-metabolized SCFAs are transported to the liver through portal circulation (Dalile et al., 2019). This pathway will be discussed in the next section.

Research has shown that in certain diseases (e.g., obesity, diabetes, and skin diseases), as well as during aging (e.g., neurodegenerative diseases), a loss of abundance and diversity of gut microbial species occurs. This decrease is associated with the dysregulation of microbial metabolites, such as a decrease in SCFAs production, which can lead to an increase in intestinal barrier permeability (Bonfili et al., 2021; Ghezzi et al., 2022; Yin et al., 2020). SCFAs also play a key role in the normal function of the intestinal barrier through other pathways such as the intestinal mechanical barrier (Bonfili et al., 2021; Yin et al., 2020). The intestinal mechanical barrier is formed by the intestinal epithelial cells, mucous layer, tight junction, and submucosal lamina propria (Hao et al., 2022; Ma, Xu, et al., 2022). Studies have shown that gut microbiota modulation and SCFAs production can promote genes involved with colon tight junction protein expression (e.g., ZO, claudin, and occludin; Table 3). This contributes to an increase in mucus thickness and the overall mechanical barrier function of the intestine (Hao et al., 2023; Ma, Xu, et al., 2022; Yang et al., 2020; Zhang, Guo, et al., 2022).

Recent work also suggested that SCFAs can impact the intestinal immune barrier, which is composed by immune factors and cells as well as, gut-associated lymphoid tissues (Hao et al., 2022; Ma, Xu, et al., 2022). SCFAs activate cellular receptors, leading to cell differentiation or proliferation. Several studies in this field suggested suppression of proinflammatory cytokines secretion (Table 3), such as interleukin 6 (IL-6) and tumor necrosis factor α (TNF-α) (Hu et al., 2022; Xiao et al., 2021; Yang et al., 2020; Zhang, Guo, et al., 2022; Zhang, Huang, et al., 2022; Zou et al., 2022). Besides, SCFAs are associated with inhibiting the toll-like receptor 4 (TLR4) signaling pathway and activating G-protein coupled receptor expression (Ma, Xu, et al., 2022). All these pathways contribute to intestinal immune function.

Regarding the chemical barrier, it is constituted by bile, gastric acid, mucus, and gastrointestinal enzymes (Hao et al., 2022; Ma, Xu, et al., 2022). Mucin is a primary compound of the intestinal layer, secreted by goblet cells, preventing the passage of harmful macromolecules through the intestinal layer. SCFAs trigger the production of anti-inflammatory factors that positively modulate the expression of genes involved in mucin production in the intestine and their secretion by pancreatic enzymes, contributing to the normal chemical barrier function (Ma, Xu, et al., 2022). Moreover, SCFAs promote the secretion of defensins, lysozyme and other antimicrobial compounds, which enhance both the intestinal mucosa immunity and the chemical barrier (Li et al., 2020; Ma, Xu, et al., 2022). Also, the re-establishment of redox balance is extensively reported in the field (Table 3) (Yang et al., 2022; Zhang, Huang, et al., 2022).

Accordingly, SCFAs have been associated with the modulation of the intestinal biological, mechanical, immunological, and chemical barrier (Li et al., 2020; Ma, Xu, et al., 2022), and, consequently, with a protective effect against inflammation and inflammatory diseases (Yin et al., 2020). As comprehensively revised in this section and in Tables 3 and 4, consuming mushroom polysaccharides (α- and β-glucans, chitin-glucan complex and other polysaccharides) is strongly connected with a significant promotion of SCFAs.

4.1.2. Effects on metabolic homeostasis

Gut microbiota modulation mediated by mushroom polysaccharides (e.g., lentinan and other β-glucans) consumption has also been associated with metabolic homeostasis, including hypocholesterolemic, antilipidemic, and anti-diabetic effects. Examples of these gut microbiota modulation effects are also presented in Table 4. In all reported experiments, gut microbiota dysbiosis is registered in the diseased mouse models.

Beyond the reduction in inflammation states, some research studies suggested a decline in blood glucose levels and insulin resistance during mushroom-derived polysaccharides ingestion (Xiao et al., 2021; Yang et al., 2020; Yang et al., 2022). Literature attributed a high influence of gut microbiota on systemic inflammation and consequent insulin resistance, resulting in a "metabolic infection" (Xiao et al., 2021). For example, a significant increase in *Enterococcus* genera has been registered through microbiota modulation and associated with increased insulin sensitivity (Yin et al., 2020).

Other findings associated with mushroom-derived polysaccharides (polysaccharides with α- and β-configurations; MW: 740 kDa; monosaccharide composition: Glc, Gal and Man) include a decrease in body weight, serum lipids and cholesterol, and fat accumulation. Typically, biochemistry analysis revealed an increase in lipid and total bile acids in feces during mushroom polysaccharides ingestion. This may suggest that mechanisms that inhibit their reabsorption are triggered by mushroom polysaccharide consumption (Nakahara et al., 2020). Also, a positive effect on lipid metabolism disorder is directly associated with gut microbiota shaping, increasing some bacteria genera such as *Prevotella* and *Anaerostipes* (Nakahara et al., 2020; Yin et al., 2020).

Furthermore, SCFAs may control gene expression and cell signaling pathways related to metabolic homeostasis at different levels (Bonfili et al., 2021; Brial et al., 2018; Yin et al., 2020). As previously mentioned, the non-metabolized SCFAs in the colonocytes reach the liver, being also an energy source in hepatocytes (Dalile et al., 2019). Beyond an energy source for peripherical gut cells and the liver, acetic acid is involved in metabolic signaling, such as lipogenesis and gluconeogenesis (Wang, Wichienchot, et al., 2019). SCFAs may also play an essential role in cholesterol metabolism. Although all the mechanisms related to lowering cholesterol levels of SCFAs are not totally understood, cholesterol-lowering by inhibiting cholesterol synthesis and promoting low-density lipoprotein (LDL) cholesterol catabolism are described as mediated effects. Most propionic acid produced by gut microbiota reaches the liver, impacting gluconeogenesis and inhibiting cholesterol synthesis (Wang, Wichienchot, et al., 2019). Therefore, these intestinal metabolites may regulate blood pressure and reduce cardiovascular disease risk (Brial et al., 2018).

4.1.3. Effects on cancer

Although literature data on a clear relationship between gut microbiota modulation through mushroom consumption and antitumor effects are limited, several studies have suggested the antitumor potential of gut microbiota modulation. Different gut microorganisms may exert opposite effects on ongoing cancer. On the one hand, some pathogenic microorganisms play important roles in cancer development through various mechanisms. Direct (e.g., deoxyribonuclease - DNAse activity) or indirect DNA damage mechanisms (e.g., production of metabolites that block DNA repair) have been reported and associated with some bacterial species producing toxins. For example, *E. coli* has been associated with a rising risk of developing some cancers. Several studies suggested that some pathogenic microorganisms promote oncogenesis through the modulation of metabolic, signal pathways, and host immune responses (Yin et al., 2020). Some microbial-derived metabolites, for instance, can block the immune effectors involved in inhibiting tumorigenesis (Araújo-Rodrigues et al., 2022).

On the other hand, some genera, such as *Lactobacillus* spp. and *Bifidobacterium* spp., have been suggested to enhance cancer immune responses (Routy et al., 2018). Additionally, gut microbiota metabolites seem to promote tumor growth inhibition (Yin et al., 2020). For instance, the scientific community has proposed that gut microbiota's influence on estrogen metabolism may impact carcinogenesis in breast cancer (Fernández et al., 2018). Furthermore, activation of the β-catenin signaling pathway, associated with carcinogenesis, has been associated with some gut microbiota-derived metabolites and toxins (Yin et al., 2020). Another example is the positive role of butyric acid in colon cancer. This gut microbiota metabolite reduces colon inflammation and regulates the apoptosis pathway (Dalile et al., 2019; Wang, Wichienchot, et al., 2019).

Khan et al. (2019) showed the effects of commercial mushroom polysaccharides from *G. lucidium* (ZhiQing-Tang Biotech Company Ltd., China) combined with saponins (also with prebiotic potential) on colorectal cancer-preventive effects in $Apc^{Min/+}$ mice. The results suggested that through gut microbiota modulation, for example, the polyps incidence was reduced, and oncogenic signaling molecules were downregulated. The isolated effect of saponins and *G. lucidium* polysaccharides was also tested. Nevertheless, the findings indicated that the combination results have a stronger cancer-preventive effect.

4.1.4. Effects on the gut-brain axis

The gut-brain axis allows bidirectional communication between the gastrointestinal tract and the central nervous system. This communication involves different pathways: neuroimmune, parasympathetic, sympathetic, and neuroendocrine. Consequently, the gut-brain axis represents a pathway of biochemical signaling that impacts numerous body functions, namely brain function (hypothalamus and frontal cortex functions) (Bonfili et al., 2021;Dalile et al., 2019 ; Ghezzi et al., 2022). Mechanisms by which the gut microbiota interacts and impacts brain function are not totally understood. However, the scientific community believes that gut-derived signaling molecules play a major role in gut-brain crosstalk. Some gut-derived mediators are cytokines, neuroactive molecules, and microbial metabolites (Bonfili et al., 2021; Ghezzi et al., 2022).

The gut microorganisms and metabolites may positively influence humoral, mental and neuronal functions through the gut-brain axis (Dalile et al., 2019; Lu et al., 2020). Beyond SCFAs, gamma-aminobutyric acid (GABA), noradrenaline, dopamine, serotonin, histamine, and acetylcholine are other vital metabolites produced by the intestinal microbial population (Bonfili et al., 2021). In recent studies, gut microbiota dysbiosis has been directly connected with the development of several clinical conditions (Dalile et al., 2019; Ghezzi et al., 2022), including Alzheimer's disease (AD), Parkinson's disease (PD),

Huntington's disease (Bonfili et al., 2021; Ghezzi et al., 2022), amyotrophic lateral sclerosis (Ghezzi et al., 2022) and other neurological diseases. For example, AD, depression, and other neurological disorders have been linked with reducing SCFAs, GABA, serotonin, and other gut microbiota metabolites (Bonfili et al., 2021; Ghezzi et al., 2022), due to a lower incidence of some gut bacteria species (Bonfili et al., 2021; Dalile et al., 2019; Ghezzi et al., 2022).

The dysregulations in amino acid metabolism have been associated with these lowered levels. Reduced concentrations of the neurotransmitter GABA, produced by several bacteria species (e.g., lactic acid bacteria) through glutamate metabolism, was found in several neurological disorders. GABA controls brain function, synaptic plasticity, and cortical re-organization and adaptation (Bonfili et al., 2021; Filosa et al., 2018; Jamwal & Kumar, 2019). Other amino acid dysregulations, namely, tryptophan, tyrosine, methionine, and purine pathways, were found in AD disease and other pathologies (Bonfili et al., 2021; Ghezzi et al., 2022). Tryptophan is a precursor of serotonin and kynurenine, both bioactive molecules of the gut-brain axis (Agus et al., 2018; Bonfili et al., 2021). For instance, serotonin is a neurotransmitter that plays important roles in cognition and mood stabilization (Bonfili et al., 2021).

Valerate, butyric, propionic, and acetic acids are SCFAs involved in gut-brain axis crosstalk (Bonfili et al., 2021; Dalile et al., 2019; Lu et al., 2020). SCFAs may reach the blood-brain barrier through the bloodstream and modulate the blood-brain barrier by increasing tight junction protein expression (Bonfili et al., 2021; Dalile et al., 2019; Parker et al., 2020). As previously mentioned, intestinal microbiota dysregulation and aging have been associated with increased permeability of the gastrointestinal tract epithelium. Moreover, different diseases, including neurodegenerative diseases, are associated with the increased permeability of the blood-brain barrier, resulting in an alteration in the transport of microbial-derived products (Bonfili et al., 2021; Ghezzi et al., 2022).

Although some medical interventions can improve the life quality of patients, effective treatment for numerous neurological disorders is not yet established. However, some efforts have been focused on the gut-brain axis, given the crucial role of the intestinal microbiome. Gut microbiota modulation has been suggested as a promising tool for preventing or alleviating neurological diseases (Bonfili et al., 2021; Ghezzi et al., 2022). Some strategies targeting gut microbiota include microbiota transplantation, probiotics, and prebiotics supplementation (Baldi et al., 2021; Hao et al., 2023). A mushroom diet reduced some neuropathological changes in animal studies (Table 3). Beyond an increase in SCFAs, most studies in the field showed modulation of neurotransmitter levels, which may positively impact brain function. Additionally, neuroinflammation is critical in neurodegenerative diseases. In these cases, reduction in oxidative stress markers and decreases in pro-inflammatory cytokines such as Il-6 and TNF-α (Hu et al., 2022; Zhang, Guo, et al., 2022), and in microglial activation (Zhang, Guo, et al., 2022) are also typically reported.

4.2. Immunomodulatory potential

Although the human body does not synthesize β-glucan, this macromolecule can promote innate and adaptive immune responses (Cerletti et al., 2021; Lu et al., 2020; Niego et al., 2021). As previously mentioned, β-glucans reach the small intestine without any gastrointestinal digestion. Beyond gut microbiota modulation, β-glucan can interact with the membrane receptors of immune cells present in the intestinal epithelium (Cerletti et al., 2021; Lu et al., 2020). TLR and C-type lectin-like are two examples of β-glucan receptors in immune cells (Cerletti et al., 2021; Chakraborty et al., 2020; Lu et al., 2020). Among C-type lectin-like receptors, dectin-1 is the most studied and characterized in immune cells (Cerletti et al., 2021; Chakraborty et al., 2020).

TLR and dectin-1 receptors activate the immune response (Chakraborty et al., 2020). Specifically, receptor recognition initiates intracellular signal transduction and consequent activation of macrophages (Cerletti et al., 2021; Lu et al., 2020). The receptors on the surface of immune cells recognize and link with (1 → 3)-β-D-glucans patterns possessing branched side chains (Chakraborty et al., 2020), triggering the production of cytokines such as TNF-α and multiple IL (Bell et al., 2022;Gong et al., 2020 ; Lu et al., 2020). Some specific TLR, namely TLR-2 and TLR-4, may also induce the expression of cytokines but, in parallel, promote the expression of chemokines and stimulate inflammatory receptors. Other essential receptors that interact with β-glucan are complement receptor-3 (CR3). These receptors are present in different macrophage populations, neutrophils, monocytes, as well as natural killer (NK) and dendritic cells (Bell et al., 2022; Chakraborty et al., 2020).

Therefore, β-glucans may activate several signaling pathways involved with innate (macrophage populations, NK, neutrophils, and dendritic cells) and adaptive immune (T and B cells) responses. The innate and adaptive systems work together to protect the human body against infections and diseases (Cerletti et al., 2021; Chakraborty et al., 2020; Lu et al., 2020). In the case of the innate immune system, which corresponds to the first line of defense, receptor recognition triggers a cascade that includes cytokines and chemokines production and other immune cell activation. NK cells are directly related to cellular defense mechanisms in the innate immune system, killing cancer cells and pathogenic microorganisms, mainly viruses. NK cells recognize some pathogens promoting infected cell lysis and stimulating immune responses (Bell et al., 2022; Chakraborty et al., 2020). The adaptive immune system is responsible for the specialized recognition and memory of specific pathogens. β-glucans may promote the activation of T cells, promoting the elimination of infected cells and long-term immunity against pathogens (Chakraborty et al., 2020).

Several studies have demonstrated the immunomodulating properties of mushroom β-glucans. In the literature, several studies showed the immunostimulant potential of β-glucans extracted from several species (e.g., *Agaricus* spp., *Ganoderma* spp., and *Pleurotus* spp.). They were shown to trigger an immune response, promoting the expression of cytokines and increasing the proliferation of lymphocytes. For example, β-glucans of *Pleurotus* spp. seems to boost immune response by enhancing the phagocytic function of macrophages. This immunostimulatory activity has been primarily observed in (1 → 3)-β-D-Glcp and (1 → 6)-β-D-Glcp β-glucans, which possess branching at position (1 → 6)-β-D-Glcp (Rodrigues Barbosa et al., 2020).

Regarding other β-glucans, pleuran (Niego et al., 2021) and lentinan (Chakraborty et al., 2020) are reported as potent immunomodulators. In the case of lentinan, its triple-helical conformation and branch distribution have been associated with its strong immunostimulant properties. Several studies have suggested the activation of immune cells by lentinan, increasing cytokine expression (Araújo-Rodrigues et al., 2022). Several studies indicate that schizophyllan plays a crucial role in modulating inflammation (e.g., periodontal disease) towards promoting the secretion of pro-inflammatory cytokines secretion and the production of anti-inflammatory cytokines (Mirończuk-Chodakowska et al., 2021; Thongsiri et al., 2021).

Concerning α-glucans, the supplementation with these macromolecules extracted from L. *edodes* also showed modulation of pro-inflammatory cytokines (Murphy et al., 2020). Furthermore, the combination of α- and β-glucans isolated from L. *edodes* species seems to have a positive immunomodulatory effect due to the reduction of proinflammatory cytokines and consequent anti-inflammatory effect (Morales et al., 2020).

4.3. Antitumor and antiproliferative effects

Antitumor effects have been extensively connected to mushroom polysaccharides. β-glucans may exhibit antitumor effects through different direct and indirect mechanisms. Based on β-glucans immune-stimulating properties, the immune cells' activation and cell

messengers (TNF-α and multiple interleukins) may be triggered (Gong et al., 2020; Lu et al., 2020), as previously described. Based on immune response activation, this indirect approach may be combined with traditional chemotherapy (Gong et al., 2020). Otherwise, these macromolecules may also promote a direct antitumor effect by enhancing cancer cells' apoptosis or growth inhibition (Gong et al., 2020; Lu et al., 2020). Specific cancer-immune responses may involve the production of chemical messengers (e.g., nitric oxide), contributing to their death or inhibiting their growth (Gong et al., 2020). Thus, prevention or delay of cancer onset and inhibition of metastasis or cell migration are positive antitumor mechanisms described during mushroom β-glucans consumption (Araújo-Rodrigues et al., 2022; Gong et al., 2020).

The stimulation of immune activity, anticancer effect, and antimetastatic activities of lentinan have been extensively reported (Cerletti et al., 2021; Gong et al., 2020; Lu et al., 2020; Zhang, Su, et al., 2019). After clinical trials, this β-glucan was approved for the clinical treatment of cancer coupled with conventional therapies (Cerletti et al., 2021; Gong et al., 2020; Lu et al., 2020) in Japan and China (Rao et al., 2021; Hui Wang et al., 2017; Zhang, Zhang, et al., 2018). This macromolecule possesses low toxicity, cost, and several therapeutic properties (Zhang, Su, et al., 2019). Generally, lentinan supplementation combined with chemotherapy improved efficacy and response rates in several cancers (e.g., lung, ovarian, colorectal) (Niego et al., 2021; Zhang, Su, et al., 2019). For example, lentinan is a promising macromolecule for chemo-immunotherapy during lung cancer therapy (Wang et al., 2020). Additionally, the supplementation with this β-glucan also showed positive effects on the adverse symptoms associated with chemotherapy (Zhang, Su, et al., 2019). Nowadays, beyond lung, ovarian, and colorectal cancers, lentinan has shown positive impacts on non-Hodgkin's lymphoma, cardiac, gastric, cervical, pancreatic, and nasopharyngeal cancers, coupled with conventional cancer therapies (Gong et al., 2020; Lu et al., 2020; Niego et al., 2021; Yadav & Negi, 2021; Zhang, Su, et al., 2019).

In the last years, continuous immunomodulatory and anticancer effects of other mushroom β-glucans have been reported (Yadav & Negi, 2021). Grifolan has been reported as an antitumor agent in mouse cancer models (Mirończuk-Chodakowska et al., 2021). Furthermore, β-glucans from *P. eryngii* showed an antiproliferative action in vitro on human breast adenocarcinoma cells (MCF-7) and hepatocarcinoma (HepG2) cell lines (Al-Saffar et al., 2020; Sharma et al., 2021).

However, α-glucans don't appear to exhibit an antitumor effect (Morales et al., 2020). This corroborates that the α- and β- and tridimensional conformation result in distinct biological properties. Another study focused on polysaccharide extracts of *Calocybe indica*, suggesting an in vitro antitumor action. The authors attribute the polysaccharides' biological properties to its structural characteristics, for instance, triple helical conformation, MW (2.46×10^3–9.37×10^4 Da), and composition of monosaccharides (Glc, Xyl, Man, Rha, Fuc, Gal and Ara) (Nataraj et al., 2022). Beyond lentinan, PSK and PSP are examples of commercial macromolecules used in cancer therapy in Asia (Bains et al., 2021; Zhang, Guo, et al., 2022).

4.4. Anti-inflammatory effects

Inflammation is a primary event that occurs in infection and several diseases coordinated by the immune system. β-glucans have been extensively reported as strong anti-inflammatory agents (Bell et al., 2022; Mirończuk-Chodakowska et al., 2021). Similar anti-inflammatory properties of glucocorticoids and non-steroidal anti-inflammatory drugs are associated with β-glucans (Mirończuk-Chodakowska et al., 2021). The anti-inflammatory suggested mechanisms of β-glucans are based on the inhibition of cyclooxygenase-2 (COX-2), nitric oxide synthase (NOS), and pro-inflammatory cytokines such as interleukin 1β (Bell et al., 2022; Mirończuk-Chodakowska et al., 2021; Muszyńska et al., 2018; Yadav & Negi, 2021). These mechanisms are extremely promising for inflammatory disorders such as periodontal diseases, AD, and PD (Mirończuk-Chodakowska et al., 2021). Beyond β-glucans, trehalose, a disaccharide found in mushrooms, has also been shown to inhibit COX-2 and NOS (Mirończuk-Chodakowska et al., 2021).

Some studies indicated that β-glucans extracted from *Pleurotus* spp. possess strong anti-inflammatory potential (Bell et al., 2022; Nidhi, 2018). For example, *P. ostreatus* β-glucans showed promising results in treating arthritis in rats. The same potential was suggested by lentinan oral ingestion (Niego et al., 2021). Moreover, Song et al. (2020) suggested that L. *edodes* polysaccharides (MW: 2.18×10^3 Da; and monosaccharide composition: Rha, Ara, Gal and Glc) also exhibit anti-inflammatory effects, suggesting that TNF-α, IL-6, and IL-1β serum levels and lipid peroxidation decreased. Moreover, a combination of α- and β-glucans isolated from *L. edodes* also exhibited immunomodulatory effects (Morales et al., 2020). A polysaccharide extract of L. *edodes* also demonstrated anti-inflammatory activity against ulcerative colitis using both in vivo and in vitro models. The authors propose this extract as an alternative and effective strategy to ulcerative colitis treatment (Alagbaoso & Mizuno, 2021).

Additionally, a study in a mouse model showed that schizophyllan modulates the anti-inflammatory response in macrophages (Thongsiri et al., 2021). Other authors studied the potential of *T. fuciformis* polysaccharides (water extract) in induced inflammation and oxidative stress. The results suggested that this macromolecule reduced oxidative stress and macrophages inflammation through miR-155 expression and nuclear factor kappa-light-chain-enhancer of activated B cell (NF-κB). miR-155 is described as an inflammation mediator, downregulating B-cells and promoting the activation of NFκB in macrophages (Ruan et al., 2018). A novel extracellular polysaccharopeptide was extracted from sanghuang mushroom (*Sanghuangporus lonicericola*), and their antioxidant and anti-inflammatory potential was evaluated, suggesting a modulation of inflammatory expression (e.g., cytokines) and reduction of oxidative stress (Zuo et al., 2021).

4.5. Neuroprotective effect

Nowadays, AD is the most prevalent neurodegenerative disease and the leading cause of dementia in the elderly, possessing a significant social and economic impact. It is characterized by a progressive loss of memory and cognitive decline, often associated with neuroinflammation, synapse, and neuron loss, cortex shrinkage, and ventricle enlargement. Moreover, sleep deprivation and visual space dysfunction have also been reported in AD patients (Bonfili et al., 2021). Although AD causes are not fully understood, β-amyloid plaques and neurofibrillary tangles are well-recognized hallmarks of the disease. Microglia overactivation has been identified as a critical stage in AD that induces the expression of inflammatory mediators, resulting in neuroinflammation and neuronal damage (Castellano et al., 2019).

The scientific community has also proposed that activation of the vitagen system may effectively help to treat neurodegenerative diseases. This is an intracellular redox system involved in neuroprotection. The vitagen system includes lipoxin A4, heat shock proteins 70, thioredoxin, and heme oxygenase 1. For example, some scientific studies reported an increase in lipoxin A4 during mushroom consumption (Bell et al., 2022). In another study, *T. versicolor* is also proposed to promote normal brain function by increasing the dendritic arborization of newly generated neurons (Ferreiro et al., 2018). In these cases, the neuroprotective mechanisms are not totally clear, and the possible interaction with gut microbiota modulation was not investigated. Additionally, in these studies, mushroom biomass was used. Although polysaccharides are the foremost common compounds, other bioactive compounds (e.g., phenolic compounds, peptides, and fatty acids) may be absorbed, reach the blood-brain barrier and impact brain function.

Beyond mushroom biomass, other studies also propose a neuroprotective potential of mushroom polysaccharides but without exploring or relating to the impact on gut microbiota. Zhang, Hu, et al. (2022) showed that *Sparassis crispa* water-soluble polysaccharides (α- and β-type glycosidic linkages; MW: 1.37×10^4 Da; monosaccharide

composition: Fuc, Gal and Glc) regulate antioxidant enzymes and promote a reduction of cell apoptosis in oxidative stress-induced hippocampal neuronal HT22 cells. In another study, the same results were reported for *Pleurotus sajor-caju* polysaccharides (α-type glycosidic linkages; MW: 44.9 kDa; monosaccharide composition: Fuc, Gal, Glc, and Man) in the same cell model (Liu et al., 2022). Consequently, mushroom consumption has been suggested to reduce the risk of developing neurodegenerative diseases associated with aging, which might be promising in helping to treat or delay AD, PD, and other neurodegenerative disorders progression (Gong et al., 2020; Yadav & Negi, 2021).

4.6. Antidiabetic effect

Diabetes mellitus is one of the most reported diseases worldwide (Gong et al., 2020; Liu et al., 2020; Sharma et al., 2021), defined by chronic hyperglycemia and insulin imbalances within the body (Liu et al., 2020; Sharma et al., 2021; Yadav & Negi, 2021). This chronic disease is associated with continuous metabolic disorders such as retinopathy, neuropathy, and angiopathy (Sharma et al., 2021). Currently, strategies to control high blood glucose levels are based on insulin administration and some conventional medicines such as acarbose (Gong et al., 2020; Govindan et al., 2023). Developing new strategies can improve diabetes treatment and the life quality of patients (Gong et al., 2020). Currently, the results of the clinical trials of some promising hypoglycemic approaches suggest side effects and/or ineffectiveness. Thus, it is of the utmost importance to propose alternative agents to treat diabetes (Sharma et al., 2021).

Several works have indicated that various mushroom polysaccharides such as β-glucans (e.g., grifolan) and polysaccharide extracts (e.g., extract with polysaccharides with MW between 8172 and 10,710 Da and constituted by Ara, Xyl, Man, Glc and Gal monosaccharides), possess hypoglycemic and antihyperglycemic properties (Gong et al., 2020; Sharma et al., 2021; Yadav & Negi, 2021; Zhang, Liu, et al., 2018). Some of these macromolecules were isolated from *Pleurotus* spp., *G. lucidium*, *H. erinaceus*, *P. cocos*, *S. crispa* and *Inonotus obliquus* mushroom species (Govindan et al., 2023). Recent studies testing new hypoglycemic agents suggested that mushroom β-glucans play important roles in diabetes-induced alterations (Gong et al., 2020). β-glucans may increase glucose uptake by stimulating insulin signaling and sensitivity (Gong et al., 2020; Govindan et al., 2023). There is potential for the development of new strategies to prevent and treat this disease using supplements or hypoglycemic drugs. However, further studies and clinical trials are necessary to determine the effectiveness of these strategies.

Grifolan has been found to be highly effective in managing diabetes-induced alterations. This suggests that it may have the potential to be used as an adjuvant for the treatment of diabetes (Mirończuk-Chodakowska et al., 2021). *Suillellus luridus* polysaccharide (composed by α-and β-glucopyranosyl residues; MW: 9.4 kDa; monosaccharide composition: Gal, Glc, Ara, and Man) also showed potential in the prevention and treatment of diabetes. The results indicated modulation of nuclear factor erythroid 2–related factor 2 (Nrf2)-mediated oxidative stress and NF-κB-mediated inflammatory responses in diabetic-induced mice (Liu et al., 2020). A polysaccharide extracted from *Hypsizygus ulmarius* (pyranose polysaccharide; MW: 2076 Da; monosaccharide composition: Glc, Gal, Rha, Fux, Xyl, and Man) exhibited in vitro and in vivo (induced diabetic rats) hypoglycemic potential. Its administration decreases the hepatic and kidney functions, resulting in a reduction of lipid peroxidation, fast blood glucose, serum lipid metabolism and body weight; and increases insulin levels, antioxidant mechanisms and glycogen storage (Govindan et al., 2023).

4.7. Hypocholesterolemic and antilipidemic effects

Beyond the antidiabetic effect, several studies have also demonstrated the hypolipidemic potential of mushroom polysaccharides (Niego et al., 2021; Yadav & Negi, 2021). Hyperlipidemia consists of high blood levels of lipids associated with several parameters, including diet, lifestyle, genetics and metabolomics. The main factors related to hyperlipidemia are hypercholesterolemia and hypertriglyceridemia, coupled with a lowered concentration of high-density lipoprotein (HDL) in plasma (Ge et al., 2022; Liang et al., 2018). High blood levels of lipids, triglycerides and cholesterol are risk factors for developing cardiovascular diseases, atherosclerosis, obesity, diabetes, and other diseases. During diabetes progression, hyperlipidemia, hypercholesterolemia, and hypertriglyceridemia conditions are also typically reported (Ge et al., 2022; Liang et al., 2018; Wang, Ma, et al., 2022).

Polysaccharides extracted from *P. eryngii* (MW: 21.7 kDa; and monosaccharide composition: Fuc, Gal, Xyl, Man, GlcA and Glc) were tested in diabetic mice, improving glucose and lipid metabolism (K.-L. Wang et al., 2019). This polysaccharide corresponds to a backbone of →4)-α-Galp-(1 → 4)-α-Galp-(1 → 2)-α-Manp-(1 → 4)-α-Galp-(1 → 2)-α-Manp-(1 → 4)-α-Galp-(1 → 4)-α-Galp-(1 → 2)-α-Manp-(1 → 4)-α-Galp-(1 → 2)-α-Manp-(1 → 4)→, with numerous branches on the O-6 position of α-Manp present in the main chain, and also secondary branches linked to the O-6 position of β-Glcp of the main branch.

Morales et al. compared some bioactive properties of L. *edodes* β-glucans. These macromolecules exhibited hypocholesterolemic effects (Morales et al., 2020). The polysaccharide fraction of *S. luridus* also showed antihyperglycemic and antihyperlipidemic activity. This study suggested the regulation of serum lipid and blood glucose levels (Zhang, Liu, et al., 2018). Additionally, in hypercholesteremic patients, β-glucans supplementation reduced LDL and cholesterol levels (Nidhi, 2018). One mechanism that may explain these antihyperlipidemic properties of β-glucans and other polysaccharides is the binding of mushroom macromolecules to cholesterol and lipids in the intestines, decreasing their absorption and promoting their excretion (Cerletti et al., 2021).

Alternatively, an analogous effect of hypocholesterolemic drugs has also been reported in mushroom polysaccharides. In these cases, modulation of cholesterol-related genes is suggested. Ge et al. (2022) isolated and studied the diet potential of a polysaccharide from *Helvella leucopus* in high-fat diet mice. The results indicated that serum levels of total cholesterol, triglycerides, and LDL decreased, while HDL increased. At the same time, modulation of mRNA levels was also suggested. Specifically, the gene expression of cholesterol-related genes peroxisome proliferator-activated receptor (PPAR-α), acyl-CoA synthetase (ACS), and carnitine palmitoyltransferase Iα (CPT-1α) in the liver was registered.

Additionally, the decrease in lipid concentration by promoting the activity of antioxidant enzymes is also reported through the consumption of mushroom polysaccharides. Liang et al. (2018) investigated the underlying mechanisms of commercial *G. lucidum* polysaccharides (Erli Biotechnology Co. Ltd., China) in obesity. Beyond the modulation of gene expression, the study suggested a positive effect in obesity. An improvement of antioxidant enzymatic systems is listed, resulting in lipid peroxidation and cell apoptosis inhibition. Similarly, the underlying mechanisms of two polysaccharide-peptides (α-type glycosidic linkages; I-MW: 9.21×10^5 and II- MW: 6.34×10^5 Da; monosaccharide compositions: Ara, Gal, Glc, Xyl and Man) from *Auricularia polytricha* were explored in vitro (HepG2 cells) and in vivo (animal model of fatty liver disease). The enhancement of antioxidant enzymatic systems and reduction of lipid peroxidation were also reported, coupled with the modulation of gene expression (Zhao et al., 2019).

4.8. Antioxidant activity

Different internal and external factors induce the production of free radicals in the human body, mainly reactive oxygen species (ROS). Normal human defense mechanisms against oxidative events prevent oxidative damage in the human body (Rodrigues Barbosa et al., 2020).

However, imbalances may promote oxidant stress, being associated with several disorders and diseases (Gong et al., 2020; Rodrigues Barbosa et al., 2020). Overproduction of ROS can damage nucleic acids, proteins, lipids, and cellular structures (Rodrigues Barbosa et al., 2020; Sudheer et al., 2019). Antioxidant macromolecules from natural sources (fruits, vegetables, herbs and macrofungi) may prevent oxidative-stress-induced damage in cancer, chronic diseases, and aging (Gong et al., 2020; Rodrigues Barbosa et al., 2020; Sudheer et al., 2019). These macromolecules possess the ability to scavenge and eliminate free radicals (Rodrigues Barbosa et al., 2020).

Antioxidant and free radical scavenging effects have been described for mushroom polysaccharides (e.g., β-glucans) (Gong et al., 2020; Sudheer et al., 2019). The scavenging capacity of these macromolecules depends on the presence of hydrogen, the number of monomers (molecular length), and branching (Gong et al., 2020). Several works demonstrated that polysaccharides fractions isolated from several *Pleurotus* spp. species such as *P. ostreatus*, *P. eryngii*, *P. sajor-caju*, *Pleurotus abalonus,* and *Pleurotus djamor* exhibit free radicals scavenging potential, possessing antioxidant and antiaging potentials (Muszyńska et al., 2018; Rodrigues Barbosa et al., 2020; Xiao et al., 2019).

Additionally, polysaccharide extracts of *G. lucidum* revealed antioxidant activity (Sudheer et al., 2019). Regarding isolated β-glucan macromolecules, several works have also demonstrated the antioxidant potential of lentinan (Chen et al., 2018; Zhang, Su, et al., 2019; Zi et al., 2020). Beyond antitumor potential, polysaccharides extracted from *C. indica* (previously described in section 4.3) exhibited high antioxidant potential in different in vitro approaches (radical scavenging, reducing ability, metal chelating and lipid peroxidation inhibition activities) (Nataraj et al., 2022). Mohamed et al. (2023) studied the antioxidant potential of a polysaccharide extracted from *Pleurotus columbinus* (α-D-glucan; MW: 54.9 kDa; monosaccharide composition: GalA, Glc and Xyl) in induced oxidative renal injury. The results suggested that the administration of this polysaccharide in mice models modulate the antioxidant kidney enzyme levels (e.g., superoxide dismutase, catalase, glutathione). This plays an important role in oxidative stress and damage reported in kidneys and other diseases.

4.9. Antimicrobial and antiviral activities

The antimicrobial potential of mushroom β-glucans against Gram-positive and Gram-negative bacteria, yeast, and mycelia fungi as well as viruses, has been described in numerous studies (Arunachalam et al., 2022; Mirończuk-Chodakowska et al., 2021; Niego et al., 2021; Yadav & Negi, 2021). The issue of antibiotic resistance makes it crucial to propose effective alternative antimicrobial solutions (Yin et al., 2020). Antibacterial, antifungal, and antiviral compounds are produced by the natural defense mechanisms of mushrooms (e.g., EPS) and other important ecological and physiological mechanisms (Yadav & Negi, 2021). The mushroom polysaccharides' primary antimicrobial and antiviral mechanisms are thought to stimulate the immune system by indirect action (e.g., phagocytosis, neutrophils, and macrophages) (Arunachalam et al., 2022; Mirończuk-Chodakowska et al., 2021). As mentioned in the previous sections, β-glucans may bind to immune cells receptors (e.g., dectin-1 and TLR), triggering a host immune response against bacterial, fungal, and viral pathogens (Mirończuk-Chodakowska et al., 2021).

The beneficial effect of mushroom bioactive compounds in several fungal infections, such as *Mycosphaerella*, *Fusarium,* and *Physalospora* has been reported (Mirończuk-Chodakowska et al., 2021). Kim et al. (2022) studied the antimicrobial potential of foodborne pathogens of *G. lucidum*, *Taiwanofungus camphoratus,* and *A. blazei* β-glucans extracts. The authors highlighted that β-glucans from *Termitomyces heimii* exhibited antibacterial potential against Gram-negative (*E. coli* and *Salmonella* spp.) and Gram-positive bacteria (*S. aureus* and *Streptococcus* spp.) (Ahmad et al., 2021).

Regarding the antiviral effects of β-glucans, the first findings in the field suggested that lentinan and schizophyllan showed an antiviral effect on tobacco plant infections. Later, lentinan was tested in combination with the antiretroviral drug didanosine in HIV patients. The results indicated a positive effect of this β-glucan, improving the numbers of T lymphocytes. In this context, nowadays, lentinan has been used in drug development targeting HIV and other viral diseases such as hepatitis and malignant pleural effusion (Niego et al., 2021). Supplementation of piglets' diet with lentinan also improved the normal gut function in rotavirus infections (Fan et al., 2021). Additionally, pleuran showed effective antiviral potential against herpes simplex virus (HSV) (Urbancikova et al., 2020). Some authors reported that pleuran may play an essential role in inhibiting viral invasion, as well as absorption and cell-to-cell transmission (Yadav & Negi, 2021).

Moreover, numerous studies suggested that respiratory infections associated with the flu were significantly reduced through β-glucans supplementation. As reviewed by previous studies, the development of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) responsible for coronavirus disease 2019 (COVID-19) is highly dependent on the host's immune system (Arunachalam et al., 2022; Mirończuk-Chodakowska et al., 2021; Sevindik, 2021). Due to the immune-stimulating potential of β-glucans in bacterial, fungal, and viral infections, these authors suggest a possible positive response of β-glucans against SARS-CoV-2. The effect of β-glucans from L. *edodes* showed potential in treating COVID-19 disease (Arunachalam et al., 2022; Murphy et al., 2020), suggesting a decline in inflammation in the lung epithelial model (Murphy et al., 2020).

4.10. Other health benefits

Other bioactive properties, namely, protective effect on DNA damage (Eid et al., 2021), anticoagulant (Nataraj et al., 2022), antiallergic (Mahmood et al., 2019), analgesic (Abreu et al., 2019), wound (Jones et al., 2020; Seo et al., 2019) and bone healing (Wang, 2020), improvement of cognitive capacity (Ferreiro et al., 2018; Pan et al., 2021) and immune system (Bell et al., 2022; Sevindik, 2021), hepatoprotective (Liu et al., 2019; Wang, 2020), antiaging (Badalyan et al., 2022; Lu et al., 2020; Wang, 2020; Yadav & Negi, 2021), and radioprotective (González et al., 2020), are also attributed to β-glucans and polysaccharide extracts. Since 2018 studies regarding these mushroom polysaccharides' effects are fewer, being crucial to increase research in this area. Some examples of studies that document these bioactive and pharmaceutical benefits are summarized in Table 5.

5. Challenges, opportunities and future research directions

Some authors have raised the hypothesis of a positive synergistic effect between several bioactive molecules in mushrooms (Araújo-Rodrigues et al., 2022; Sousa et al., 2023; Venturella et al., 2021). Although several studies and review papers raise this hypothesis, studies showing the interaction between mushroom bioactive molecules are scarce and limited. Most studies focus on the interaction between mushroom macromolecules with other matrixes or external macromolecules (e.g., vitamins, chitosan, and flavonoids) (Tong et al., 2020).

Specifically, in the mushroom matrix, a positive interaction between mushroom polysaccharides and selenium was reviewed by Rodrigues Barbosa et al. (2020). This study suggested that this synergistic effect may be positive in anti-inflammatory, antioxidant, antitumor, hepatoprotective, antidiabetic, and neuroprotective properties. Also, a possible positive interaction between mushroom polysaccharides and vitamin D enrichment through ultraviolet B radiation was reviewed. Regarding these polysaccharides and vitamin D interaction, the authors suggested that this interaction may positively impact the anti-inflammatory potential compared with isolated macromolecules (Muszyńska et al., 2018).

However, proving this synergistic effect in a specific matrix may be a difficult task due to, for example, the multiple macromolecules present

Table 5
Other bioactive properties of mushroom polysaccharides.

Mushroom species	Polysaccharide fraction	Bioactivity	Main results	Reference
Pholiota nameko	β-glucan (main chain of (1 → 3)-β-D-Glcp units, branches at O-6 with single β-D-Glcp units or (1 → 6)-β-D-Glcp)	Analgesic	Ameliorate inflammatory pain on mice model with induced injury.	(Abreu et al., 2019)
Agaricus blazei Hericium erinaceus Grifola frondosa	Andosan™ (82 % *A.blazei* Murill, 15 % *H. erinaceus*, and 3 % *G. frondosa*)	Antiallergic	Decreased allergy and asthma symptoms during the pollen season by reduction of specific IgE blood (clinical trial).	(Mahmood et al., 2019)
Calocybe indica	Polysaccharides extract (α- and β- glycosidic linkages; MW: 2.5×10^3–9.4×10^4 Da; molecular ratio: Gal 66.2, Glc 15.5, Fuc 5.6, Ara 3.6, Man 2.9, Xyl 3.1, GlcA 2, Rha 1.2)	Anticoagulant	A prolongation of APTT and TT action and no effect on PT were reported, suggesting anticoagulant properties.	(Nataraj et al., 2022)
Lentinula edodes	β-glucan ((1 → 3)-β−/(1 → 6)-β-glucan)	Cognitive capacity improvement	Nutritional supplementation in obese mice showed prevention of cognitive decline associated with obesity.	(Pan et al., 2021)
Inonotus obliquus	Polysaccharide extract (molecular ratio: Ino 12.5, Glc 12.3, Gal 14.3, Man 9.9, Rha 9.3 and Xylulo 7.7)	DNA damage reduction	Genotoxic effects and DNA damage were significantly reduced in UVB-exposed zebrafish by improving the expression of DNA repair genes.	(Eid et al., 2021; Eid & Das, 2020)
Pleurotus citrinipileatus	Polysaccharide extract (pyran-type structure linked by β-type glycosidic linkages; MW: 1.30×10^5 Da; composed by Xyl 27 %, Ara 21 %, Gal 19 %, Glu 10 %, Man 9 %, GalA 6 %, Rha 5 % and GlcA 4 %)	Hepatoprotective	Amelioration of liver fibrosis by a decrease of TGF- β1 level (cytokine involved in the degradation and synthesis of extracellular matrix).	(Liu et al., 2019)
Schizophyllum commune	Commercial β-glucan ((1 → 6)-β branched (1 → 3)-β glucan; QUEGEN biotech)	Wound healing	Accelerate wound closure in mice by promoting keratinocyte migration and activation of dermal fibroblast differentiation.	(Seo et al., 2019)

IgE - Immunoglobulin E; APTT- prolong activated partial thromboplastin time; TT – thrombin time; PT – prothrombin time; TGF- β1 - Transforming growth factor beta 1; DNA - Deoxyribonucleic acid; UVB - Ultraviolet B. Ara – arabinose; Fuc – fucose; Gal – galactose; GalA - galacturonic acid; Glc – glucose; GlcA - glucuronic acid; Ino – Inositol; Man – mannose; ManA - mannuronic acid; Rha – Rhamnose; Xyl – xylose; Xylulo – xylulose.

in extracts and the entire mushroom fraction (e.g., anti-nutrients) and their possible interactions as well as the different impact of gastrointestinal digestion on the distinctive macromolecules either individually and in combination. Consequently, it is crucial to evaluate and better understand the possible interaction between mushroom bioactive compounds and their underlying mechanisms.

Further investigation is of utmost importance to clarify the different mechanisms of action of the different polysaccharide structures. Regarding the structure-function relationship, several studies suggested that conformation, MW branching degree, and other properties play key roles in polysaccharides' biological properties. However, most studies lack comprehensive and detailed information concerning chemical structure. Identifying the chemical structure of mushroom polysaccharides is essential to understand their interaction with biological systems. The current review has revealed a gap in the literature regarding the correlation between the structure and function of mushroom polysaccharides, which presents an area for further research. Such research could open new possibilities in pharmaceutical and drug design.

Another identified limitation in the field corresponds to the scarce scientific data on α-glucans available, making further research on this subject mandatory to decipher in more detail their chemical structures and identify possible uncovered bioactive properties. Furthermore, studies regarding other health effects of mushroom polysaccharides (Section 4.10) are scarce, so it is important to increase research in this area to have more in-depth studies and specific conclusions. These effects included: the protective effect on DNA damage, anticoagulant, antiallergic, analgesic, wound and bone healing, improvement of cognitive capacity and immune system, hepatoprotective, antiaging and radioprotective.

Additionally, some underlying mechanisms of mushroom polysaccharides have yet to be totally understood, making it essential to investigate them. Although some clinical trials focusing on mushroom polysaccharides are in progress it is vital to increase the number of clinical trials to foster the use of mushroom polysaccharides in preventing or treating diseases. The design of clinical trials is important to overcome the limitations of existing clinical trials, being crucial to develop structured, randomized, double-blinded, and placebo-controlled studies with a higher number of participants. This may be a paramount move to multiple drugs approvement, some of which are extensively applied in clinical treatments in Asia.

6. Concluding remarks

Mushrooms possess a rich nutritional value, being a good source of dietary fiber, digestible proteins, essential amino acids, vitamins, and minerals. Besides their nutritional potential, numerous biological and functional properties have been reported, increasing mushroom popularity and market value. Due to their attractive attributes, mushrooms have been classified as next-generation food. Therefore, macrofungi species can be used beyond diet as functional foods, supplements, nutraceuticals, and pharmaceutical products. Polysaccharides are the most representative bioactive group present in mushrooms, typically described as "biological response modifiers".

β-glucan is the most studied mushroom polysaccharide, with numerous medicinal properties such as prebiotic, anticancer, anti-inflammatory, antioxidant, antiviral, and neuroprotective being reported. Although α-glucans and chitin studies are scarcer and more limited, an increasing interest in these macromolecules has been raised due to their prebiotic capacity as well as the antimicrobial and wound-healing potential of chitin and its derivatives. The mushroom polysaccharide content and composition depend on several parameters such as species, growing conditions, development stage, and extraction methodologies.

The bioactive properties of mushroom polysaccharides depend on their structural properties (structure-function relationship). While significant limitations were reported in this review, some key correlations were identified. A higher MW is generally recognized to have a positive influence on biological properties but low MW polysaccharides may exhibit increased antioxidant properties. Chemical modifications, association with other molecules and branching commonly enhance the β-glucans and other mushroom polysaccharides' biological properties. Although it is a challenge to establish a connection between the function and monosaccharide composition of polysaccharides, heteropolysaccharides with high monosaccharide diversity seem to have a positive impact on health. Moreover, the triple helical conformation

may play a pivotal role in the biological properties of mushroom polysaccharides even though there is still limited data.

Beyond the numerous medicinal properties of mushrooms, an increasing interest in the mushrooms' prebiotic potential has also been raised due to the multiple impacts of gut microbiota modulation. Prebiotic studies can be divided into in vitro fermentation with single strains, in vitro human fecal fermentation, animal studies, and clinical trials. Still, the most prevalent are human fecal fermentation studies. The gastrointestinal simulation suggested no significant impact of the polysaccharide fraction. Generally, the mushroom polysaccharides fractions tested promoted the growth of probiotic strains or showed the capacity to modulate human intestinal microbiota and stimulate the production of SCFAs (e.g., propionic, acetic, and butyric acids). Several studies also focus on the gut microbiota modulation effects, mainly through mouse models with induced diseases. SCFAs showed a positive impact on the intestinal biological, mechanical, chemical, and immunological barriers. Additionally, some of the most relevant gut microbiota-mediated effects are the reduction of proinflammatory cytokines secretion and re-establishing of redox balance, positively impacting intestinal, cardiovascular, metabolic, and neurological diseases.

Additionally, the most reported bioactivities of mushrooms are anticancer and immunomodulatory, and L. *edodes* is the most explored species. This may be due to the intense stimulation of immune responses of mushroom β-glucans and the approval and extensive use of lentinan in cancer treatment in Asia (Japan and China). β-glucans immune-stimulating potential plays essential roles in their anticancer, immunomodulatory, anti-inflammatory, antiviral, and antimicrobial effects. Some antibacterial (*S. aureus*, *E. coli,* and *Salmonella* spp.), antifungal (*Mycosphaerella*, *Fusarium,* and *Physalospora*) and antiviral (HSV, HIV, and COVID-19) effects of mushroom polysaccharides (mainly β-glucans) are also extensively reported.

β-glucans and other polysaccharide extracts also play an important role in metabolic diseases, for instance, diabetes, obesity, and high cholesterol levels. These macromolecules typically stimulate insulin signaling and sensitivity. Concerning hypocholesterolemic and anti-lipidemic effects, three main mechanisms are reported. The first corresponds to the decrease of lipids absorption and increase in their excretion by binding polysaccharides to cholesterol and lipids in the intestine. Alternatively, mushroom polysaccharides have also been associated with the regulation of gene expression of cholesterol-related genes and the promotion of activity of antioxidant enzymes.

Oxidative stress has been associated with several diseases. Antioxidant and neuroprotective potential are reported for mushroom polysaccharides. One of the strategies proposed by the scientific community for treating neurodegenerative diseases is activating the Vitagen system. While the mushroom neuroprotective mechanisms are not totally clear, some mushroom species seem to increase lipoxin A4. Although polysaccharides are the foremost common compounds, other bioactive compounds (e.g., phenolic compounds, peptides, and fatty acids) present in mushroom biomass may be absorbed, reach the blood-brain barrier and impact brain function.

Thus, the available literature corroborates the high value of mushroom β-glucans in several human diseases and disorders. Consequently, lentinan, pleuran, schizophyllan, and other β-glucans are highly valued in cosmetic, food, and medical markets. Nowadays, these are incorporated in numerous pharmaceutic formulations, holding an expected increasing market value.

CRediT authorship contribution statement

Helena Araújo-Rodrigues: Writing – original draft, Visualization, Methodology, Formal analysis, Conceptualization. **Ana Sofia Sousa:** Writing – review & editing, Validation. **João Bettencourt Relvas:** Validation, Supervision. **Freni K. Tavaria:** Writing – review & editing, Validation, Supervision. **Manuela Pintado:** Writing – review & editing, Validation, Supervision, Project administration.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

Acknowledgments

We would like to thank the National Funds from FCT - Fundação para a Ciência e a Tecnologia through project UIDB/50016/2020 and FCT individual PhD grants number 2020.05798.BD (H. Araújo-Rodrigues) and 2021.07407.BD (A.S. Sousa).

References

Abreu, H., Simas, F. F., Smiderle, F. R., Sovrani, V., Dallazen, J. L., Maria-Ferreira, D., … Iacomini, M. (2019). Gelling functional property, anti-inflammatory and antinociceptive bioactivities of β-D-glucan from the edible mushroom Pholiota nameko. *International Journal of Biological Macromolecules, 122*, 1128–1135. https://doi.org/10.1016/j.ijbiomac.2018.09.062

Agus, A., Planchais, J., & Sokol, H. (2018). Gut microbiota regulation of tryptophan metabolism in health and disease. *Cell Host & Microbe, 23*(6), 716–724. https://doi.org/10.1016/j.chom.2018.05.003

Ahmad, R., Sellathoroe, S., Ngadi, E., Tengku Saharuddin, T. S., Zakaria, I. I., Selvakumaran, S., … W. A.. (2021). Isolation, identification, cultivation and determination of antimicrobial β-glucan from a wild-termite mushroom Termitomyces heimii RFES 230662. *Biocatalysis and Agricultural Biotechnology, 37*(8), Article 102187. https://doi.org/10.1016/j.bcab.2021.102187

Alagbaoso, C. A., & Mizuno, M. (2021). Polysaccharides from shiitake culinary-medicinal mushroom Lentinus edodes (Agaricomycetes) suppress pMLKL-mediated Necroptotic cell death and colitis in mice. *International Journal of Medicinal Mushrooms, 23*(7), 13–26. https://doi.org/10.1615/IntJMedMushrooms.2021038850

Al-Saffar, A. Z., Hadi, N. A., & Khalaf, H. M. (2020). Antitumor activity of β-glucan extracted from Pleurotus Eryngii. *Indian Journal of Forensic Medicine and Toxicology, 14*(3), 2492–2499. https://doi.org/10.37506/ijfmt.v14i3.10811

Araújo-Rodrigues, H., Sofia Sousa, A., Pintado, M. E., & Barros, D. (2022). Chapter 6. Macromolecules in Fungi with pharmaceutical potential. In L. Stojković (Ed.), *Edible Fungi: Chemical composition, nutrition and health effects* (36th ed., pp. 232–272). Royal Society of Chemistry. https://doi.org/10.1039/9781839167522-00232.

Arunachalam, K., Sasidharan, S. P., & Yang, X. (2022). A concise review of mushrooms antiviral and immunomodulatory properties that may combat against COVID-19. *Food Chemistry Advances, 1*(2), Article 100023. https://doi.org/10.1016/j.focha.2022.100023

Badalyan, S. M., Barkhudaryan, A., & Rapior, S. (2022). Medicinal macrofungi as cosmeceuticals: A review. *International Journal of Medicinal Mushrooms, 24*(4), 1–13. https://doi.org/10.1615/IntJMedMushrooms.2022043124

Bae, I. Y., Kim, H. W., Yoo, H. J., Kim, E. S., Lee, S., Park, D. Y., & Lee, H. G. (2013). Correlation of branching structure of mushroom β-glucan with its physiological activities. *Food Research International, 51*(1), 195–200. https://doi.org/10.1016/j.foodres.2012.12.008

Bains, A., Chawla, P., Kaur, S., Najda, A., Fogarasi, M., & Fogarasi, S. (2021). Bioactives from mushroom: Health attributes and food industry applications. *Materials, 14*(24). https://doi.org/10.3390/ma14247640

Balakrishnan, K., Dhanasekaran, D., Krishnaraj, V., Anbukumaran, A., Ramasamy, T., & Manickam, M. (2021). Edible mushrooms: A promising bioresource for prebiotics. In *Advances in probiotics* (pp. 81–97). Elsevier. https://doi.org/10.1016/B978-0-12-822909-5.00005-8.

Baldi, S., Mundula, T., Nannini, G., & Amedei, A. (2021). Microbiota shaping - the effects of probiotics, prebiotics, and fecal microbiota transplant on cognitive functions: A systematic review. *World Journal of Gastroenterology, 27*(39), 6715–6732. https://doi.org/10.3748/wjg.v27.i39.6715

Bell, V., Silva, C. R. P. G., Guina, J., & Fernandes, T. H. (2022). Mushrooms as future generation healthy foods. *Frontiers in Nutrition, 9*. https://doi.org/10.3389/fnut.2022.1050099

Bijla, S., & Sharma, V. P. (2023). Status of mushroom production: Global and national scenario. *Mushroom Research, 32*(2), 91–98. https://doi.org/10.36036/MR.32.2.2023.146647

Bonfili, L., Cecarini, V., Gogoi, O., Gong, C., Cuccioloni, M., Angeletti, M., … Eleuteri, A. M. (2021). Microbiota modulation as preventative and therapeutic approach in Alzheimer's disease. *The FEBS Journal, 288*(9), 2836–2855. https://doi.org/10.1111/febs.15571

Brial, F., Le Lay, A., Dumas, M. E., & Gauguier, D. (2018). Implication of gut microbiota metabolites in cardiovascular and metabolic diseases. *Cellular and Molecular Life Sciences, 75*(21), 3977–3990. https://doi.org/10.1007/s00018-018-2901-1

Castellano, J. M., Garcia-Rodriguez, S., Espinosa, J. M., Millan-Linares, M. C., Rada, M., & Perona, J. S. (2019). Oleanolic acid exerts a neuroprotective effect against microglial cell activation by modulating cytokine release and antioxidant defense systems. *Biomolecules, 9*(11), 683. https://doi.org/10.3390/biom9110683

Cateni, F., Gargano, M. L., Procida, G., Venturella, G., Cirlincione, F., & Ferraro, V. (2022). Mycochemicals in wild and cultivated mushrooms: Nutrition and health. *Phytochemistry Reviews, 21*(2), 339–383. https://doi.org/10.1007/s11101-021-09748-2

Cerletti, C., Esposito, S., & Iacoviello, L. (2021). Edible mushrooms and Beta-glucans: Impact on human health. *Nutrients, 13*(7), 2195. https://doi.org/10.3390/nu13072195

Chakraborty, N., Banerjee, A., Sarkar, A., Ghosh, S., & Acharya, K. (2020). Mushroom polysaccharides: A potent immune-modulator. *Biointerface Research in Applied Chemistry, 11*(2), 8915–8930. https://doi.org/10.33263/BRIAC112.89158930

Chaudhary, P., Sharma, A., Singh, B., & Nagpal, A. K. (2018). Bioactivities of phytochemicals present in tomato. *Journal of Food Science and Technology, 55*(8), 2833–2849. https://doi.org/10.1007/s13197-018-3221-z

Chen, H.-P., Zhao, Z.-Z., Li, Z.-H., Huang, Y., Zhang, S.-B., Tang, Y., … Liu, J.-K. (2018). Anti-proliferative and anti-inflammatory Lanostane triterpenoids from the polish edible mushroom Macrolepiota procera. *Journal of Agricultural and Food Chemistry, 66*(12), 3146–3154.

Chen, L., Ge, M.-D., Zhu, Y.-J., Song, Y., Cheung, P. C. K., Zhang, B.-B., & Liu, L.-M. (2019). Structure, bioactivity and applications of natural hyperbranched polysaccharides. *Carbohydrate Polymers, 223*(July), Article 115076. https://doi.org/10.1016/j.carbpol.2019.115076

Chen, Z., Yin, C., Fan, X., Ma, K., Yao, F., Zhou, R., Shi, D., Cheng, W., & Gao, H. (2020). Characterization of physicochemical and biological properties of Schizophyllum commune polysaccharide extracted with different methods. *International Journal of Biological Macromolecules, 156*, 1425–1434. https://doi.org/10.1016/j.ijbiomac.2019.11.183

Choudhary, S. (2020). Characterization and applications of mushroom exopolysaccharides. In *New and future developments in microbial biotechnology and bioengineering* (pp. 171–181). Elsevier. https://doi.org/10.1016/B978-0-12-821007-9.00014-0.

Dalile, B., Van Oudenhove, L., Vervliet, B., & Verbeke, K. (2019). The role of short-chain fatty acids in microbiota–gut–brain communication. *Nature Reviews Gastroenterology and Hepatology, 16*(8), 461–478. https://doi.org/10.1038/s41575-019-0157-3

Damián, M. R., Cortes-Perez, N. G., Quintana, E. T., Ortiz-Moreno, A., Garfias Noguez, C., Cruceño-Casarrubias, C. E., … Bermúdez-Humarán, L. G. (2022). Functional foods, nutraceuticals and probiotics: A focus on human health. *Microorganisms, 10*(5), 1065. https://doi.org/10.3390/microorganisms10051065

Deveci, E., Çayan, F., Tel-Çayan, G., & Duru, M. E. (2019). Structural characterization and determination of biological activities for different polysaccharides extracted from tree mushroom species. *Journal of Food Biochemistry, 43*(9), 1–13. https://doi.org/10.1111/jfbc.12965

Du, B., Meenu, M., Liu, H., & Xu, B. (2019). A concise review on the molecular structure and function relationship of β-glucan. *International Journal of Molecular Sciences, 20*(16), 4032. https://doi.org/10.3390/ijms20164032

Du, B., Nie, S., Peng, F., Yang, Y., & Xu, B. (2022). A narrative review on conformational structure characterization of natural polysaccharides. *Food Frontiers, 3*(4), 631–640. https://doi.org/10.1002/fft2.150

Eid, J. I., Al-Tuwaijri, M. M., Mohanty, S., & Das, B. (2021). Chaga mushroom (Inonotus obliquus) polysaccharides exhibit genoprotective effects in UVB-exposed embryonic zebrafish (Danio rerio) through coordinated expression of DNA repair genes. *Heliyon, 7*(2), Article e06003. https://doi.org/10.1016/j.heliyon.2021.e06003

Eid, J. I., & Das, B. (2020). Molecular insights and cell cycle assessment upon exposure to Chaga (Inonotus obliquus) mushroom polysaccharides in zebrafish (Danio rerio). *Scientific Reports, 10*(1), 1–9. https://doi.org/10.1038/s41598-020-64157-3

Fan, X., Hu, H., Chen, D., Yu, B., He, J., Yu, J., Luo, J., Eckhardt, E., Luo, Y., Wang, J., Yan, H., & Mao, X. (2021). Lentinan administration alleviates diarrhea of rotavirus-infected weaned pigs via regulating intestinal immunity. *Journal of Animal Science and Biotechnology, 12*(1), 43. https://doi.org/10.1186/s40104-021-00562-6

Farias, D. D. P., de Araújo, F. F., Neri-Numa, I. A., & Pastore, G. M. (2019). Prebiotics: Trends in food, health and technological applications. *Trends in Food Science & Technology, 93*(9), 23–35. https://doi.org/10.1016/j.tifs.2019.09.004

Fernández, M. F., Reina-Pérez, I., Astorga, J. M., Rodríguez-Carrillo, A., Plaza-Díaz, J., & Fontana, L. (2018). Breast cancer and its relationship with the microbiota. *International Journal of Environmental Research and Public Health, 15*(8), 1–20. https://doi.org/10.3390/ijerph15081747

Ferreira, S. S., Passos, C. P., Madureira, P., Vilanova, M., & Coimbra, M. A. (2015). Structure-function relationships of immunostimulatory polysaccharides: A review. *Carbohydrate Polymers, 132*, 378–396. https://doi.org/10.1016/j.carbpol.2015.05.079

Ferreiro, E., Pita, I. R., Mota, S. I., Valero, J., Ferreira, N. R., Fernandes, T., … Rego, A. C. (2018). Coriolus versicolor biomass increases dendritic arborization of newly-generated neurons in mouse hippocampal dentate gyrus. *Oncotarget, 9*(68), 32929–32942. https://doi.org/10.18632/oncotarget.25978

Filosa, S., Di Meo, F., & Crispi, S. (2018). Polyphenols-gut microbiota interplay and brain neuromodulation. *Neural Regeneration Research, 13*(12), 2055. https://doi.org/10.4103/1673-5374.241429

Fu, C., Ye, K., Ma, S., Du, H., Chen, S., Liu, D., Ma, G., & Xiao, H. (2023). Simulated gastrointestinal digestion and gut microbiota fermentation of polysaccharides from Agaricus bisporus. *Food Chemistry, 418*(March), Article 135849. https://doi.org/10.1016/j.foodchem.2023.135849

Ge, Y., Qiu, H., & Zheng, J. (2022). Physicochemical characteristics and anti-hyperlipidemic effect of polysaccharide from BaChu mushroom (Helvella leucopus). *Food Chemistry: X, 15*(July), Article 100443. https://doi.org/10.1016/j.fochx.2022.100443

Ghezzi, L., Cantoni, C., Rotondo, E., & Galimberti, D. (2022). The gut microbiome–brain crosstalk in neurodegenerative diseases. *Biomedicines, 10*(7), 1–17. https://doi.org/10.3390/biomedicines10071486

Giavasis, I. (2014). Bioactive fungal polysaccharides as potential functional ingredients in food and nutraceuticals. *Current Opinion in Biotechnology, 26*, 162–173. https://doi.org/10.1016/j.copbio.2014.01.010

Gibson, G. R., Hutkins, R., Sanders, M. E., Prescott, S. L., Reimer, R. A., Salminen, S. J., … Reid, G. (2017). Expert consensus document: The international scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. *Nature Reviews Gastroenterology and Hepatology, 14*(8), 491–502. https://doi.org/10.1038/nrgastro.2017.75

Gong, P., Wang, S., Liu, M., Chen, F., Yang, W., Chang, X., Liu, N., Zhao, Y., Wang, J., & Chen, X. (2020). Extraction methods, chemical characterizations and biological activities of mushroom polysaccharides: A mini-review. *Carbohydrate Research, 494*(June), Article 108037. https://doi.org/10.1016/j.carres.2020.108037

González, A., Atienza, V., Montoro, A., & Soriano, J. M. (2020). Use of ganoderma lucidum (Ganodermataceae, basidiomycota) as radioprotector. *Nutrients, 12*(4), 1–9. https://doi.org/10.3390/nu12041143

Govindan, S., Shanmugam, J., Rajendran, G., Ramani, P., Unni, D., Venkatachalam, B., … Ahn, B.-C. (2023). Antidiabetic activity of polysaccharide from Hypsizygus ulmarius in streptozotocin-nicotinamide induced diabetic rats. *Bioactive Carbohydrates and Dietary Fibre, 29*(October 2022), Article 100350. https://doi.org/10.1016/j.bcdf.2023.100350

Hao, R., Zhou, X., Zhao, X., Lv, X., Zhu, X., Gao, N. N., … Li, D. (2023). Flammulina velutipes polysaccharide counteracts cadmium-induced gut injury in mice via modulating gut inflammation, gut microbiota and intestinal barrier. *Science of the Total Environment, 877*(March), Article 162910. https://doi.org/10.1016/j.scitotenv.2023.162910

Hao, W., Hao, C., Wu, C., Xu, Y., & Jin, C. (2022). Aluminum induced intestinal dysfunction via mechanical, immune, chemical and biological barriers. *Chemosphere, 288*(P2), Article 132556. https://doi.org/10.1016/j.chemosphere.2021.132556

He, Z., Lin, J., He, Y., & Liu, S. (2022). Polysaccharide-peptide from Trametes versicolor: The potential medicine for colorectal cancer treatment. *Biomedicines, 10*(11), 1–11. https://doi.org/10.3390/biomedicines10112841

Hu, M., Zhang, P., Wang, R., Zhou, M., Pang, N., Cui, X., … Yu, Y. (2022). Three different types of β-glucans enhance cognition: The role of the gut-brain Axis. *Frontiers in Nutrition, 9*(3), 1–14. https://doi.org/10.3389/fnut.2022.848930

Hu, W., Di, Q., Liang, T., Zhou, N., Chen, H., Zeng, Z., Luo, Y., & Shaker, M. (2023). Effects of in vitro simulated digestion and fecal fermentation of polysaccharides from straw mushroom (Volvariella volvacea) on its physicochemical properties and human gut microbiota. *International Journal of Biological Macromolecules, 239*(March), Article 124188. https://doi.org/10.1016/j.ijbiomac.2023.124188

Inyod, T., Ayimbila, F., Payapanon, A., & Keawsompong, S. (2022). Antioxidant activities and prebiotic properties of the tropical mushroom Macrocybe crassa. *Bioactive Carbohydrates and Dietary Fibre, 27*(9), Article 100298. https://doi.org/10.1016/j.bcdf.2021.100298

Jamwal, S., & Kumar, P. (2019). Insight into the emerging role of striatal neurotransmitters in the pathophysiology of Parkinson's disease and Huntington's disease: A review. *Current Neuropharmacology, 17*(2), 165–175. https://doi.org/10.2174/1570159X16666180302115032

Jędrzejewski, T., Pawlikowska, M., Sobocińska, J., & Wrotek, S. (2023). COVID-19 and Cancer diseases—The potential of Coriolus versicolor mushroom to combat Global Health challenges. *International Journal of Molecular Sciences, 24*(5), 4864. https://doi.org/10.3390/ijms24054864

de Jesus, L. I., Smiderle, F. R., Cordeiro, L. M. C., de Freitas, R. A., Van Griensven, L. J. L. D., & Iacomini, M. (2018). Simple and effective purification approach to dissociate mixed water-insoluble α- and β-D-glucans and its application on the medicinal mushroom Fomitopsis betulina. *Carbohydrate Polymers, 200*(July), 353–360. https://doi.org/10.1016/j.carbpol.2018.08.004

Jones, M., Kujundzic, M., John, S., & Bismarck, A. (2020). Crab vs. mushroom: A review of crustacean and fungal chitin in wound treatment. *Marine Drugs, 18*(1), 64. https://www.mdpi.com/1660-3397/18/1/64.

Khan, I., Huang, G., Li, X. A., Liao, W., Leong, W. K., Xia, W., … Hsiao, W. L. W. (2019). Mushroom polysaccharides and jiaogulan saponins exert cancer preventive effects by shaping the gut microbiota and microenvironment in ApcMin/+ mice. *Pharmacological Research, 148*(6), Article 104448. https://doi.org/10.1016/j.phrs.2019.104448

Khan, I., Huang, G., Li, X., Leong, W., Xia, W., & Hsiao, W. L. W. (2018). Mushroom polysaccharides from Ganoderma lucidum and Poria cocos reveal prebiotic functions. *Journal of Functional Foods, 41*(12), 191–201. https://doi.org/10.1016/j.jff.2017.12.046

Kim, J. H., Tam, C. C., Chan, K. L., Mahoney, N., Cheng, L. W., Friedman, M., & Land, K. M. (2022). Antimicrobial efficacy of edible mushroom extracts: Assessment of fungal resistance. *Applied Sciences, 12*(9), 4591. https://doi.org/10.3390/app12094591

Knoema. (2022). *Production of mushrooms and truffles in the World* (p. 2021). https://knoema.com/data/agriculture-indicators-production+mushrooms-and-truffles.

Kulshreshtha, S. (2023). Mushroom as prebiotics: A sustainable approach for healthcare. *Probiotics and Antimicrobial Proteins.* , Article 0123456789. https://doi.org/10.1007/s12602-023-10164-5

Lai, Y., Fang, Q., Guo, X., Lei, H., Zhou, Q., Wu, N., & Song, C. (2022). Effect of polysaccharides from Dictyophora indusiata on regulating gut microbiota and short-chain fatty acids in mice. *Journal of Food Measurement and Characterization.* https://doi.org/10.1007/s11694-022-01596-8

Levy, M., Wu, J., Shi, J., Cheng, H., Qu, X., Bernstein, I., … Tian, J. (2021). Proof-of-concept and feasibility study to evaluate the effect of β-glucan on protective qi deficiency in adults. *Chinese Journal of Integrative Medicine, 27*(9), 666–673. https://doi.org/10.1007/s11655-020-3430-y

Li, H., Wang, Y., Zhao, P., Guo, L., Huang, L., Li, X., & Gao, W. (2023). Naturally and chemically acetylated polysaccharides: Structural characteristics, synthesis, activities, and applications in the delivery system: A review. *Carbohydrate Polymers, 313*(92), Article 120746. https://doi.org/10.1016/j.carbpol.2023.120746

Li, X., He, Y., Zeng, P., Liu, Y., Zhang, M., Hao, C., Wang, H., Lv, Z., & Zhang, L. (2019). Molecular basis for Poria cocos mushroom polysaccharide used as an antitumour drug in China. *Journal of Cellular and Molecular Medicine, 23*(1), 4–20. https://doi.org/10.1111/jcmm.13564

Li, X.-Y., He, C., Zhu, Y., & Lu, N.-H. (2020). Role of gut microbiota on intestinal barrier function in acute pancreatitis. *World Journal of Gastroenterology, 26*(18), 2187–2193. https://doi.org/10.3748/wjg.v26.i18.2187

Liang, Z., Yuan, Z., Li, G., Fu, F., & Shan, Y. (2018). Hypolipidemic, antioxidant, and Antiapoptotic effects of polysaccharides extracted from Reishi mushroom, Ganoderma lucidum (Leysser: Fr) karst, in mice fed a high-fat diet. *Journal of Medicinal Food, 21*(12), 1218–1227. https://doi.org/10.1089/jmf.2018.4182

Liu, M., Dai, Y., Song, C., Wang, J., Liu, Y., & Wang, Q. (2022). Structural characterization of a Pleurotus sajor-caju polysaccharide and its neuroprotection related to the inhibition of oxidative stress. *Nutrients, 14*(19). https://doi.org/10.3390/nu14194047

Liu, X., Pang, H., Gao, Z., Zhao, H., Zhang, J., & Jia, L. (2019). Antioxidant and hepatoprotective activities of residue polysaccharides by Pleurotus citrinipileatus. *International Journal of Biological Macromolecules, 131*, 315–322. https://doi.org/10.1016/j.ijbiomac.2019.03.074

Liu, Y., Liu, Y., Zhang, M., Li, C., Zhang, Z., Liu, A., Wu, Y., Wu, H., Chen, H., Hu, X., Lin, B., & Wu, W. (2020). Structural characterization of a polysaccharide from Suillellus luridus and its antidiabetic activity via Nrf2/HO-1 and NF-κB pathways. *International Journal of Biological Macromolecules, 162*, 935–945. https://doi.org/10.1016/j.ijbiomac.2020.06.212

Lu, H., Lou, H., Hu, J., Liu, Z., & Chen, Q. (2020). Macrofungi: A review of cultivation strategies, bioactivity, and application of mushrooms. *Comprehensive Reviews in Food Science and Food Safety, 19*(5), 2333–2356. https://doi.org/10.1111/1541-4337.12602

Ma, G., Xu, Q., Du, H., Muinde Kimatu, B., Su, A., Yang, W., Hu, Q., & Xiao, H. (2022). Characterization of polysaccharide from Pleurotus eryngii during simulated gastrointestinal digestion and fermentation. *Food Chemistry, 370*(9), Article 131303. https://doi.org/10.1016/j.foodchem.2021.131303

Ma, G., Yang, W., Zhao, L., Pei, F., Fang, D., & Hu, Q. (2018). A critical review on the health promoting effects of mushrooms nutraceuticals. *Food Science and Human Wellness, 7*(2), 125–133. https://doi.org/10.1016/j.fshw.2018.05.002

Ma, J., Piao, X., Mahfuz, S., Long, S., & Wang, J. (2022). The interaction among gut microbes, the intestinal barrier and short chain fatty acids. *Animal Nutrition, 9*, 159–174. https://doi.org/10.1016/j.aninu.2021.09.012

Mahmood, F., Hetland, G., Nentwich, I., Mirlashari, M. R., Ghiasvand, R., & Nissen-Meyer, L. S. H. (2019). Agaricus blazei-based mushroom extract supplementation to birch allergic blood donors: A randomized clinical trial. *Nutrients, 11*(10), 1–15. https://doi.org/10.3390/nu11102339

Maity, P., Sen, I. K., Chakraborty, I., Mondal, S., Bar, H., Bhanja, S. K., … Maity, G. N. (2021). Biologically active polysaccharide from edible mushrooms: A review. *International Journal of Biological Macromolecules, 172*, 408–417. https://doi.org/10.1016/j.ijbiomac.2021.01.081

Marçal, S., Sousa, A. S., Taofiq, O., Antunes, F., Morais, A. M. M. B., Freitas, A. C., … Pintado, M. (2021). Impact of postharvest preservation methods on nutritional value and bioactive properties of mushrooms. *Trends in Food Science & Technology, 110* (January), 418–431. https://doi.org/10.1016/j.tifs.2021.02.007

Martinez-Medina, G. A., Chávez-González, M. L., Verma, D. K., Prado-Barragán, L. A., Martínez-Hernández, J. L., Flores-Gallegos, A. C., … Aguilar, C. N. (2021). Bio-funcional components in mushrooms, a health opportunity: Ergothionine and huitlacohe as recent trends. *Journal of Functional Foods, 77*, Article 104326. https://doi.org/10.1016/j.jff.2020.104326

Meng, Y., Lyu, F., Xu, X., & Zhang, L. (2020). Recent advances in chain conformation and bioactivities of triple-Helix polysaccharides. *Biomacromolecules, 21*(5), 1653–1677. https://doi.org/10.1021/acs.biomac.9b01644

Mirończuk-Chodakowska, I., Kujawowicz, K., & Witkowska, A. M. (2021). Beta-glucans from Fungi: Biological and health-promoting potential in the COVID-19 pandemic era. *Nutrients, 13*(11), 3960. https://doi.org/10.3390/nu13113960

Mohamed, S. S., Ibrahim, G. S., Ghoneim, M. A. M., & Hassan, A. I. (2023). Evaluating the role of polysaccharide extracted from Pleurotus columbinus on cisplatin-induced oxidative renal injury. *Scientific Reports, 13*(1), 1–14. https://doi.org/10.1038/s41598-022-27081-2

Morales, D., Rutckeviski, R., Villalva, M., Abreu, H., Soler-Rivas, C., Santoyo, S., … Smiderle, F. R. (2020). Isolation and comparison of α- and β-D-glucans from shiitake mushrooms (Lentinula edodes) with different biological activities. *Carbohydrate Polymers, 229*(July 2019), Article 115521. https://doi.org/10.1016/j.carbpol.2019.115521

Moumita, S., & Das, B. (2022). Assessment of the prebiotic potential and bioactive components of common edible mushrooms in India and formulation of synbiotic microcapsules. *LWT, 156*, Article 113050. https://doi.org/10.1016/j.lwt.2021.113050

Murphy, E. J., Masterson, C., Rezoagli, E., O'Toole, D., Major, I., Stack, G. D., … Rowan, N. J. (2020). β-Glucan extracts from the same edible shiitake mushroom Lentinus edodes produce differential in-vitro immunomodulatory and pulmonary cytoprotective effects — Implications for coronavirus disease (COVID-19) immunotherapies. *Science of the Total Environment, 732*(January), Article 139330. https://doi.org/10.1016/j.scitotenv.2020.139330

Muszyńska, B., Grzywacz-Kisielewska, A., Kała, K., & Gdula-Argasińska, J. (2018). Anti-inflammatory properties of edible mushrooms: A review. *Food Chemistry, 243*(July 2017), 373–381. https://doi.org/10.1016/j.foodchem.2017.09.149

Nakahara, D., Nan, C., Mori, K., Hanayama, M., Kikuchi, H., Hirai, S., & Egashira, Y. (2020). Effect of mushroom polysaccharides from Pleurotus eryngii on obesity and gut microbiota in mice fed a high-fat diet. *European Journal of Nutrition, 59*(7), 3231–3244. https://doi.org/10.1007/s00394-019-02162-7

Nataraj, A., Govindan, S., Ramani, P., Subbaiah, K. A., Sathianarayanan, S., Venkidasamy, B., … Pateiro, M. (2022). Antioxidant, anti-tumour, and anticoagulant activities of polysaccharide from Calocybe indica (APK2). *Antioxidants, 11*(9), 1–20. https://doi.org/10.3390/antiox11091694

National Library of Medicine, U. S. (2023). *ClinicalTrials.gov database*. NIH. https://clinicaltrials.gov/ct2/results?term=mushroom.

NCT03300947. (2019). *Psilocybin for treatment of obsessive compulsive disorder (PSILOCD)*. National Library of Medicine. https://clinicaltrials.gov/study/NCT03300947.

NCT04186780. (2018). *Effects of Lentinula Edodes bars on dyslipidemia and oxidative stress in cholesterol individuals: Randomized study*. National Library of Medicine. https://clinicaltrials.gov/study/NCT04186780.

NCT04501653. (2021). *Precision functional brain mapping in psilocybin (psilocybin PFM)*. National Library of Medicine. https://clinicaltrials.gov/study/NCT04501653.

NCT04667247. (2020). *Mushroom-based product for COVID-19 (MACH19)*. National Library of Medicine. https://clinicaltrials.gov/study/NCT04667247.

NCT04951336. (2021). *RCT of mushroom based natural product to enhance immune response to COVID-19 vaccination*. National Library of Medicine. https://clinicaltrials.gov/study/NCT04951336.

NCT05190432. (2021). *Taxifolin/Ergothioneine and immune biomarkers in healthy volunteers (TaxEr) (TaxEr)*. National Library of Medicine. https://clinicaltrials.gov/study/NCT05190432.

Nidhi, D. (2018). Mushroom polysaccharides as a potential prebiotics. *International Journal of Health Sciences and Research, 2*(1), 115–126.

Niego, A. G., Rapior, S., Thongklang, N., Raspé, O., Jaidee, W., Lumyong, S., & Hyde, K. D. (2021). Macrofungi as a nutraceutical source: Promising bioactive compounds and market value. *Journal of Fungi, 7*(5), 397. https://doi.org/10.3390/jof7050397

Nishimoto, Y., Kawai, J., & Mori, K. (2023). *Dietary supplement of mushrooms promotes SCFA production and moderately associates with IgA production : A pilot clinical study. January* pp. 1–13). https://doi.org/10.3389/fnut.2022.1078060

Nowak, R., Nowacka-Jechalke, N., Juda, M., & Malm, A. (2018). The preliminary study of prebiotic potential of polish wild mushroom polysaccharides: The stimulation effect on Lactobacillus strains growth. *European Journal of Nutrition, 57*(4), 1511–1521. https://doi.org/10.1007/s00394-017-1436-9

Pan, W., Jiang, P., Zhao, J., Shi, H., Zhang, P., Yang, X., … Yu, Y. (2021). β-Glucan from Lentinula edodes prevents cognitive impairments in high-fat diet-induced obese mice: Involvement of colon-brain axis. *Journal of Translational Medicine, 19*(1), 1–17. https://doi.org/10.1186/s12967-021-02724-6

Panda, S. K., & Luyten, W. (2022). Medicinal mushrooms: Clinical perspective and challenges. *Drug Discovery Today, 27*(2), 636–651. https://doi.org/10.1016/j.drudis.2021.11.017

Parker, A., Fonseca, S., & Carding, S. R. (2020). Gut microbes and metabolites as modulators of blood-brain barrier integrity and brain health. *Gut Microbes, 11*(2), 135–157. https://doi.org/10.1080/19490976.2019.1638722

Rao, Z., Dong, Y., Zheng, X., Tang, K., & Liu, J. (2021). Extraction, purification, bioactivities and prospect of lentinan: A review. *Biocatalysis and Agricultural Biotechnology, 37*(September), Article 102163. https://doi.org/10.1016/j.bcab.2021.102163

Reddy, P., Rajeswari, U., & Kumar, S. (2021). A comprehensive review on α -D-glucans : Structural and functional diversity, derivatization and bioapplications. *Carbohydrate Research, 503*(12), Article 108297. https://doi.org/10.1016/j.carres.2021.108297

Rizkyana, A. D., Ho, T. C., Roy, V. C., Park, J. S., Kiddane, A. T., Do Kim, G., & Chun, B. S. (2022). Sulfation and characterization of polysaccharides from oyster mushroom (Pleurotus ostreatus) extracted using subcritical water. *Journal of Supercritical Fluids, 179*(September 2021), Article 105412. https://doi.org/10.1016/j.supflu.2021.105412

Rodrigues Barbosa, J., dos Santos Freitas, M. M., da Silva Martins, L. H., & de Carvalho, R. N. (2020). Polysaccharides of mushroom Pleurotus spp.: New extraction techniques, biological activities and development of new technologies. *Carbohydrate Polymers, 229*(9), Article 115550. https://doi.org/10.1016/j.carbpol.2019.115550

Rout, D., Mondal, S., Chakraborty, I., & Islam, S. S. (2008). The structure and conformation of a water-insoluble (1→3)-,(1→6)-β-d-glucan from the fruiting bodies of Pleurotus florida. *Carbohydrate Research, 343*(5), 982–987. https://doi.org/10.1016/j.carres.2007.12.022

Routy, B., Gopalakrishnan, V., Daillère, R., Zitvogel, L., Wargo, J. A., & Kroemer, G. (2018). The gut microbiota influences anticancer immunosurveillance and general health. *Nature Reviews Clinical Oncology, 15*(6), 382–396. https://doi.org/10.1038/s41571-018-0006-2

Ruan, Y., Li, H., Pu, L., Shen, T., & Jin, Z. (2018). Tremella fuciformis polysaccharides attenuate oxidative stress and inflammation in macrophages through miR-155. *Analytical Cellular Pathology, 2018*, 1–10. https://doi.org/10.1155/2018/5762371

Sarkar, R., Nandan, C. K., Bhunia, S. K., Maiti, S., Maiti, T. K., Sikdar, S. R., & Islam, S. S. (2012). Glucans from alkaline extract of a hybrid mushroom (backcross mating between PfloVv12 and Volvariella volvacea): Structural characterization and study of immunoenhancing and antioxidant properties. *Carbohydrate Research, 347*(1), 107–113. https://doi.org/10.1016/j.carres.2011.10.043

Seo, G., Hyun, C., Choi, S., Kim, Y. M., & Cho, M. (2019). The wound healing effect of four types of beta-glucan. *Applied Biological Chemistry, 62*(1), 20. https://doi.org/10.1186/s13765-019-0428-2

Sevindik, M. (2021). Mushrooms as natural antiviral sources and supplements foods against coronavirus (COVID-19). *Journal of Bacteriology & Mycology: Open Access, 9*(2), 73–76. https://doi.org/10.15406/jbmoa.2021.09.00299

Shang, H., Chen, S., Li, R., Zhou, H., Wu, H., & Song, H. (2018). Influences of extraction methods on physicochemical characteristics and activities of Astragalus cicer L. polysaccharides. *Process Biochemistry, 73*(2888), 220–227. https://doi.org/10.1016/j.procbio.2018.07.016

Sharma, A., Sharma, A., & Tripathi, A. (2021). Biological activities of Pleurotus spp. polysaccharides: A review. *Journal of Food Biochemistry, 45*(6), 1–16. https://doi.org/10.1111/jfbc.13748

Song, X., Ren, Z., Wang, X., Jia, L., & Zhang, C. (2020). Antioxidant, anti-inflammatory and renoprotective effects of acidic-hydrolytic polysaccharides by spent mushroom compost (Lentinula edodes) on LPS-induced kidney injury. *International Journal of Biological Macromolecules, 151*, 1267–1276. https://doi.org/10.1016/j.ijbiomac.2019.10.173

Sousa, A. S., Araújo-Rodrigues, H., & Pintado, M. E. (2023). The health-promoting potential of edible mushroom proteins. *Current Pharmaceutical Design, 29*(11), 804–823. https://doi.org/10.2174/1381612829666221223103756

Su, Y., Cheng, S., Ding, Y., Wang, L., Sun, M., Man, C., Zhang, Y., & Jiang, Y. (2023). A comparison of study on intestinal barrier protection of polysaccharides from Hericium erinaceus before and after fermentation. *International Journal of Biological Macromolecules, 233*(November 2022), Article 123558. https://doi.org/10.1016/j.ijbiomac.2023.123558

Su, Y., Li, H., Hu, Z., Zhang, Y., Guo, L., Shao, M., Man, C., & Jiang, Y. (2023). Research on degradation of polysaccharides during Hericium erinaceus fermentation. *LWT, 173*(November 2022), Article 114276. https://doi.org/10.1016/j.lwt.2022.114276

Sudheer, S., Alzorqi, I., Manickam, S., & Ali, A. (2019). Bioactive compounds of the wonder medicinal mushroom "Ganoderma lucidum". In *Reference Series in Phytochemistry* (pp. 1863–1893). https://doi.org/10.1007/978-3-319-78030-6_45

Surenjav, U., Zhang, L., Xu, X., Zhang, X., & Zeng, F. (2006). Effects of molecular structure on antitumor activities of (1→3)-β-d-glucans from different Lentinus Edodes. *Carbohydrate Polymers, 63*(1), 97–104. https://doi.org/10.1016/j.carbpol.2005.08.011

Synytsya, A., & Novák, M. (2013). Structural diversity of fungal glucans. *Carbohydrate Polymers, 92*(1), 792–809. https://doi.org/10.1016/j.carbpol.2012.09.077

Tepsongkroh, B., Thaihuttakij, C., Supawong, S., & Jangchud, K. (2023). Impact of high pressure pre-treatment and hot water extraction on chemical properties of crude polysaccharide extract obtained from mushroom (Volvariella volvacea). *Food Chemistry: X, 19*(July), Article 100864. https://doi.org/10.1016/j.fochx.2023.100864

Thimmaraju, A., Govindan, S., Rajendran, A., Ramani, P., Pateiro, M., & Lorenzo, J. M. (2023). Enhancement of physicochemical properties, antioxidant, antitumor, and anticoagulant activities via acetylation of Hypsizygus ulmarius polysaccharide. *International Journal of Food Science & Technology, 58*(6), 3478–3487. https://doi.org/10.1111/ijfs.16439

Thongsiri, C., Nagai-Yoshioka, Y., Yamasaki, R., Adachi, Y., Usui, M., Nakashima, K., Nishihara, T., & Ariyoshi, W. (2021). Schizophyllum commune β-glucan: Effect on interleukin-10 expression induced by lipopolysaccharide from periodontopathic bacteria. *Carbohydrate Polymers, 253*(7). https://doi.org/10.1016/j.carbpol.2020.117285

Tian, B., Geng, Y., Xu, T., Zou, X., Mao, R., Pi, X., … Sun, P. (2022). Digestive characteristics of Hericium erinaceus polysaccharides and their positive effects on fecal microbiota of male and female volunteers during in vitro fermentation. *Frontiers in Nutrition, 9*(March), 1–17. https://doi.org/10.3389/fnut.2022.858585

Tomoda, M., Gonda, R., Kasahara, Y., & Hikino, H. (1986). Glycan structures of ganoderans b and c, hypoglycemic glycans of ganoderma lucidum fruit bodies. *Phytochemistry, 25*(12), 2817–2820. https://doi.org/10.1016/S0031-9422(00)83748-6

Tong, A. J., Hu, R. K., Wu, L. X., Lv, X. C., Li, X., Zhao, L. N., & Liu, B. (2020). Ganoderma polysaccharide and chitosan synergistically ameliorate lipid metabolic disorders and modulate gut microbiota composition in high fat diet-fed golden hamsters. *Journal of Food Biochemistry, 44*(1), 1–9. https://doi.org/10.1111/jfbc.13109

Urbancikova, I., Hudackova, D., Majtan, J., Rennerova, Z., Banovcin, P., & Jesenak, M. (2020). Efficacy of Pleuran (β-glucan from Pleurotus ostreatus) in the Management of Herpes Simplex Virus Type 1 infection. *Evidence-based Complementary and Alternative Medicine, 2020*. https://doi.org/10.1155/2020/8562309

Venturella, G., Ferraro, V., Cirlincione, F., & Gargano, M. L. (2021). Medicinal mushrooms: Bioactive compounds, use, and clinical trials. *International Journal of Molecular Sciences, 22*(2), 634. https://doi.org/10.3390/ijms22020634

Wang, C.-Y. (2020). A review on the potential reuse of functional polysaccharides extracted from the by-products of mushroom processing. *Food and Bioprocess Technology, 13*(2), 217–228. https://doi.org/10.1007/s11947-020-02403-2

Wang, H., Ma, J. X., Zhou, M., Si, J., & Cui, B. K. (2022). Current advances and potential trends of the polysaccharides derived from medicinal mushrooms sanghuang. *Frontiers in Microbiology, 13*(1968). https://doi.org/10.3389/fmicb.2022.965934

Wang, H., Cai, Y., Zheng, Y., Bai, Q., Xie, D., & Yu, J. (2017). Efficacy of biological response modifier lentinan with chemotherapy for advanced cancer: A meta-analysis. *Cancer Medicine, 6*(10), 2222–2233. https://doi.org/10.1002/cam4.1156

Wang, K.-L., Lu, Z.-M., Mao, X., Chen, L., Gong, J.-S., Ren, Y., Geng, Y., Li, H., Xu, H.-Y., Xu, G.-H., Shi, J.-S., & Xu, Z.-H. (2019). Structural characterization and anti-alcoholic liver injury activity of a polysaccharide from Coriolus versicolor mycelia. *International Journal of Biological Macromolecules, 137*, 1102–1111. https://doi.org/10.1016/j.ijbiomac.2019.06.242

Wang, M., Xie, Z., Li, L., Chen, Y., Li, Y., Wang, Y., … Liao, Q. (2019). Supplementation with compound polysaccharides contributes to the development and metabolic activity of young rat intestinal microbiota. *Food & Function, 10*(5), 2658–2675. https://doi.org/10.1039/C8FO02565G

Wang, M., Wichienchot, S., He, X., Fu, X., Huang, Q., & Zhang, B. (2019). In vitro colonic fermentation of dietary fibers: Fermentation rate, short-chain fatty acid production and changes in microbiota. *Trends in Food Science & Technology, 88*(2), 1–9. https://doi.org/10.1016/j.tifs.2019.03.005

Wang, T., Han, J., Dai, H., Sun, J., Ren, J., Wang, W., Qiao, S., Liu, C., Sun, L., Liu, S., Li, D., Wei, S., & Liu, H. (2022). Polysaccharides from Lyophyllum decastes reduce obesity by altering gut microbiota and increasing energy expenditure. *Carbohydrate Polymers, 295*(1), Article 119862. https://doi.org/10.1016/j.carbpol.2022.119862

Wang, X., Wang, Y., Zhou, Q., Peng, M., Zhang, J., Chen, M., … Xie, G. (2020). Immunomodulatory effect of Lentinan on aberrant T subsets and cytokines profile in non-small cell lung Cancer patients. *Pathology & Oncology Research, 26*(1), 499–505. https://doi.org/10.1007/s12253-018-0545-y

Wang, X.-Y., Zhang, D., Yin, J.-Y., Nie, S.-P., & Xie, M.-Y. (2019). Recent developments in Hericium erinaceus polysaccharides: Extraction, purification, structural characteristics and biological activities. *Critical Reviews in Food Science and Nutrition, 59*(sup1), S96–S115. https://doi.org/10.1080/10408398.2018.1521370

Wu, D. T., An, L. Y., Liu, W., Hu, Y. C., Wang, S. P., & Zou, L. (2022). In vitro fecal fermentation properties of polysaccharides from Tremella fuciformis and related modulation effects on gut microbiota. *Food Research International, 156*(January), Article 111185. https://doi.org/10.1016/j.foodres.2022.111185

Wu, S., Zhang, S., Peng, B., Tan, D., Wu, M., Wei, J., … Luo, H. (2024). Ganoderma lucidum : A comprehensive review of phytochemistry, efficacy, safety and clinical study. *Food Science and Human Wellness, 13*(2), 568–596. https://doi.org/10.26599/FSHW.2022.9250051

Xiao, C., Jiao, C., Xie, Y., Ye, L., Li, Q., & Wu, Q. (2021). Grifola frondosa GF5000 improves insulin resistance by modulation the composition of gut microbiota in diabetic rats. *Journal of Functional Foods, 77*(November 2020), Article 104313. https://doi.org/10.1016/j.jff.2020.104313

Xiao, H., Chen, C., Li, C., Huang, Q., & Fu, X. (2019). Physicochemical characterization, antioxidant and hypoglycemic activities of selenized polysaccharides from Sargassum pallidum. *International Journal of Biological Macromolecules, 132*, 308–315. https://doi.org/10.1016/j.ijbiomac.2019.03.138

Yadav, D., & Negi, P. S. (2021). Bioactive components of mushrooms: Processing effects and health benefits. *Food Research International, 148*(4), Article 110599. https://doi.org/10.1016/j.foodres.2021.110599

Yang, D., Zhou, Z., & Zhang, L. (2019). *An overview of fungal glycan-based therapeutics* (pp. 135–163). https://doi.org/10.1016/bs.pmbts.2019.02.001

Yang, R., Li, Y., Mehmood, S., Yan, C., Huang, Y., Cai, J., & Ji, J. (2020). Polysaccharides from Armillariella tabescens mycelia ameliorate renal damage in type 2 diabetic mice. *International Journal of Biological Macromolecules, 162*, 1682–1691. https://doi.org/10.1016/j.ijbiomac.2020.08.006

Yang, X., Zheng, M., Zhou, M., Zhou, L., Ge, X., Pang, N., … Yu, Y. (2022). Lentinan supplementation protects the gut–liver axis and prevents steatohepatitis: the role of gut microbiota involved. *Frontiers in Nutrition, 8*(1). https://doi.org/10.3389/fnut.2021.803691

Yin, C., Noratto, G. D., Fan, X., Chen, Z., Yao, F., Shi, D., & Gao, H. (2020). The impact of mushroom polysaccharides on gut microbiota and its beneficial effects to host: A review. *Carbohydrate Polymers, 250*(June), Article 116942. https://doi.org/10.1016/j.carbpol.2020.116942

Zhang, L., Hu, Y., Duan, X., Tang, T., Shen, Y., Hu, B., Liu, A., Chen, H., Li, C., & Liu, Y. (2018). Characterization and antioxidant activities of polysaccharides from thirteen boletus mushrooms. *International Journal of Biological Macromolecules, 113*, 1–7. https://doi.org/10.1016/j.ijbiomac.2018.02.084

Zhang, L., Liu, Y., Ke, Y., Liu, Y., Luo, X., Li, C., Zhang, Z., Liu, A., Shen, L., Chen, H., Hu, B., Wu, H., Wu, W., Lin, D., & Li, S. (2018). Antidiabetic activity of polysaccharides from Suillellus luridus in streptozotocin-induced diabetic mice. *International Journal of Biological Macromolecules, 119*, 134–140. https://doi.org/10.1016/j.ijbiomac.2018.07.109

Zhang, M., Zhang, Y., Zhang, L., & Tian, Q. (2019). Mushroom polysaccharide lentinan for treating different types of cancers: A review of 12 years clinical studies in China. In (1st ed.), *163. Progress in molecular biology and translational science*. Elsevier Inc.. https://doi.org/10.1016/bs.pmbts.2019.02.013

Zhang, S., Lei, L., Zhou, Y., Ye, F., & Zhao, G. (2022). Roles of mushroom polysaccharides in chronic disease management. *Journal of Integrative Agriculture, 21*(7), 1839–1866. https://doi.org/10.1016/S2095-3119(21)63871-6

Zhang, T., Huang, S., Qiu, J., Wu, X., Yuan, H., & Park, S. (2022). Beneficial effect of Gastrodia elata Blume and Poria cocos wolf administration on acute UVB irradiation by alleviating inflammation through promoting the gut-skin Axis. *International Journal of Molecular Sciences, 23*(18), Article 10833. https://doi.org/10.3390/ijms231810833

Zhang, W., Guo, Y., Cheng, Y., Yao, W., & Qian, H. (2022). Neuroprotective effects of polysaccharide from Sparassis crispa on Alzheimer's disease-like mice: Involvement of microbiota-gut-brain axis. *International Journal of Biological Macromolecules, 225*(April 2022), 974–986. https://doi.org/10.1016/j.ijbiomac.2022.11.160

Zhang, W., Hu, B., Han, M., Guo, Y., Cheng, Y., & Qian, H. (2022). Purification, structural characterization and neuroprotective effect of a neutral polysaccharide from Sparassis crispa. *International Journal of Biological Macromolecules, 201*, 389–399. https://doi.org/10.1016/j.ijbiomac.2021.12.165

Zhang, W. N., Su, R. N., Gong, L. L., Yang, W. W., Chen, J., Yang, R., … Chen, Y. (2019). Structural characterization and in vitro hypoglycemic activity of a glucan from Euryale ferox Salisb. Seeds. *Carbohydrate Polymers, 209*(September 2018), 363–371. https://doi.org/10.1016/j.carbpol.2019.01.044

Zhang, X., Cai, Z., Mao, H., Hu, P., & Li, X. (2021). Isolation and structure elucidation of polysaccharides from fruiting bodies of mushroom Coriolus versicolor and evaluation of their immunomodulatory effects. *International Journal of Biological Macromolecules, 166*, 1387–1395. https://doi.org/10.1016/j.ijbiomac.2020.11.018

Zhang, Y., Zhang, M., Jiang, Y., Li, X., He, Y., Zeng, P., … Zhang, L. (2018). Lentinan as an immunotherapeutic for treating lung cancer: A review of 12 years clinical studies in China. *Journal of Cancer Research and Clinical Oncology, 144*(11), 2177–2186. https://doi.org/10.1007/s00432-018-2718-1

Zhang, Z., Zhao, L., Qu, H., Zhou, H., Yang, H., & Chen, H. (2022). Physicochemical characterization, adsorption function and prebiotic effect of chitin-glucan complex from mushroom Coprinus comatus. *International Journal of Biological Macromolecules, 206*(12), 255–263. https://doi.org/10.1016/j.ijbiomac.2022.02.152

Zhao, J., Hu, Y., Qian, C., Hussain, M., Liu, S., Zhang, A., … Sun, P. (2023). The interaction between mushroom polysaccharides and gut microbiota and their effect on human health: A review. *Biology, 12*(1), 122. https://doi.org/10.3390/biology12010122

Zhao, S., Zhang, S., Zhang, W., Gao, Y., Rong, C., Wang, H., … Ng, T. (2019). First demonstration of protective effects of purified mushroom polysaccharide-peptides against fatty liver injury and the mechanisms involved. *Scientific Reports, 9*(1), 1–13. https://doi.org/10.1038/s41598-019-49925-0

Zheng, M., Pi, X., Li, H., Cheng, S., Su, Y., Zhang, Y., … Jiang, Y. (2022). Ganoderma spp. polysaccharides are potential prebiotics: A review. *Critical Reviews in Food Science and Nutrition, 0*(0), 1–19. https://doi.org/10.1080/10408398.2022.2110035

Zi, Y., Jiang, B., He, C., & Liu, L. (2020). Lentinan inhibits oxidative stress and inflammatory cytokine production induced by benzo(a)pyrene in human keratinocytes. *Journal of Cosmetic Dermatology, 19*(2), 502–507. https://doi.org/10.1111/jocd.13005

Zou, M. Y., Wang, Y. J., Liu, Y., Xiong, S. Q., Zhang, L., & Wang, J. H. (2022). Huangshan floral mushroom polysaccharide ameliorates dextran sulfate sodium-induced colitis in mice by modulating Th17/Treg balance in a gut microbiota-dependent manner. *Molecular Nutrition & Food Research, 2200408*, 1–14. https://doi.org/10.1002/mnfr.202200408

Zuo, K., Tang, K., Liang, Y., Xu, Y., Sheng, K., Kong, X., … Wang, Y. (2021). Purification and antioxidant and anti-inflammatory activity of extracellular polysaccharopeptide from sanghuang mushroom, Sanghuangporus lonicericola. *Journal of the Science of Food and Agriculture, 101*(3), 1009–1020. https://doi.org/10.1002/jsfa.10709