DOI: 10.26599/FSHW.2025.9250590

Contents lists available at SciOpen

Food Science and Human Wellness

journal homepage: https://www.sciopen.com/journal/2097-0765

China Food Publishing Co.

Advances in the Preparation, Structure-Activity Relationship, and Biological Mechanisms of *Agaricus* Polysaccharides

Zhixuan Li[a,#], Ming Zhang[a,#], Yuying Liu[a,b], MingLei Li[b,c,*], Jianzhao Qi[a,b,c,*]

[a] *Shaanxi Key Laboratory of Natural Products & Chemical Biology, College of Chemistry & Pharmacy, Northwest A&F University, Yangling 712100, China*

[b] *Center of Edible Fungi, Northwest A&F University, Yangling 712100, China*

[c] *School of Soil and Water Conservation Science and Engineering, Northwest A&F University, Yangling 712100, China,*

ABSTRACT: Polysaccharides derived from the *Agaricus* genus have garnered considerable attention due to their diverse biological activities and potential applications in functional foods and pharmaceuticals. This review focuses on the preparation methods, structure-activity relationships, and underlying biological mechanisms of *Agaricus* polysaccharides. Key advances in their extraction and purification techniques, structural characterization using modern analytical tools, and their association with biological activities are discussed. The role of polysaccharide structure, including glycosidic linkages, branching degrees, and molecular weight, in determining their physicochemical properties and biofunctions is highlighted. Moreover, the biological mechanisms underpinning their antitumor, immunomodulatory, antioxidant effects are elaborated. Finally, future perspectives on the challenges and opportunities for developing *Agaricus* polysaccharides as functional biomaterials are provided.

Key word: *Agaricus* Polysaccharides; Structure; Activity Relationship

1. Introduction

Polysaccharides, a crucial class of natural macromolecules, are ubiquitous in the realms of flora, fauna, and microorganisms [1, 2]. Due to their excellent biocompatibility and bioactivity, they have found extensive applications in fields such as medicine [3-5], food science [6], and environmental conservation [7]. Edible-medicinal fungi, renowned for their polysaccharide constituents[8, 9], exhibit potent biological activities and are particularly esteemed for their roles in immune modulation, anti-neoplastic properties, anti-oxidative capabilities, and hypoglycemic effects [10-14]. Among these fungi, *Agaricus* species, which are consumed globally, have become a focal point in health research due to their polysaccharide constituents [15]. Notably, polysaccharides extracted from *Agaricus blazei* [16-20], *Agaricus brasiliensis* [21-23], and *Agaricus bisporus* [24, 25] have been the subject of extensive research and scientific scrutiny. *Agaricus* subrufescens, exhibit however, presents, significant variations in polysaccharide composition and biological

# These authors contributed equally to this work.
***Corresponding author**
mlli@nwsuaf.edu.cn (M.L.); qjz@nwafu.edu.cn (J.Q.)

Received 13 December 2024
Received in revised from 13 January 2025
Accepted 31 January 2025

activity, which are influenced by factors such as environmental conditions, cultivation practices, and genetic diversity [26].

Agaricus polysaccharides are known for their diverse biological functions, encompassing anti-neoplastic, immunomodulatory, anti-oxidative, anti-inflammatory, and anti-aging effects [11, 27-31]. *Agaricus* polysaccharides exhibit anti-tumor activity by enhancing immune responses and inhibiting the proliferation and invasion of tumor cells [32-34]. Additionally, their antioxidant activity helps effectively scavenge free radicals, slow down the aging process, and hold potential therapeutic effects on various diseases associated with oxidative stress [35].

Agaricus species are distributed across the globe, with a particular affinity for tropical and temperate climates. Their distribution is notably concentrated in Asia, Europe, and the Americas, where cultivation has a long-standing history [36, 37]. The biosynthesis of polysaccharides in these fungi may be influenced by climatic conditions, soil composition, and agricultural techniques, especially in the warm and humid environments that foster higher growth rates and the accumulation of bioactive compounds in *Agaricus* species. Polysaccharides, as a primary bioactive component, exhibit a distinct structure-function correlation that is pivotal to their manifold biological activities [38]. The molecular structure of *Agaricus* polysaccharides varies between sources, leading to differences in biological activity, with molecular weight, glycosidic linkage types, and degree of polymerization being key determinants of their functions [39, 40].

Despite the substantial progress in *Agaricus* polysaccharide research, a comprehensive understanding of their mechanisms of action remains elusive. The primary challenges lie in deciphering the structure-function relationships, investigating their metabolic pathways *in vivo*, and uncovering the bioactivity disparities among polysaccharides from different *Agaricus* species. The existing literature predominantly focuses on specific biological functions, with a scarcity of systematic overviews on their collective bioactivity. Furthermore, enhancing the bioactivity of these polysaccharides through structural modifications is a critical research domain, encompassing the discovery of novel functions and a deeper comprehension of their structural nuances.

To bridge these knowledge gaps, this review endeavors to provide a systematic synthesis of the current state of research on the extraction, isolation, structural characteristics, and biological activities of *Agaricus* polysaccharides. It will underscore their principal functions, such as anti-neoplastic, immunomodulatory, and anti-oxidative effects, and offer an analysis of their mechanisms of action based on the most recent scientific insights. By critically reviewing and consolidating existing studies, this paper aspires to lay a theoretical groundwork for future investigations into *Agaricus* polysaccharides and to inform their development and application in biomedicine and nutraceuticals.

2. Effects the properties of *Agaricus* Polysaccharides

The intricate composition of carbohydrates and other macromolecules within mushrooms is subject to a variety of influences, including the specific *Agaricus* species, growth conditions—such as substrate type and

environmental parameters—and the developmental phase of the fungi. The choice of processing and extraction methods critically determines the concentration and bioactivity of these macromolecules[41]. It is noteworthy that distinct bioactive macromolecules can be isolated from both the fruiting bodies and the mycelia of the same mushroom species. Therefore, the cultivation and extraction techniques utilized for *Agaricus* species have a profound bearing on the functional attributes of their bioactive macromolecules. This underscores the necessity for meticulous selection and optimisation of these processes to ensure the maximization of the polysaccharides' therapeutic potential.

2.1 Cultivation Effects on Agaricus polysaccharides

The cultivation techniques employed for *Agaricus* species are paramount in shaping the profile and bioactivity of their functional constituents. A spectrum of factors, including substrate type, nutrient composition, pH levels, temperature, humidity, and light exposure, exert a significant influence on the biosynthesis and accumulation of bioactive compounds, such as polysaccharides, proteins, and secondary metabolites [42]. The cultivation conditions (such as the cultivation formula) are crucial factors influencing the structure and yield of polysaccharides, where specific environmental conditions may stimulate the production of antioxidants or immune-regulating compounds. Studies by Shu et al. have underscored the pivotal role of cultivation temperature in the biosynthesis and bioactivity of polysaccharides in *A. blaze*i. Polysaccharides derived from cultivation under low-temperature conditions have been found to possess higher β-glucan content and molecular weight, which correlates with enhanced biological activity. These polysaccharides have been shown to exert immunomodulatory effects by stimulating the release of TNF-α, thereby bolstering macrophage-mediated immune responses [43]. In a similar vein, the substrate utilized for cultivation is crucial in determining the functional quality of the harvested mushrooms. Wang et al. have demonstrated that the cultivation of *Agaricus* mushrooms on asparagus straw as the primary substrate, with various composts as supplements, results in significant variations in both the total dry weight of the fruiting bodies and their polysaccharide content [44].

In fact, the properties of *Agaricus* polysaccharides are not only influenced by the cultivation environment but also vary at different stages of cultivation. The profiles of bioactive compounds can exhibit substantial variation between different stages (such as mycelial and fruiting body), with certain metabolites being preferentially synthesised and accumulated at specific growth phases. For instance, Cardozo et al. extracted polysaccharides from both the mycelium (MI) and fruiting bodies (FR) of *A. brasiliensis* Wasser, and noted significant differences in their monosaccharide composition and structural characteristics. The polysaccharides from the mycelium were predominantly composed of glucose and mannose, while those from the fruiting bodies included glucose, mannose, and galactose. This indicates that the developmental stages not only influence the diversity of the polysaccharides but also their functional and structural properties [21]. These variations highlight the critical importance of selecting the appropriate developmental stage for harvesting, tailored to the desired functional components. This precision in timing is essential to ensure the optimal yield and efficacy of the bioactive compounds within the *Agaricus* species.

2.2 Extraction methods Effects on Agaricus polysaccharides

To accommodate the diverse nature of polysaccharides, a plethora of extraction methodologies has been devised. These varied techniques can result in substantial differences in the molecular weight, monosaccharide composition, and structural features of the isolated polysaccharides [45]. The conditions under which extraction is performed, including temperature, pH, solid-liquid ratio, and the type of solvent used, as well as supplementary extraction technologies such as enzymatic hydrolysis, ultrasound, and microwave treatment, have a significant bearing on the molecular architecture and physicochemical attributes of polysaccharides. These factors may induce hydrolysis of molecular chains and the cleavage of intermolecular hydrogen bonds, yielding polysaccharides with distinct physicochemical properties and biological activities [46]. As delineated in **Table 1**, a comprehensive list of extraction methods for *Agaricus* polysaccharides is provided.

2.2.1 Solvent extraction method

Solvent extraction is a widely utilized and traditional method for isolating polysaccharides [47], capitalizing on the ability to adjust the acidity, alkalinity, and polarity of the solvent to selectively extract specific compounds. Common solvent extraction techniques include hot water extraction, cold water extraction, acid extraction, and alkali extraction [48]. The selection of solvents and extraction conditions is primarily determined by the physicochemical properties of the target polysaccharides, which also influence the extraction yield, structural attributes, and biological activities. To date, solvent-based methods have been extensively used in the extraction of polysaccharides from various natural source [47, 49]. Many studies on *Agaricus* mushrooms have employed such approaches, Liu et al. used a 5% NaOH solution to extract a water-soluble polysaccharide (ABP-AW1) from *A. blazei* fruiting bodies[50]. In addition to alkali extraction, acid treatment is also an efficient method. Furthermore, the acid extraction process can alter the properties of the polysaccharides. In previous studies, Cardozo et al. demonstrated that the structural and functional attributes of sulfated polysaccharides differ from their non-sulfated counterparts, indicating that the extraction method can impact the final product [21]. Although acid and alkali treatments are effective in release polysaccharides [51, 52], they often leave residual salts and may cause partial degradation of the polysaccharides, further complicating purification and potentially diminishing the quality of the extracted compounds.

In addition to solvent-based extraction (acid or alkali), hot water extraction is another widely applied method for isolating polysaccharides from *Agaricus* mushrooms. By facilitating the separation of the cell wall at elevated temperatures, hot water extraction enables vacuolar contents to diffuse into the solvent [52, 53], and obtains some polysaccharides with relatively complete structure. Wang et al. isolated an acidic heteropolysaccharide from the fermentation broth using hot water extraction. The acidic polysaccharide was composed of (1→4)-β-D-galactan, (1→4)-α-D-galacturonic acid, (1→5)-α-L-arabinan, (1→2)-linked ribopyranose, (1→2)-linked rhamnopyranose, and terminal α-fucopyranose structures, with constituent

monosaccharides including arabinose, galactose, glucose, fucose, mannose, rhamnose, xylose, galacturonic acid, and glucuronic acid [54]. In addition to *A. blazei*, Kozarski and colleagues successfully extracted polysaccharides from the fruiting bodies of *A. bisporus* and *A. brasiliensi* using hot water extraction [55]. Further analysis revealed that these polysaccharides exhibited a certain degree of diversity in their monosaccharide composition. Moreover, Bei Wu and colleagues also utilized the hot water extraction method to isolate and purify a polysaccharide, ABP-1a, from the fruiting bodies of *A. blazei*. High-performance liquid chromatography analysis indicated that ABP-1a is a heteropolysaccharide primarily composed of glucose, mannose, galactose, and trace amounts of rhamnose [20]. These findings demonstrate that hot water extraction offers significant advantages in maintaining the structural integrity and extraction efficiency of polysaccharides, establishing it as a core technique for the study of polysaccharides from *Agaricus* mushrooms. However, hot water extraction presents limitations, such as extended extraction times, polysaccharide degradation at high temperatures, and impacts on efficiency and product quality [56].

2.2.2 Other extraction methods

While solvent-based methods, such as acid and alkali treatments, are widely used, their drawbacks——including increased purification complexity, polysaccharide degradation, and potential loss of biological activity——have spurred the development of alternative extraction techniques. To address these limitations, physical methods, including ultrasound- and microwave-assisted extraction, have gained considerable attention for their efficiency and ability to preserve functional properties.

2.2.2.1 Ultrasound-assisted extraction

To overcome these challenges, novel physical and enzymatic methods have emerged as promising alternatives. Ultrasound-assisted extraction (UAE) leverages high-frequency sound waves to disrupt cell walls and enhance solvent penetration, thereby significantly improving extraction yields [57, 58]. For instance, Tian et al. optimized UAE conditions for polysaccharides from *Agaricus bisporus* and demonstrated not only an increase in yield but also the antioxidant bioactivity of the extracted polysaccharides. This method avoids the use of extreme temperatures or harsh acid/alkali treatments, thereby reducing damage to the extracted compounds and preserving their functional properties [59].

2.2.2.2 Microwave-assisted extraction

Similarly, microwave-assisted extraction (MAE) utilizes electromagnetic radiation for rapid heating, promoting cell wall disruption and polysaccharide release. Zhang et al. demonstrated that optimizing MAE conditions for *A. blazei* significantly enhanced extraction efficiency, while the extracted polysaccharides (PMAE) exhibited notable antioxidant activity, highlighting their potential as functional foods and therapeutic agents [60]. Similarly, Zhang et al. employed microwave treatment to extract polysaccharides from *A. brasiliensis*, which are composed of glucose, mannose, and galactose and play a crucial role in immunomodulation[22]. Beyond physical methods, enzymatic hydrolysis represents another promising strategy.

2.2.2.3 Enzymatic-assisted technology

Enzymatic-assisted technology is undoubtedly an emerging technique in the field of polysaccharide extraction, gaining widespread attention for its advantages, including high extraction yield and low energy demand, high reproducibility in a shorter period of time, and simplified operation [61, 62]. Enzymes can degrade cell wall components under mild conditions, effectively preserving the biological activity of the polysaccharides, Li et al. used snail enzyme to treat *A. bisporus*, successfully obtaining three weakly acidic polysaccharides, which were shown to have significant antioxidant and anti-aging abilities, further validating the effectiveness of this method [27]. Furthermore, Jia et al. investigated the extraction effects of cellulase, pectinase, and papain on polysaccharides from *A. blazei*. By comparing the yield and activity of polysaccharides extracted using hot water, single enzymes, and enzyme combinations, they found that enzyme treatment with a combination of enzymes resulted in higher yields and stronger antioxidant activity. This suggests that enzymatic extraction is gentler than hot water extraction and more conducive to the efficient extraction of polysaccharides from *A. blazei* [63]. However, the high cost of enzymes and challenges in scaling enzymatic methods for industrial applications remain significant hurdles. The refinement of traditional extraction methods and the introduction of innovative techniques have significantly improved the efficiency and quality of polysaccharide extraction. At present, given the structural diversity of polysaccharides and the specific requirements of various applications, further development of efficient extraction methods will help optimize the structural modifications and functional properties of polysaccharides to meet the needs of different fields.

Table 1. Extraction Methods Based on *Agaricus* Polysaccharides

Extraction Method	Yield (%)	Principle	Advantages	Limitations	References
Hot Water	4.20-51.7	Heat generated by hot water treatment causes the separation of the plasma membrane of the cells.	Convenient, economical, simple operation.	Low efficiency, high temperature, polysaccharide degradation.	[20, 23, 24, 54, 64-69]
Alkali Treatment	4.31-11.93	In alkaline solution, cells and cell walls absorb water and expand or rupture, leading to the release of polysaccharides.	Low energy consumption, simple operation, high efficiency.	Impurities , introduced, high consumption.	[70-72]
Enzymatic Treatment	5.27-17.44	Enzymes break down the cell wall and membrane structure	Gentle reaction conditions, high efficiency.	Limited by enzyme activity and cost.	[27, 63, 73]
Ultrasound-Assisted	3.43-6.02	Ultrasonic cavitation and mechanical shear break the cell wall, releasing and dissolving nutrients inside the cells	Low temperature, simple operation, energy-saving.	Destruction of active components, reduced extract stability.	[56, 59]
Microwave-Assisted	7.18-12.35	Microwave heating increases the temperature and pressure inside cells, causing the cell wall to rupture.	Strong penetration, high selectivity, high heating efficiency.	Expensive equipment, microwave radiation.	[22, 60]

Ultra-High Pressure Extraction	-	Ultra-high pressure causes structural changes such as cell perforation, loosening, or rupture, allowing full contact between the effective cell components and solvents.	High efficiency, low temperature, simple operation.	Harsh reaction conditions, not suitable for industrialization.	[74]

3. Structure and Bioactivity of *Agaricus* Polysaccharides

The primary structure of polysaccharides is defined by the type of monosaccharide residues, their linkage positions, glycosidic bond configurations, and the sequence of the residues. These factors contribute to a high degree of structural variability, which enhances the potential of polysaccharides to carry and transmit biological information [75]. A series of extracts, structure and functions of *Agaricus* Polysaccharides are listed in **Table 1**. Specifically, *Agaricus* polysaccharides are notable for their structural complexity and biological functions [56]. These polysaccharides are composed of various monosaccharides such as glucose, galactose, mannose, and xylose, which are connected by different types of glycosidic bonds, including β-(1→3), β-(1→6), and α-(1→6) [76]. The structural diversity of these compounds is a key determinant of their biological activity, with several factors such as functional groups, molecular weight, and monosaccharide composition playing essential roles in modulating their bioactivity. Furthermore, molecular modifications can alter the structure of polysaccharides, thereby influencing their biological activity [46, 77, 78]. Several chemical modification methods have been developed to enhance or expand the biological properties of polysaccharides, including carboxymethylation [79]，sulfation [21, 24, 79-81], and acetylation[82, 83]. These modifications can improve or introduce new biological activities, broadening the potential applications of polysaccharides [77].

Table 2. Extraction, Structure, and Activity of *Agaricus* Polysaccharides

Source	component	Extraction	Mw	Monosaccharide composition	Biological activity	Ref
A. blazei	Fruiting bodies	Aqueous ammonium oxalate and sodium hydroxide,	1-5×10^4 Da	Glc: Xyl: Man: Gal =100:4:1:5	Antitumor	[83]
A. blazei	Fruiting bodies	Hot water extraction	5×10^4 Da	Glc, Gal, Man, Xyl, Fuc	Antitumor	[84]
A. blazei	Fruiting bodies	Hot water extraction	2×10^6 Da	Glc, Gal, Man, Xyl, Fuc	Antitumor	[84]
A. blazei	Fruiting bodies	Hot water extraction		Glc, Gal, Man, Xyl, Ara, Fuc, Rib	Antitumor	[84]
A. blazei	Fruiting bodies	Hot water extraction	5×10^4 Da	Glc, Gal, Man, Rib	Antitumor	[84]
A. blazei		Water extracted； Precipitation with ethanol				[85]
A. blazei	Mycelia	Supercritical fluid carbon dioxide extraction	757 kDa		Antioxidant	[72]
A. blazei	Mycelia	Supercritical fluid carbon dioxide extraction	887 kDa		Antioxidant	[72]
A. blazei	Mycelia	Supercritical fluid carbon dioxide extraction	1,318 kDa		Antioxidant	[72]
A. blazei	Mycelia	Supercritical fluid carbon dioxide extraction	631 kDa		Antioxidant	[72]
A. blazei	Mycelia	Supercritical fluid carbon dioxide extraction	1, 226 kDa		Antioxidant	[72]
A. blazei	Fruiting bodies	EtOH extraction	48 kDa		Antitumor	[86]
A. blazei		Water extraction	48 kDa		Antitumor, Immunostimulatory	[87-89]
A. brasiliensis		Extracted with 4:1 (v/v) chloroform–methanol	19.4×10^3g/mol	Fuc: Gal = 86.1: 13.9	Antinociceptive	[28]
A. bisporus var. hortensis		Extracted with 4:1 (v/v) chloroform–methanol	31.1×10^3g/mol	Fuc, Gal, 3-O-methyl-Gal	Anti-inflammatory, Antinociceptive	[28]
A. blazei		Repeated extraction with hot water, cold NaOH, and then hot NaOH		Glc: Man: Ara= 93.87: 3.54: 2.25	Promote burn wound healing	[19]
A. brasiliensis		Hot water extraction		Glc: Ara: Man= 78.38: 10.46:8.51	Anti-cardiovascular	[90]
A. brasiliensis	Mycelia	Hot water extraction	86 kDa		Antiherpetic	[91]
A. bisporus	Fruiting body	Hot water extraction and precipitation with ethanol	2.9×10^4g/mol		Immunomodulatory	[64]

A. brasiliensis	Fruiting body	Hot water extraction and precipitation with ethanol	4.5×10^4g/mol		Immunomodulatory	[64]
A. bisporus	Fruiting body	Hot water extraction		Glc: Gal: Xyl= 96.3: 2.9: 0.8	Immunomodulatory, Antioxidant	[55]
A. brasiliensis	Fruiting body	Hot water extraction		Glc: Gal: Man/Xyl: Fuc: Rha: Ara: GlcN: Fruc= 57.5:27.7:7.3: 1.2: 1.2: 0.9: 0.7	Immunomodulatory, Antioxidant	[55]
A. blazei	Fruiting bodies	Alkaline extraction	50 kDa	Gal: Glc: Fuc: Ara: Man= 29: 20: 6: 2: 2	Antitumor	[50]
A. blazei	Fruiting bodies	Ethanol and water extraction	390 kDa	D-Gal: D-Glc= 1:2		[92]
A. blazei	Fruiting bodies	Microwave-assisted extraction, Heat reflux extraction, Ultrasonic extraction, maceration extraction			Antioxidant	[60]
A. bisporus	Fruiting body	Hot water	2,000 kDa	Rib: Rha: Fuc: Xyl: Man: Fructose: Glc=2.86:4.24:1.85:25.53:39.21:12.84:13.47	Antitumor	[93]
A. bisporus	Fruiting body	Hot water	40-70 kDa	Rha: Fuc: Xyl: Man: Fructose: Glu= 2.16:5.13:8.45:18.61:24.43:41.23	Antitumor	[93]
A. bisporus				Rib: Fuc: Xyl: Gal: Man: Fructose: Glc=4.06:2.40:4.27:5.64:25.49:45.67:12.46		[93]
A. bisporus	Fruiting body	Ultrasonic assisted extraction	158 kDa	D-glucose	Antioxidant	[59]
A. blazei	Fruiting bodies	95%EtOH defatted and water extraction	420 kDa	Glu: Man: Gal=1:1:1, and a trace of Rha	Antitumor	[20]
A. bisporus	Fruiting bodies	Water extraction	43.8×10^4 g mol^{-1}	Fuc: Gal:3-*O*-methyl-Gal= 6:84:10	Antiinflammatory	[94]
A. brasiliensis	Fruiting body	Hot water extraction, precipitation with ethanol	609 kDa	Glu: Man: Gal= 63.67 ± 4.08:1.76 ± 0.13:4.55 ± 1.44		[21]
A. brasiliensis	Mycelium	Hot water extraction, precipitation with ethanol	310 kDa	Glc: Man= 19.35 ± 3.12: 58.65 ± 2.74		[21]
A. brasiliensis		Hot water extraction, precipitation with ethanol	127 kDa	Glc: Man: Gal= 68.98 ± 1.26: 1.16 ± 0.34: 2.86 ± 1.31	Antitumor	[21]
A. brasiliensis		Hot water extraction, precipitation with ethanol	86 kDa	Glc: Man= 24.72 ± 4.12: 55.28 ± 3.12	Antitumor	[21]
A. bisporus	Fruiting body	Successive cold and hot aqueous extraction	2.9×10^4 g/mol	Glc	Cytotoxic	[95]
A. bisporus	Fruiting body	Hot water extraction	2.9×10^4 g/mol	Man, Gal, Glc	Immunostimulatory	[96]
A. brasiliensis	Fruiting body	Hot water extraction	4.5×10^4 g/mol	Man, Gal, Glc	Immunostimulatory	[96]

A. bisporus	Fruiting bodies	Aqueous extraction	3.71×10^5 g/mol	Fuc: Gal: 3-*O*-methyl-Gal= 11.2: 74.2: 14.6	Anti-sepsis, Anti-inflammatory	[97]
A. brasiliensis					Antiviral	[79]
A. bisporus	Fruiting body	Hot water extraction	51.7 kDa	Glc: Man: Gal: Xyl= 2.25:2.00:0.35:0.20		[69]
A. bisporus	Mycelia	Ultrasound-assisted extraction				[98]
A. brasiliensis		Hot water extraction				[99]
A. blazei		Freeze drying; hot water extraction			Antioxidant	[68]
A. blazei		Vacuum drying; Hot water extraction			Antioxidant	[68]
A. blazei		Air drying; Hot water extraction			Antioxidant	[68]
A. bisporus		Enzyme-Assisted Extraction		Glc: Gal: Xyl: Man: Fuc= 58.81: 14.49: 10.82: 13.3: 2.58	Antioxidant, Immune response, pro-anti-inflammatory	[73]
A. bisporus		Enzyme-Assisted Extraction		Glc: Gal: Xyl: Man= 61.05: 16.17: 10.36: 12.42	Antioxidant	[73]
A. bisporus	Fruiting body	Aqueous extraction	1.28×10^4g/mol	Fuc: Gal: 3-*O*-Me-Gal= 9.58:75.85:14.56%	Anticoagulant	[24]
A. brasiliensis	Mycelia, Culture medium	Hot water extraction	351-375 kDa	Rha and Man	Antioxidant Antiaging	[23]
A. brasiliensis	Mycelia, culture medium	hot water extraction	(50-198)kDa	Rha and Man	Antioxidant activity	[23]
A. brasiliensis	Mycelia, culture medium	hot water extraction	(21-81) kDa	Rha: Rib: Man= 3.69:1:1.03	Antioxidant activity	[23]
A. brasiliensis	Mycelia, culture medium	hot water extraction	(129-159) kDa	Rha: Myoinositol: Man: Glu= 1.3:1.1:1:2	Antioxidant activity	[23]
A. brasiliensis	Mycelia, culture medium	hot water extraction	(216-270) kDa	Rha: Man: Glu: Gal = 10.5:1.2:1.9:1	Antioxidant activity	[23]
A. brasiliensis	Mycelia, culture medium	hot water extraction	(150-188)kDa	Rha: Man = 1.4:1	Antioxidant activity	[23]

A. bisporus	Fruiting body	Alkaline extraction	34.7 kDa	Fuc: Rib: Xyl: Man: Gal: Glu = 12.96:0.58:1.16:2.2:28.82:54.28	Antioxidant, antiaging, hepatoprotective	[70]
A. bisporus	Fruiting body	Alkaline extraction	53.2 kDa	Fuc: Rib: Xyl: Man: Gal: Glc = 16.5: 1 :7.9: 10.5: 57: 45.1	Antioxidant, antiaging, hepatoprotective	[70]
A. bisporus	Fruiting body	Alkaline extraction	25.3 kDa	Fuc: Rib: Xyl: Man: Gal: Glc= 3.3: 1.1: 1: 16.6: 9.9: 14.3	Antioxidant, antiaging, hepatoprotective	[70]
A. bisporus	Fruiting body	Alkaline extraction	79.6 kDa	Rib: Man: Gal: Glc = 1: 1.7: 8.5: 24.3	Antioxidant, antiaging, hepatoprotective	[70]
A. bisporus	Fruiting bodies	Successive aqueous and alkaline extraction	1.8×10^4 g/mol	Man: Gal: Glc = 27.3:24.4:48.3	Antitumor against HepG2	[25]
A. blazei	Fruiting bodies	High-speed shearing homogenization extraction	7,340 kDa	Glc		[74]
A. brasiliensis		microwave extraction	1,150 kDa	Glc: Man: Gal = 99.2:0.2:0.6	potent stimulator of macrophage proliferation and activation	[22]
A. bisporus	Fruiting body	Enzyme assisted extraction		Rha: Fuc: Xyl: Man: Gal: Glc = 1:3.6:2.8:55.3:9:10.2	Antioxidant, Anti-aging activities	[27]
A. bisporus	Fruiting body	Enzyme assisted extraction		Rha: Fuc: Xyl: Man: Gal: Glc = 1:1.6:1.1:1.4:4:6.7	Antioxidant, Anti-aging activities	[27]
A. bisporus	Fruiting body	Enzyme assisted extraction		Rha: Fuc: Xyl: Man: Gal: Glc = 1:7.2:2.8:30.9:29.4:12.7	Antioxidant, Antiaging activities	[27]
A. bisporus	Fruiting body	Enzyme assisted extraction		Xyl: Man: Gal: Glc = 1:5.4:2.5:10.7	Antioxidant, Anti-aging activities	[27]
A. bisporus	Fruiting body	Acidic extraction		Fuc: Rha: Xyl: Gal: Glc: Man= 1.9:1.1:1:15.9:34.6:18	Antioxidant activity, anti-aging, Hepatoprotective	[35]
A. bisporus	Fruiting body	Acidic extraction		Rha: Glc: Xyl: Man: Fuc: Gal= 1:37.5:1.9:13.6:1.6:15.9	Antioxidant activity, anti-aging, Hepatoprotective	[35]
A. bisporus	Fruiting body	Acidic extraction		Rha: Glu: Man: Fuc: Xyl: Gal= 3.2:37.1:3.6:5.3:1:12.3	Antioxidant activity, anti-aging, Hepatoprotective	[35]

A. bisporus	Fruiting body	Acidic extraction		Glc: Man: Fuc: Xyl: Gal= 10.4:5.2:1.9:1:2.4	Antioxidant activity, anti-aging, Hepatoprotective	[35]
A. bisporus	Fruiting body	Hot water extraction		Glc: Man: Gal: Fuc: Ara: Glucuronic =70.3:8.7;12.88:0.79:5.04:1.57	Hepatoprotective	[67]
A. blazei	Sub-merged fermentation	Hot water extraction	350 kDa	Fuc: Ara: Xyl= 6.4:15.5:14.7, and less amount of Rha, Glc, and Man		[54]
A. bitorquis	Fruiting bodies	Hot water extraction			Anti-hypoxic activity	[66]
A. bitorquis	Fermentation medium	Hot water extraction			Anti-hypoxic activity	[66]
A. bitorquis	Fermentation medium	Hot water extraction			Antioxidant activities, anti-hypoxic activity	[66]
A. bitorquis	Fruiting bodies	Hot water extraction	30.4 kDa	Man: Rha: Glc: Gal =1.3:0.2:4.8:0.8	Antioxidant	[66]
A. bitorquis	Fruiting bodies	Hot water extraction	9.7 kDa	Man: Rha: Glu: Gal = 1.5:0.4:60.2:1.0	Antioxidant	[66]
A. bitorquis	Fruiting bodies	Hot water extraction	3.1 kDa	Man: Glu: Gal= 0.1:5.2:0.1	Antioxidant	[66]
A. blazei	Fruiting bodies	Water extraction		Glc: Gal: Man: Glc: Fuc= 79.1:12.4: 4.5: 2.7: 1.3	Lipid-lowering activity	[16]
A. blazei	Fruiting bodies	Water extraction	10 kDa	Glc: GlcA: Gal: Xyl: Fuc= 95.1:3.7:0.9:0.2:0.1	Lipid-lowering activity	[16]
A. blazei	Fruiting bodies	Water extraction	360 kDa	Glc: Gal: GlcA: Fuc= 69.2:24.3:4.3:2.2		[16]
A. bisporus		Hot-water extraction	784 kDa	Rib: Rha: Ara: Xyl: Man: Glc: Gal= 2.08:4.61:2.45:22.25:36.45:89.22:1.55	Immunobiological activity	[65]

Glc: Glucose, Xyl: Xylose, Man: Mannose, Gal: Galactose, Fuc: Fucose, Ara: Arabinose, Rib: Ribose, Rha: Rhamnose, GluN: Glucosamine, GluA: Gluconic acid, 3-*O*-methyl-Gal: 3-*O*-methyl-Galactose, GlcUA: Glucuronic acid, GalA: Galacturonic acid

3.1 Antitumor Activity

Polysaccharides extracted from the *Agaricus* genus have demonstrated significant antitumor activities, which have been extensively investigated through both in vitro and *in vivo* studies. The potential antitumor mechanisms of *Agaricus* polysaccharides are highly similar to those of currently studied polysaccharides[100] (**Figure 1**). In the figure 1, we present the antitumor molecular mechanisms of these polysaccharides. These polysaccharides exert their antitumor effects via multiple pathways, including the modulation of tumor suppressor gene expression and the enhancement of antioxidant properties, which further amplify their therapeutic potential. Specifically, these polysaccharides combat cancer cell invasion by stimulating the host immune system through various mechanisms. First, they activate several types of effector immune cells, including macrophages, T lymphocytes, B lymphocytes, cytotoxic T lymphocytes (CTLs), and natural killer (NK) cells. In turn, these activated immune cells promote the secretion of key cytokines such as tumor necrosis factor-α (TNF-α), interferon-γ (IFN-γ), and interleukin-1β (IL-1β), which play critical roles in the antitumor response [75]. These cytokines not only inhibit tumor cell proliferation but also induce apoptosis and promote the differentiation of tumor cells, weakening tumor growth. In addition, polysaccharides stimulate the release of reactive nitrogen and oxygen intermediates, as well as other immune-regulating molecules, further enhancing the antitumor immune response.

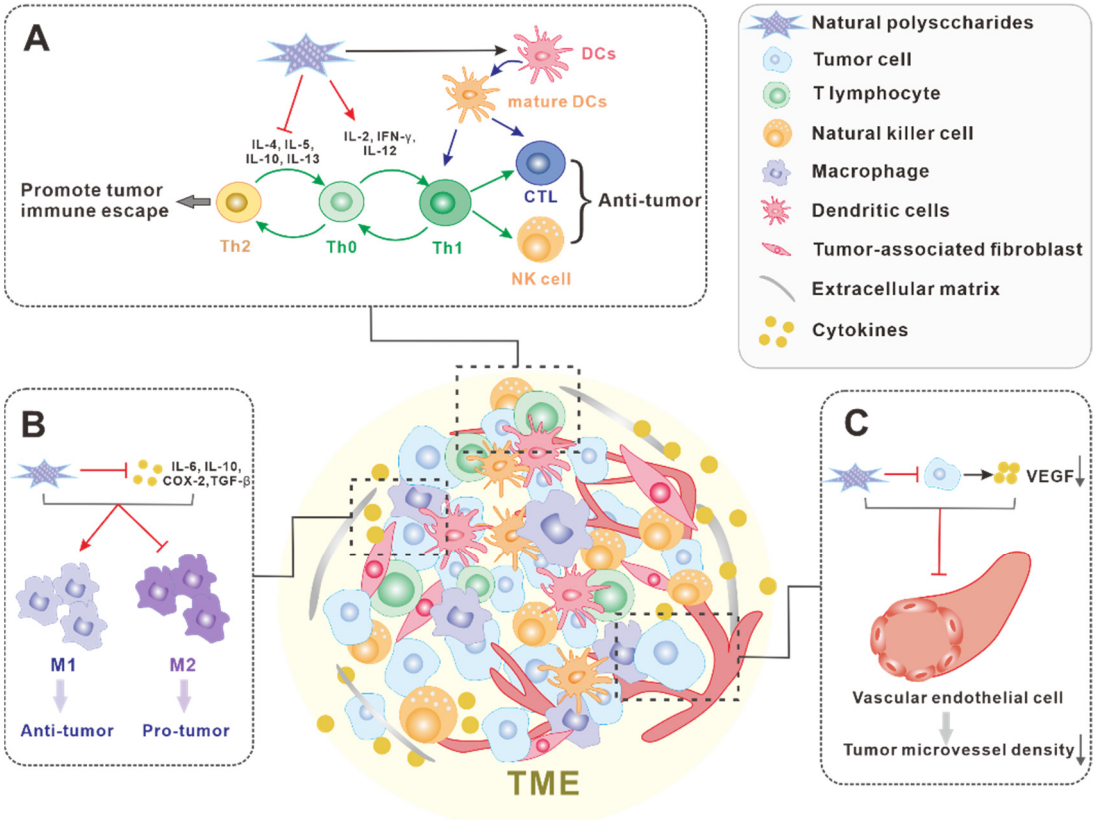

Figure 1. Anti-tumor mechanism of natural polysaccharides. Polysaccharides not only induce apoptosis by directly acting on tumor cells, but also inhibit the occurrence; (A) indicates that natural polysaccharides promote the expression of cytokines such as IL-2, IFN-γ and IL-12, inhibit the expression of cytokines such as IL-4, IL-5, IL-10 and IL-13, resulting in promoting the differentiation of Th0 cells into Th1 cells, which have anti-tumor effect. What's more, natural polysaccharides activate DC cells, allowing them to function normally in antigen presentation;(B) indicates that polysaccharide reduces the concentration of cytokines such as IL-6, IL-10, COX-2 and TGF-β in TME, so as to promote the differentiation of M1 macrophages, which play an anti-tumor role; (C) indicates that polysaccharides down regulate the expression of VEGF and so inhibit tumor related angiogenesis.

The anti-tumor effects of some *Agaricus* Polysaccharides were analyzed in **Table 3**. For example, Niu et al. isolated a low-molecular-weight antitumor polysaccharide (LMPAB) from *A. blazei Murill*, which exhibits significant immune-stimulating activity. Studies have shown that its antitumor effect is closely related to the activation of NK cells and the expression of INF-γ [101]. These multi-level mechanisms demonstrate the powerful antitumor potential of polysaccharides derived from the *Agaricus* genus.

Table 3. Anti-Tumor Effects and Mechanisms of *Agaricus* Polysaccharides

Source	Experimental model	Principle	Reference
A. blazei	mouse sarcoma 180	Enhanced the splenic NK cell activity, splenocyte proliferation, indexes of spleen and thymus, and antitumor cytokines production in tumor-bearing mice.	[33, 89]
A.. bisporus	HepG2 cells	Through promoted an increase of cytochrome c release and a decrease of ATP content to promote cell death by apoptosis by the mitochondrial death pathway.	[25, 95]
A. brasiliensis	A549 cells	cytotoxic activity	[21]
A. blazei	HT-29 cells	Through the metastasizing capacity of cancer cells through interfering with the interaction between E-selectin and sLe^x.	[86]
A. blazei	HOS cells	The could induce apoptosis of HOS cells and inhibit the DNA inhibition synthesis by blockading the tritium uptake in HOS cells.	[20]
A. bisporus	Sarcoma 180 cells	Inhibits the growth of tumor cells by enhancing the immune response	[93]

Antitumor polysaccharides exhibit significant diversity in their chemical structures and physical properties. Specifically, the polysaccharide ABP-W1 derived from *A. blazei* Murill adopts a triple-helical conformation in aqueous solution. Polysaccharides with triple-helical structures generally demonstrate stronger anticancer activities compared to those in random coil or linear conformations [75, 92]. Dong et al. isolated and purified a polysaccharide, WAAP-2 (121 kDa), with a triple-helix structure from *A. bisporus*. This polysaccharide is composed of mannitol, glucose, and galactose, with its backbone rich in β-D-(1,6)-glucose and β-D-(1,3,6)-glucose. The antitumor activity of WAAP-2 is associated with its monosaccharide composition, the abundance of β-D-glucose, and its spatial conformation [102]. Furthermore, β-glucans can enhance phagocytosis and trigger the expression of cytokines such as TNF-α and various interleukins, thereby exerting immunomodulatory effects [103]. β-glucans from *A. blazei*, characterized by β-(1→3) and β-(1→6) linkages, have been reported to act as immune enhancers against cancer cells [104]. For instance, Liu et al. extracted a low molecular weight polysaccharide (LMW-ABP) from the fruiting bodies of *A. blazei*, primarily composed of a (1→3)-linked β-d-glucan backbone. This polysaccharide was found to suppress FucT-VII mRNA expression on the surface of HT-29 cells, functioning as an immunoenhancer [86]. Pires et al. have confirmed that the mannan-galactan polysaccharide (RK2-Ab) extracted from *A. bisporus* can reduce the cell viability of HepG2 cells, indicating that RK2-Ab may have the potential to inhibit the proliferation of liver cancer cells [25].

Polysaccharides with varying structures exhibit distinct molecular weights (MW), which are closely associated with their antitumor activities. Studies have demonstrated that polysaccharides with molecular weights ranging from 10 to 1000 kDa generally exhibit optimal immunoactivity in numerous investigations.

Polysaccharides with MW <10 kDa often fail to maintain proper chain conformations, which is critical for exhibiting effective biological activity [105]. Currently, low molecular weight (LMW) polysaccharides from *Agaricus* species appear to dominate in terms of antitumor efficacy [17, 106, 107]. Niu et al. conducted extensive studies on melanoma and sarcoma mouse models, which showed that LMW polysaccharides from *A. blazei* can reduce lung metastasis in melanoma and inhibit the growth and metastasis of sarcoma[17, 107]. The mechanism underlying the reduction in tumor growth is primarily through anti-angiogenic effects [107], while the regulation of anti-metastatic activity is mediated by matrix metalloproteinase-9 and the metastasis suppressor factor nm23-H1[17]. These structurally diverse polysaccharides exert different functions *in vivo*, and their antitumor efficacy can be influenced by factors such as molecular weight, conformation, and monosaccharide composition. Further research is needed to fully understand how these polysaccharides interact with various molecular targets to enhance their antitumor potential.

3.2 Antioxidant Activity and Anti-Aging Ability

The antioxidant capacity of polysaccharides is closely related to their structural characteristics, with active sites playing a decisive role in their function. **Figure 2** illustrates some potential mechanisms of the antioxidant and anti-aging effects of *Agaricus* polysaccharides, which is similar to most polysaccharides [108, 109]. The antioxidant effects of *Agaricus* polysaccharides are primarily mediated through various mechanisms, including free radical scavenging, metal ion chelation, and antioxidant enzyme activation [27, 35, 66].

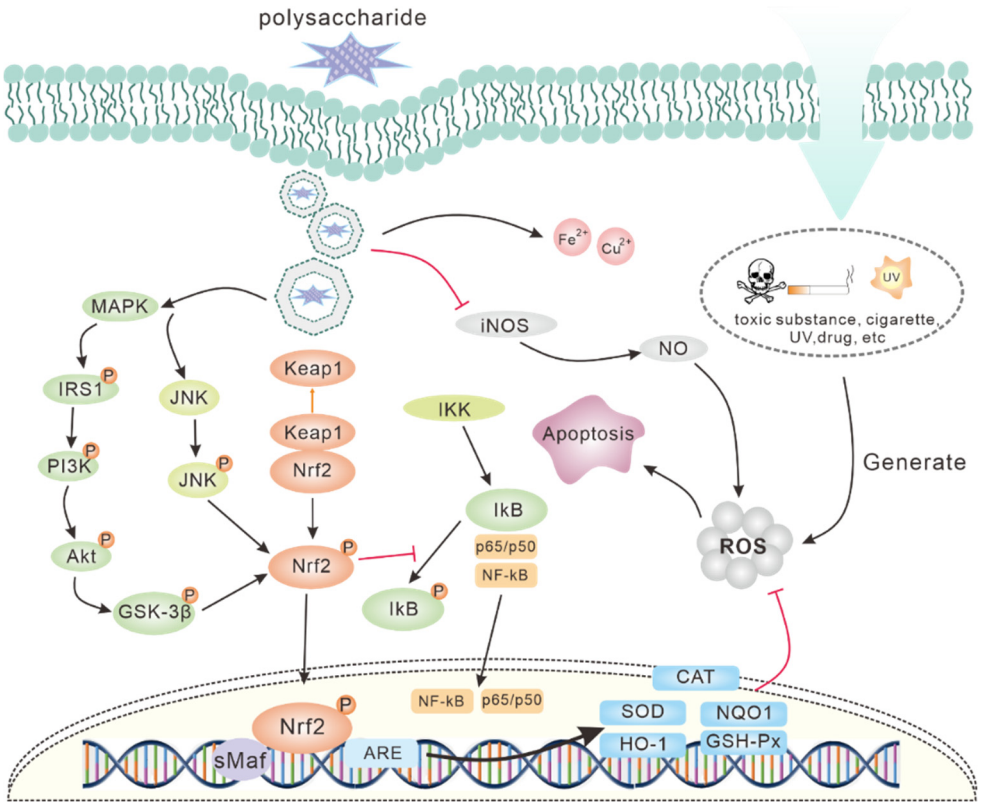

Figure 2. Potential regulatory mechanisms of the Antioxidant and Anti-Aging activities of *Agaricus* polysaccharides.

The antioxidant activity of polysaccharides can directly initiate anti-aging effects *in vivo*. Firstly, these polysaccharides can directly scavenge free radicals, thereby reducing oxidative damage [27, 35]. For instance, five polysaccharide components extracted from *A. blazei* mycelium demonstrated significant free radical scavenging ability at specific concentrations, exhibiting strong antioxidant activity. Moreover, these polysaccharides can also bind to metal ions (such as Fe^{2+}), reducing metal-catalyzed free radical generation and further inhibiting oxidative damage. Li et al. extracted polysaccharides (EnAPS), which demonstrated significant antioxidant effects, particularly in the d-Gal-induced aging mouse model. These antioxidant effects were primarily achieved through the scavenging of free radicals, metal ion chelation, and reducing oxidative stress, mechanisms closely associated with aging [27]. Interesting, the free radical scavenging ability of polysaccharides is proportional to their structure (eg. molecular weight) [72], a characteristic possibly influenced by the extraction method. For example, polysaccharides extracted using microwave heating exhibited stronger antioxidant properties compared to those obtained through traditional methods, likely due to their higher solubility and structural modifications [60].

Moreover, *Agaricus* polysaccharides can activate the body's antioxidant enzyme systems, enhancing cellular antioxidant defenses. Harikrishnan et al. demonstrated that *A. bisporus* polysaccharides (ABPs) could enhance the antioxidant capacity in fish by regulating the expression of antioxidant enzyme genes [110]. Furthermore, some *Agaricus* polysaccharides protect cells by inhibiting oxidative stress. For example, Kuang et al. isolated intracellular polysaccharides from *A. bitorquis* (ABSC) and found that IPS-III displayed strong antioxidant activity in HepG2 cells, protecting them from H_2O_2-induced cytotoxicity. This protection was achieved by scavenging excess ROS and inhibiting the depletion of SOD, CAT, and GSH, thereby reducing lipid peroxidation [66].

Actually, the antioxidant effects of *Agaricus* polysaccharides can exert deeper biological effects *in vivo*. These polysaccharides alleviate oxidative stress-induced damage to liver cells by inhibiting the activation of the TGF-β1 and Smad3 signaling pathways, while simultaneously enhancing the activity of antioxidant enzymes such as GSH and SOD [67]. Similarly, researchers induced aging in mice by injecting D-galactose, which resulted in a significant decrease in the activities of SOD, GSH-Px, CAT, and T-AOC, as well as a significant increase in the levels of MDA and LPO. Interestingly, treatment with *Agaricus* polysaccharides significantly improved the activity of antioxidant enzymes and reduced lipid peroxide content, suggesting that the extracted and purified *Agaricus* polysaccharides can alleviate and improve aging characteristics by scavenging excess free radicals or promoting antioxidant enzyme activity [70].

The antioxidative effects of *Agaricus* polysaccharides were closely related to its anti-aging mechanism. This is because free radicals are generated during normal physiological processes, particularly from the mitochondrial electron transport chain. The body also has a free radical scavenging system to maintain balance [111, 112]. However, with aging, it becomes increasingly difficult to maintain this balance, leading to the excessive accumulation of free radicals. These excess free radicals can easily convert unsaturated fatty acids in biological membranes into lipid peroxides. Additionally, since mitochondria provide energy to cells

and regulate the cell cycle, the excess free radicals cause severe damage to mitochondria, further accelerating the aging process [113]. As previously discussed, *Agaricus* polysaccharides, through their antioxidant mechanisms, can play a key role in mitigating oxidative stress and preventing age-related cellular damage, thus contributing to anti-aging effects. *Agaricus* polysaccharides exhibit their potential for antioxidant defense and cellular protection through multiple mechanisms. These findings highlight their broad application prospects in health management and disease prevention.

3.3 Other Functional Applications

In addition to well-known biological activities such as anti-tumor, antioxidant, and anti-aging effects, the unique sugar chain structures and functional groups of *Agaricus* polysaccharides can modulate various biological signaling pathways, thereby exhibiting a broad range of biological functions.

Among these, the lipid-lowering effects of fungal polysaccharides have attracted increasing attention as an emerging research focus. Recent studies have demonstrated that glucans, mannans, and heteropolysaccharides, play a pivotal role in reducing blood lipid levels [16]. Li et al. extracted polysaccharides from the fruiting body of *A. blazei* and demonstrated their lipid-lowering ability. However, their study mainly focused on the relationship between the lipid-lowering activity of the polysaccharides and the regulation of gut microbiota, without in-depth analysis of the specific structural mechanisms of action [114]. In the same year, Li et al. also isolated a polysaccharide mainly composed of Glc dextran from *A. blazei*, which significantly reduced total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C) levels while increasing high-density lipoprotein cholesterol (HDL-C) levels. This effect was closely linked to the polysaccharide's structural characteristics, particularly its affinity with lipid metabolism receptors [16].

The structural modifications of *Agaricus* polysaccharides further demonstrate the critical impact of molecular structure on their bioactivity. For example, sulfate-modified *Agaricus* polysaccharides exhibit significant antiviral activity, highlighting the critical role of polysaccharide structure in its bioactivity. The sulfate-modified polysaccharides may exhibit enhanced antiviral abilities, likely through inhibition of viral enzyme expression and replication [115]. Zhao et al. improved the anti-HIV activity of *A. blazei* polysaccharides through sulfate modification [116]. Furthermore, Cardozo confirmed the inhibitory effect of the sulfate-modified polysaccharides on herpes simplex virus [91]. Comparative studies by Yamamoto et al. revealed that sulfate-modified polysaccharides with higher β-glucan content were particularly effective in inhibiting herpesvirus replication, highlighting the essential role of structural modifications in enhancing antiviral properties [79]. Specifically, sulfate modification enhanced the bioactivity of *Agaricus* polysaccharides, demonstrating that antiviral effects are strongly associated with molecular structure modifications.

Despite these advances, most current studies are confined to in vitro experiments and animal models, the underlying mechanisms governing these effects and their safety profiles in humans remain inadequately understood. Future research should focus on elucidating the molecular mechanisms underlying

structure-function relationships, as well as assessing the clinical feasibility of these modifications. These foundational studies provide a promising basis for the functional development and application of *Agaricus* polysaccharides in health-related fields.

4. Future outlook

The exploration of extraction methodologies and biological activities of *Agaricus* polysaccharides will persist as a pivotal research avenue. While a variety of extraction techniques, such as hot water extraction, alkali treatment, ultrasonic-assisted extraction, microwave-assisted extraction, and enzymatic extraction, are currently at our disposal and are effective in obtaining *Agaricus* polysaccharides while preserving their biological activity. Actually, traditional extraction methods have their limitations in modulating the structure-function relationship of these polysaccharides. Therefore, *Agaricus* polysaccharides could be modified through genetic modification of fungi and post-treatment of polysaccharides to obtain more excellent performance of polysaccharides.

Recent advances in genetic and molecular biology techniques have enabled more precise control over the polysaccharide synthesis pathway, thereby altering their structure and, consequently, their functional properties. For instance, modulating the expression of enzyme genes involved in polysaccharide synthesis can control the structural characteristics of the polysaccharides, which in turn affects their biological activities such as antioxidant and immune-modulatory functions. Enhancing or suppressing the expression of genes encoding glycosyltransferases, glycogen synthases, and polymerases can fine-tune polysaccharide structure and function at the molecular level [117]. The biosynthetic regulation of mushroom polysaccharides must rely on their genomic information, and the genomes of several *Agaricu*s species have been revealed [118, 119]. Beyond genetic regulation, chemical modification offers an effective means to alter the structure-function relationship of polysaccharides. Phosphorylation, acetylation, and sulfation are chemical modifications that can enhance polysaccharide bioactivity [120]. These chemical modifications introduce functional groups, including sulfate, phosphate, carboxymethyl, inorganic selenium, methyl, and acetyl groups, into the polysaccharide chains. Such alterations not only modify the chain structure but also influence the tertiary conformation, thereby affecting biological activities [121]. For instance, the incorporation of sulfate groups can enhance immune responses by facilitating interactions with immune cell receptors through oxygen binding and electrostatic attraction, ultimately inhibiting tumour cell proliferation [120]. However, it is important to note that structural modifications can also occur during polysaccharide extraction, particularly when solvents such as acids or bases are used. These unintended alterations may impact polysaccharide functionality. Optimising extraction conditions to harness these structural changes could potentially reduce additional modification steps, thus improving operational efficiency. Building on the potential for multiple functional modifications, polysaccharides can also be tailored to optimize their properties. Their inherent biocompatibility and water solubility make them ideal candidates for modification as drug delivery carriers, enabling the integration of specific functionalities to enhance therapeutic efficacy [122, 123]. For example,

Zhang et al. introduced hydrophobic groups to *Angelica* polysaccharides, forming amphiphilic conjugates that self-assembled into nanoparticles for targeted drug delivery. This modification not only altered the physicochemical properties of the polysaccharides but also enhanced their drug delivery performance [124]. Similarly, *Agaricus* polysaccharides exhibit diverse bioactivities, such as antitumor and antiviral effects, making them promising candidates for drug delivery and other advanced applications. Beyond this, polysaccharide-based composites have shown potential in various fields, including gene carriers, immunomodulators, and conductive neural repair materials. These materials have broad applications in drug delivery, tissue engineering, and immunotherapy. Furthermore, combining *Agaricus* polysaccharides with antimicrobial peptides or metal oxides can significantly enhance their functionality, leading to the development of novel materials with substantial potential for medical applications. Such structural modifications or the preparation of composite materials directly influence the functional properties of polysaccharides, driving innovative advancements in *Agaricus*-based polysaccharide materials and opening up broad prospects for their diverse applications in the biomedical field [125]. By optimizing extraction, modification, and structural design technologies, the use of *Agaricus* polysaccharides in medicine, food, and other industries can be significantly expanded, accelerating their industrialization.

Many fungal polysaccharides currently exhibit active functions, and with deeper research into *Agaricus* polysaccharides, it has been found that the structural diversity and multifunctional potential of these polysaccharides make them stand out in various fields. Recent studies suggest that *Agaricus* polysaccharides can regulate the composition and activity of the gut microbiota, promoting the growth of beneficial bacteria such as Bifidobacterium and Lactobacillus, while inhibiting the proliferation of pathogenic bacteria. This dual function not only helps improve gut health but also brings systemic benefits, such as enhancing immune function and metabolic regulation, by maintaining microbiota balance. In addition, *Agaricus* polysaccharides exhibit significant anti-inflammatory properties by inhibiting the secretion of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1*β*[110]. These mechanisms make *Agaricus* polysaccharides potentially valuable in the treatment of inflammatory diseases. In the field of neuroprotection, *Agaricus* polysaccharides show great application potential[126]. For example, their antioxidant properties help scavenge free radicals, thereby preventing oxidative damage to neural cells.

In summary, while substantial progress has been made in the study of *Agaricus* polysaccharides, the mechanisms underlying their bioactivity remain incompletely understood. The primary challenges lie in elucidating the structure-function relationships, understanding their *in vivo* metabolic processes, and addressing the activity differences among polysaccharides from various sources. Current literature mainly focuses on isolated biological functions, with limited comprehensive reviews on their overall bioactivity. Additionally, enhancing bioactivity through structural modification remains an important research avenue. Future studies will likely explore novel functional possibilities and conduct deeper analyses of existing structures. The research prospects for *Agaricus* polysaccharides are vast, with future efforts focused on

developing more efficient, environmentally friendly, and biologically active polysaccharide formulations to overcome current technical challenges and promote broader applications in diverse industries.

Conflicts of interest

The authors have no conflict of interest to declare.

Acknowledgements

This work was funded by financial support from Key R&D Projects in Shaanxi Province of China (No. 2023-YBSF-164), Key Core Technology Research and Development in Shaanxi Province Agriculture (No. 2024NYGG010) and the National Key Research and Development Program (No. 2021YFD1600401).

Reference

[1.] Benalaya, I, Alves, G, Lopes, J, et al. A Review of Natural Polysaccharides: Sources, Characteristics, Properties, Food, and Pharmaceutical Applications. Int J Mol Sci. 2024;25(2).doi.org/10.3390/ijms25021322

[2.] Lu, X, Fei, L, Li, Y, et al. Effect of different plant growth regulators on callus and adventitious shoots induction, polysaccharides accumulation and antioxidant activity of Rhodiola dumulosa. Chinese Herbal Medicines. 2023;15(2):271-7.doi.org/10.1016/j.chmed.2022.07.005

[3.] Gong, H, Li, W, Sun, J, et al. A review on plant polysaccharide based on drug delivery system for construction and application, with emphasis on traditional Chinese medicine polysaccharide. Int J Biol Macromol. 2022;211:711-28.doi.org/10.1016/j.ijbiomac.2022.05.087

[4.] Mohammed, ASA, Naveed, M, Jost, N. Polysaccharides; Classification, Chemical Properties, and Future Perspective Applications in Fields of Pharmacology and Biological Medicine (A Review of Current Applications and Upcoming Potentialities). J Polym Environ. 2021;29(8):2359-71.doi.org/10.1007/s10924-021-02052-2

[5.] Tian, H, An, L, Wang, P, et al. Review of *Astragalus membranaceus* polysaccharides: Extraction process, structural features, bioactivities and applications. Chinese Herbal Medicines. 2024;16.doi.org/10.1016/j.chmed.2024.09.004

[6.] Yang, X, Li, A, Li, X, et al. An overview of classifications, properties of food polysaccharides and their links to applications in improving food textures. Trends in Food Sci Tech. 2020;102:1-15.doi.org/10.1016/j.tifs.2020.05.020

[7.] Al-Hazmi, HE, Luczak, J, Habibzadeh, S, et al. Polysaccharide nanocomposites in wastewater treatment: A review. Chemosphere. 2024;347:140578.doi.org/10.1016/j.chemosphere.2023.140578

[8.] Fu, G-Q, Li, Y-X, He, Y, et al. Extraction, structure and bioactivity of *Tremella Fuciformis* polysaccharides: A review. Food & Medicine Homology. 2025;2.doi.org/10.26599/FMH.2025.9420038

[9.] Xie, Y-K, Pan, X-Y, Liang, X-R, et al. Research progress on structural characterization and bioactivities of *Poria cocos* and *Ganoderma* polysaccharides. Food & Medicine Homology. 2025;2(1):9420040.doi.org/10.26599/FMH.2025.9420040

[10.] Yu, W, Zhang, Y, Yao, L, et al. Research progress on the prevention of tumor by fungal polysaccharides. Trends in Food Sci Tech. 2024;147.doi.org/10.1016/j.tifs.2024.104422

[11.] Wang, W, Tan, J, Nima, L, et al. Polysaccharides from fungi: A review on their extraction, purification, structural features, and biological activities. Food Chem X. 2022;15:100414.doi.org/10.1016/j.fochx.2022.100414

[12.] Cui, Y-L, Li, B. Hypoglycemic effects of edible fungus polysaccharides: A mini review. Food & Medicine Homology. 2025;2(1):9420046.doi.org/10.26599/FMH.2025.9420046

[13.] Wang, Z-X, Huang, K, Pu, K-L, et al. *Naematelia aurantialba*: a comprehensive review of its medicinal, nutritional, and cultivation aspects. Food & Medicine Homology. 2025;2.doi.org/10.26599/FMH.2025.9420072

[14.] Yuan, Q, Xie, F, Tan, J, et al. Extraction, structure and pharmacological effects of the polysaccharides from Cordyceps sinensis: A review. Journal of Functional Foods. 2022;89:104909.doi.org/10.1016/j.jff.2021.104909

[15.] Maity, P, Sen, IK, Chakraborty, I, et al. Biologically active polysaccharide from edible mushrooms: A review. Int J Biol Macromol. 2021;172:408-17.doi.org/10.1016/j.ijbiomac.2021.01.081

[16.] Li, Y, Sheng, Y, Lu, X, et al. Isolation and purification of acidic polysaccharides from *Agaricus blazei* Murill and evaluation of their lipid-lowering mechanism. Int J Biol Macromol. 2020;157:276-87.doi.org/10.1016/j.ijbiomac.2020.04.190

[17.] Niu, YC, Liu, JC, Zhao, XM, et al. A low molecular weight polysaccharide isolated from *Agaricus blazei* Murill (LMPAB) exhibits its anti-metastatic effect by down-regulating metalloproteinase-9 and up-regulating Nm23-H1. Am J Chin Med. 2009;37(5):909-21.doi.org/10.1142/S0192415X09007351

[18.] Győri, J. Study on the mushroom species *Agaricus blazei* (Murill). Int J Hortic Sci. 2007;13(4).doi.org/10.31421/ijhs/13/4/772

[19.] Sui, Z, Yang, R, Liu, B, et al. Chemical analysis of *Agaricus blazei* polysaccharides and effect of the polysaccharides on IL-1β mRNA expression in skin of burn wound-treated rats. Int J Biol Macromol. 2010;47(2):155-7.doi.org/10.1016/j.ijbiomac.2010.05.006

[20.] Wu, B, Cui, J, Zhang, C, et al. A polysaccharide from *Agaricus blazei* inhibits proliferation and promotes apoptosis of osteosarcoma cells. Int J Biol Macromol. 2012;50(4):1116-20.doi.org/10.1016/j.ijbiomac.2012.02.023

[21.] Cardozo, FT, Camelini, CM, Cordeiro, MN, et al. Characterization and cytotoxic activity of sulfated derivatives of polysaccharides from *Agaricus brasiliensis*. Int J Biol Macromol. 2013;57:265-72.doi.org/10.1016/j.ijbiomac.2013.03.026

[22.] Zhang, Y, Liu, D, Fang, L, et al. A galactomannoglucan derived from *Agaricus brasiliensis*: Purification, characterization and macrophage activation via MAPK and IkappaB/NFkappaB pathways. Food Chem. 2018;239:603-11.doi.org/10.1016/j.foodchem.2017.06.152

[23.] Zhang, J, Gao, Z, Li, S, et al. Purification, Characterization, Antioxidation, and Antiaging Properties of Exopolysaccharides and Endopolysaccharides of the Royal Sun Medicinal Mushroom, *Agaricus brasiliensis* (Agaricomycetes). Int J Med Mushrooms. 2016;18(12):1071-81.doi.org/10.1615/IntJMedMushrooms.v18.i12.20

[24.] Roman, Y, Iacomini, M, Sassaki, GL, et al. Optimization of chemical sulfation, structural characterization and anticoagulant activity of *Agaricus bisporus* fucogalactan. Carbohydr Polym. 2016;146:345-52.doi.org/10.1016/j.carbpol.2016.03.061

[25.] Pires, A, Ruthes, AC, Cadena, S, et al. Cytotoxic effect of a mannogalactoglucan extracted from *Agaricus bisporus* on HepG2 cells. Carbohydr Polym. 2017;170:33-42.doi.org/10.1016/j.carbpol.2017.04.050

[26.] da Silva Campelo, M, Neto, JFC, Lima, ABN, et al. Polysaccharides and extracts from *Agaricus brasiliensis* Murill - A comprehensive review. Int J Biol Macromol. 2021;183:1697-714.doi.org/10.1016/j.ijbiomac.2021.05.112

[27.] Li, S, Liu, M, Zhang, C, et al. Purification, in vitro antioxidant and in vivo anti-aging activities of soluble polysaccharides by enzyme-assisted extraction from *Agaricus bisporus*. Int J Biol Macromol. 2018;109:457-66.doi.org/10.1016/j.ijbiomac.2017.12.108

[28.] Komura, DL, Carbonero, ER, Gracher, AH, et al. Structure of *Agaricus* spp. fucogalactans and their anti-inflammatory and antinociceptive properties. Bioresour Technol. 2010;101(15):6192-9.doi.org/10.1016/j.biortech.2010.01.142

[29.] Firenzuoli, F, Gori, L, Lombardo, G. The Medicinal Mushroom *Agaricus blazei* Murrill: Review of Literature and Pharmaco-Toxicological Problems. Evid Based Complement Alternat Med. 2008;5(1):3-15.doi.org/10.1093/ecam/nem007

[30.] Wisitrassameewong, K, Karunarathna, SC, Thongklang, N, et al. *Agaricus subrufescens*: A review. Saudi J Biol Sci. 2012;19(2):131-46.doi.org/10.1016/j.sjbs.2012.01.003

[31.] Mingyi, Y, Belwal, T, Devkota, HP, et al. Trends of utilizing mushroom polysaccharides (MPs) as potent nutraceutical components in food and medicine: A comprehensive review. Trends in Food Sci Tech. 2019;92:94-110.doi.org/10.1016/j.tifs.2019.08.009

[32.] Wu, QC, Zhang, YY, Li, YB, et al. A novel cell-wall polysaccharide derived from the stipe of *Agaricus bisporus* inhibits mouse melanoma proliferation and metastasis. Arch Biochem Biophys. 2023;744:109678.doi.org/10.1016/j.abb.2023.109678

[33.] Niu Y C, LJC, Zhao X M. Immunostimulatory activities of a low molecular weight antitumoral polysaccharide isolated from *Agaricus blazei* Murill (LMPAB) in Sarcoma 180 ascitic tumor-bearing mice. Die Pharmazie. 2009;64(7):472-6.doi.org/10.1691/ph.2009.8806

[34.] Zhang, N, Liu, Y, Tang, FY, et al. Structural characterization and in vitro anti-colon cancer activity of a homogeneous polysaccharide from *Agaricus bisporus*. Int J Biol Macromol. 2023;251:126410.doi.org/10.1016/j.ijbiomac.2023.126410

[35.] Li, S, Liu, H, Wang, W, et al. Antioxidant and anti-aging effects of acidic-extractable polysaccharides by *Agaricus bisporus*. Int J Biol Macromol. 2018;106:1297-306.doi.org/10.1016/j.ijbiomac.2017.08.135

[36.] Zhao, R, Karunarathna, S, Raspé, O, et al. Major clades in tropical Agaricus. Fungal Divers. 2011;51(1):279-96.doi.org/10.1007/s13225-011-0136-7

[37.] He, MQ, Chen, J, Zhou, JL, et al. Tropic origins, a dispersal model for saprotrophic mushrooms in *Agaricus* section Minores with descriptions of sixteen new species. Sci Rep. 2017;7(1):5122.doi.org/10.1038/s41598-017-05203-5

[38.] Araujo-Rodrigues, H, Sousa, AS, Relvas, JB, et al. An Overview on Mushroom Polysaccharides: Health-promoting Properties, Prebiotic and Gut Microbiota Modulation Effects and Structure-function Correlation. Carbohydr Polym. 2024;333:121978.doi.org/10.1016/j.carbpol.2024.121978

[39.] Liu, J, Willför, S, Xu, C. A review of bioactive plant polysaccharides: Biological activities, functionalization, and biomedical applications. Bioact Carbohydr Diet Fibre. 2015;5(1):31-61.doi.org/10.1016/j.bcdf.2014.12.001

[40.] Zhang, M, Zhao, L, Tang, F, et al. Chemical Structures, Biological Activities, and Biosynthetic Analysis of Secondary Metabolites from *Agaricus* Mushrooms: A Review. J Agric Food Chem. 2024;72(22):12387-97.doi.org/10.1021/acs.jafc.4c01861

[41.] Zhang, H-N, Liu, Y, Zhang, H-L, et al. Effect of different drying and grinding techniques on the physicochemical properties and biological activities of fungal polysaccharides. Food & Medicine Homology. 2025;2(1):9420045.doi.org/10.26599/FMH.2025.9420045

[42.] Berger, RG, Bordewick, S, Krahe, NK, et al. Mycelium vs. Fruiting Bodies of Edible Fungi-A Comparison of Metabolites. Microorganisms. 2022;10(7).doi.org/10.3390/microorganisms10071379

[43.] Shu, CH, Lin, KJ, Wen, BJ. Effects of culture temperature on the production of bioactive polysaccharides by *Agaricus blazei* in batch cultures. J Chem Technol Biotechnol. 2007;82(9):831-6.doi.org/10.1002/jctb.1748

[44.] Wang, Q, Li, BB, Li, H, et al. Yield, dry matter and polysaccharides content of the mushroom *Agaricus blazei* produced on asparagus straw substrate. Sci Hortic. 2010;125(1):16-8.doi.org/10.1016/j.scienta.2010.02.022

[45.] Yi, Y, Xu, W, Wang, HX, et al. Natural polysaccharides experience physiochemical and functional changes during preparation: A review. Carbohydr Polym. 2020;234:115896.doi.org/10.1016/j.carbpol.2020.115896

[46.] Chen, Y, Zhang, N, Chen, X. Structurally Modified Polysaccharides: Physicochemical Properties, Biological Activities, Structure-Activity Relationship, and Applications. J Agric Food Chem. 2024;72(7):3259-76.doi.org/10.1021/acs.jafc.3c06433

[47.] Leong, YK, Yang, FC, Chang, JS. Extraction of polysaccharides from edible mushrooms: Emerging technologies and recent advances. Carbohydr Polym. 2021;251:117006.doi.org/10.1016/j.carbpol.2020.117006

[48.] Lu, X. Changes in the structure of polysaccharides under different extraction methods. eFood. 2023;4(2):e82.doi.org/10.1002/efd2.82

[49.] Lei, S. Bioactivities, isolation and purification methods of polysaccharides from natural products: A review. Int J Biol Macromol. 2016;92:37-48.doi.org/10.1016/j.ijbiomac.2016.06.100

[50.] Liu, J, Sun, Y. Structural analysis of an alkali-extractable and water-soluble polysaccharide (ABP-AW1) from the fruiting bodies of *Agaricus blazei* Murill. Carbohydr Polym. 2011;86(2):429-32.doi.org/10.1016/j.carbpol.2011.01.027

[51.] Huang, SQ, Li, JW, Wang, Z, et al. Optimization of alkaline extraction of polysaccharides from *Ganoderma lucidum* and their effect on immune function in mice. Molecules. 2010;15(5):3694-708.doi.org/10.3390/molecules15053694

[52.] Trygg, J, Beltrame, G, Yang, B. Rupturing fungal cell walls for higher yield of polysaccharides: Acid treatment of the basidiomycete prior to extraction. Innov Food Sci Emerg Technol. 2019;57.doi.org/10.1016/j.ifset.2019.102206

[53.] Li, M, Law, D, Zhu, S, et al. Extraction, purification, characterization and antidiabetic mechanisms of plant polysaccharides: a critical review. Turk J Bioch. 2024;49(5):596-611.doi.org/10.1515/tjb-2024-0071

[54.] Wang, HT, Yang, LC, Yu, HC, et al. Characteristics of fucose-containing polysaccharides from submerged fermentation of *Agaricus blazei* Murill. J Food Drug Anal. 2018;26(2):678-87.doi.org/10.1016/j.jfda.2017.07.006

[55.] Kozarski, M, Klaus, A, Niksic, M, et al. Antioxidative and immunomodulating activities of polysaccharide extracts of the medicinal mushrooms *Agaricus bisporus*, *Agaricus brasiliensis*, *Ganoderma lucidum* and *Phellinus linteus*. Food Chem. 2011;129(4):1667-75.doi.org/10.1016/j.foodchem.2011.06.029

[56.] Feng, Y, Zhang, J, Wen, C, et al. Recent advances in *Agaricus bisporus* polysaccharides: Extraction, purification, physicochemical characterization and bioactivities. Process Biochem. 2020;94:39-50.doi.org/10.1016/j.procbio.2020.04.010

[57.] Shen, L, Pang, S, Zhong, M, et al. A comprehensive review of ultrasonic assisted extraction (UAE) for bioactive components: Principles, advantages, equipment, and combined technologies. Ultrason Sonochem. 2023;101:106646.doi.org/10.1016/j.ultsonch.2023.106646

[58.] Zhao, F, Wang, Z, Huang, H. Physical Cell Disruption Technologies for Intracellular Compound Extraction from Microorganisms. Processes. 2024;12(10).doi.org/10.3390/pr12102059

[59.] Tian, Y, Zeng, H, Xu, Z, et al. Ultrasonic-assisted extraction and antioxidant activity of polysaccharides recovered from white button mushroom (*Agaricus bisporus*). Carbohydr Polym. 2012;88(2):522-9.doi.org/10.1016/j.carbpol.2011.12.042

[60.] Zhang, Z, Lv, G, Pan, H, et al. Optimization of the Microwave-Assisted Extraction Process for Polysaccharides in Himematsutake (*Agaricus blazei* Murrill) and Evaluation of Their Antioxidant Activities. Food Sci Technol Res. 2011;17(6):461-70.doi.org/10.3136/fstr.17.461

[61.] Costa, JR, Tonon, RV, Cabral, L, et al. Valorization of Agricultural Lignocellulosic Plant Byproducts through Enzymatic and Enzyme-Assisted Extraction of High-Value-Added Compounds: A Review. ACS Sustainable Chem Eng. 2020;8(35):13112-25.doi.org/10.1021/acssuschemeng.0c02087

[62.] Ke, L-q. Optimization of Ultrasonic Extraction of Polysaccharides from *Lentinus Edodes* Based on Enzymatic Treatment. J Food Process Preserv. 2015;39(3):254-9.doi.org/10.1111/jfpp.12228

[63.] Jia, S, Li, F, Liu, Y, et al. Effects of extraction methods on the antioxidant activities of polysaccharides from *Agaricus blazei* Murrill. Int J Biol Macromol. 2013;62:66-9.doi.org/10.1016/j.ijbiomac.2013.08.031

[64.] Smiderle F R, RAC, van Arkel J, et al. . Polysaccharides from *Agaricus bisporus* and *Agaricus brasiliensis* show similarities in their structures and their immunomodulatory effects on human monocytic THP-1 cells. BMC Complement Altern Med. 2011;11(11):1-11.doi.org/10.1186/1472-6882-11-58

[65.] Liu, G, Ye, J, Li, W, et al. Extraction, structural characterization, and immunobiological activity of ABP Ia polysaccharide from *Agaricus bisporus*. Int J Biol Macromol. 2020;162:975-84.doi.org/10.1016/j.ijbiomac.2020.06.204

[66.] Kuang, H, Jiao, Y, Wang, W, et al. Characterization and antioxidant activities of intracellular polysaccharides from *Agaricus bitorquis* (QueL.) Sacc. Chaidam ZJU-CDMA-12. Int J Biol Macromol. 2020;156:1112-25.doi.org/10.1016/j.ijbiomac.2019.11.142

[67.] Liu, Y, Zheng, D, Su, L, et al. Protective effect of polysaccharide from *Agaricus bisporus* in Tibet area of China against tetrachloride-induced acute liver injury in mice. Int J Biol Macromol. 2018;118(Pt B):1488-93.doi.org/10.1016/j.ijbiomac.2018.06.179

[68.] Wu, S, Li, F, Jia, S, et al. Drying effects on the antioxidant properties of polysaccharides obtained from *Agaricus blazei* Murrill. Carbohydr Polym. 2014;103:414-7.doi.org/10.1016/j.carbpol.2013.11.075

[69.] He, J, Zhang, A, Ru, Q, et al. Structural characterization of a water-soluble polysaccharide from the fruiting bodies of *Agaricus bisporus*. Int J Mol Sci. 2014;15(1):787-97.doi.org/10.3390/ijms15010787

[70.] Li, S, Li, J, Zhang, J, et al. The Antioxidative, Antiaging, and Hepatoprotective Effects of Alkali-Extractable Polysaccharides by *Agaricus bisporus*. Evid Based Complement Alternat Med. 2017;2017:7298683.doi.org/10.1155/2017/7298683

[71.] Wang X L, LGQ, Zhang H Y, et al. Extraction of Mycelial Polysaccharides from Submerged-Cultured *Agaricus blazei*. 4th International Conference on Bioinformatics and Biomedical Engineering; IEEE2010 p. 1-4.

[72.] Ker, Y-B, Chen, K-C, Chyau, C-C, et al. Antioxidant Capability of Polysaccharides Fractionated from Submerge-Cultured *Agaricus blazei* Mycelia. J Agric Food Chem. 2005;53(18):7052-8.doi.org/10.1021/jf0510034

[73.] Yin X, YQ, Zhou X. . Complex enzyme-assisted extraction, purification, and antioxidant activity of polysaccharides from the Button Mushroom, *Agaricus bisporus* (Higher Basidiomycetes). Int J Med Mushrooms. 2015;17(10):987-96.doi.org/10.1615/intjmedmushrooms.v17.i10.80

[74.] Zhang, A, Deng, J, Liu, X, et al. Structure and conformation of *α*-glucan extracted from *Agaricus blazei* Murill by high-speed shearing homogenization. Int J Biol Macromol. 2018;113:558-64.doi.org/10.1016/j.ijbiomac.2018.02.151

[75.] Meng, X, Liang, H, Luo, L. Antitumor polysaccharides from mushrooms: a review on the structural characteristics, antitumor mechanisms and immunomodulating activities. Carbohydr Res. 2016;424:30-41.doi.org/10.1016/j.carres.2016.02.008

[76.] Ohno, N, Furukawa, M, Miura, NN, et al. Antitumor beta glucan from the cultured fruit body of *Agaricus blazei*. Biol Pharm Bull. 2001;24(7):820-8.doi.org/10.1248/bpb.24.820

[77.] Xie, L, Shen, M, Hong, Y, et al. Chemical modifications of polysaccharides and their anti-tumor activities. Carbohydr Polym. 2020;229:115436.doi.org/10.1016/j.carbpol.2019.115436

[78.] Huang, L, Shen, M, Morris, GA, et al. Sulfated polysaccharides: Immunomodulation and signaling mechanisms. Trends in Food Sci Tech. 2019;92:1-11.doi.org/10.1016/j.tifs.2019.08.008

[79.] Yamamoto, KA, Galhardi, LC, Rincao, VP, et al. Antiherpetic activity of an *Agaricus brasiliensis* polysaccharide, its sulfated derivative and fractions. Int J Biol Macromol. 2013;52:9-13.doi.org/10.1016/j.ijbiomac.2012.09.029

[80.] Roman Ochoa, Y, Iacomini, M, Sassaki, GL, et al. Sulfation of fucogalactan from *Agaricus bisporus*: Different patterns in the chemical structure and their effects on anticoagulant activity. Int J Biol Macromol. 2017;97:357-64.doi.org/10.1016/j.ijbiomac.2017.01.035

[81.] Cardozo, FT, Larsen, IV, Carballo, EV, et al. In vivo anti-herpes simplex virus activity of a sulfated derivative of *Agaricus brasiliensis* mycelial polysaccharide. Antimicrob Agents Chemother. 2013;57(6):2541-9.doi.org/10.1128/AAC.02250-12

[82.] Kawagishi, H, Kanao, T, Inagaki, R, et al. Formolysis of a potent antitumor (1 → 6)-β-d-glucan-protein complex from *Agaricus blazei* fruiting bodies and antitumor activity of the resulting products. Carbohydrate Polymers. 1990;12(4):393-403.doi.org/10.1016/0144-8617(90)90089-B

[83.] Kawagishi, H, Inagaki, R, Kanao, T, et al. Fractionation and antitumor activity of the water-in-soluble residue of *Agaricus blazei* fruiting bodies. Carbohydr Polym. 1989;186(2):267-73.doi.org/10.1016/0008-6215(89)84040-6

[84.] Mizuno, T, Hagiwara, T, Nakamura, T, et al. Antitumor Activity and Some Properties of Water-soluble Polysaccharides from "Himematsutake," the Fruiting Body of *Agavicus blazei* Murill. Appl Biol Chem. 1990;54(11):2889-96.doi.org/10.1080/00021369.1990.10870406

[85.] Gonzaga, MLC, Ricardo, N, Heatley, F, et al. Isolation and characterization of polysaccharides from *Agaricus blazei* Murill. Carbohydr Polym. 2005;60(1):43-9.doi.org/10.1016/j.carbpol.2004.11.022

[86.] Liu, J, Yue, L, Zhang, C, et al. A polysaccharide isolated from *Agaricus blazei* Murill inhibits sialyl Lewis X/E-selectin-mediated metastatic potential in HT-29 cells through down-regulating α-1,3-fucosyltransferase-VII (FucT-VII). Carbohydr Polym. 2010;79(4):921-6.doi.org/10.1016/j.carbpol.2009.10.023

[87.] Liu, J, Sun, J. A Study on the Extraction, Separation, and Anti-Tumor Activity Screening of Low Molecular Weight Polysaccharides from *Agaricus blazei* Murill. Chin J Tradit Chin Med Pharm. 2006(05):298-300.doi.org/10.3969/j.issn.1673-1727.2006.05.015

[88.] Niu, Y-C, Liu, J-C, Zhao, X-M, et al. Immunostimulatory activities of a low molecular weight antitumoral polysaccharide isolated from *Agaricus blazei* Murill (LMPAB) in Sarcoma 180 ascitic tumor-bearing mice. Pharmazie. 2009;64(7):472-6.doi.org/10.1691/ph.2009.8806

[89.] Niu, YC, Liu, JC, Zhao, XM, et al. A low molecular weight polysaccharide isolated from *Agaricus blazei* suppresses tumor growth and angiogenesis in vivo. Oncol Rep. 2009;21.doi.org/10.3892/or_00000201

[90.] Zhang, S, He, B, Ge, J, et al. Characterization of chemical composition of *Agaricus brasiliensis* polysaccharides and its effect on myocardial SOD activity, MDA and caspase-3 level in ischemia-reperfusion rats. Int J Biol Macromol. 2010;46(3):363-6.doi.org/10.1016/j.ijbiomac.2010.01.008

[91.] Cardozo, FT, Camelini, CM, Mascarello, A, et al. Antiherpetic activity of a sulfated polysaccharide from *Agaricus brasiliensis* mycelia. Antiviral Res. 2011;92(1):108-14.doi.org/10.1016/j.antiviral.2011.07.009

[92.] Liu, J, Zhang, C, Wang, Y, et al. Structural elucidation of a heteroglycan from the fruiting bodies of *Agaricus blazei* Murill. Int J Biol Macromol. 2011;49(4):716-20.doi.org/10.1016/j.ijbiomac.2011.07.003

[93.] Jeong, SC, Koyyalamudi, SR, Jeong, YT, et al. Macrophage immunomodulating and antitumor activities of polysaccharides isolated from *Agaricus bisporus* white button mushrooms. J Med Food. 2012;15(1):58-65.doi.org/10.1089/jmf.2011.1704

[94.] Ruthes, AC, Rattmann, YD, Carbonero, ER, et al. Structural characterization and protective effect against murine sepsis of fucogalactans from *Agaricus bisporus* and Lactarius rufus. Carbohydr Polym. 2012;87(2):1620-7.doi.org/10.1016/j.carbpol.2011.09.071

[95.] Andrade Pires, AdR, Ruthes, AC, Suter Correia Cadena, SM, et al. Cytotoxic effect of *Agaricus bisporus* and *Lactarius rufus* *β*-D-glucans on HepG2 cells. Int J Biol Macromol. 2013;58:95-103.doi.org/10.1016/j.ijbiomac.2013.03.040

[96.] Smiderle, FR, Alquini, G, Tadra-Sfeir, MZ, et al. *Agaricus bisporus* and *Agaricus brasiliensis* (1 → 6)-β-D-glucans show immunostimulatory activity on human THP-1 derived macrophages. Carbohydr Polym. 2013;94(1):91-9.doi.org/10.1016/j.carbpol.2012.12.073

[97.] Ruthes, AC, Rattmann, YD, Malquevicz-Paiva, SM, et al. *Agaricus bisporus* fucogalactan: Structural characterization and pharmacological approaches. Carbohydr Polym. 2013;92(1):184-91.doi.org/10.1016/j.carbpol.2012.08.071

[98.] Chen, QS, Zhou, TY, Li, XY, et al. Applied Orthogonal Experiment Design for Optimization of Ultrasonic-Assisted Extraction of Polysaccharides from *Agaricus bisporus* Mycelia. Adv Mate Res. 2014;3384(1010-1012):1779-82.doi.org/10.4028/www.scientific.net/AMR.1010-1012.1779

[99.] Gonzaga, MLC, Menezes, TMF, Rebêlo, LM, et al. *Agaricus brasiliensis* mushroom betaglucans solutions: Physicochemical properties and griseofulvin solubilization by self-assembly micro-nano particles formation. Bioact Carbohydr Diet Fibre. 2014;4(2):144-54.doi.org/10.1016/j.bcdf.2014.09.004

[100.] Ying, Y, Hao, W. Immunomodulatory function and anti-tumor mechanism of natural polysaccharides: A review. Front Immunol. 2023;14:1147641.doi.org/10.3389/fimmu.2023.1147641

[101.] Niu, Y-C, Liu, J-C, Zhao, X-M, et al. Immunostimulatory activities of a low molecular weight antitumoral polysaccharide isolated from *Agaricus blazei* Murill (LMPAB) in Sarcoma 180 ascitic tumor-bearing mice. Pharmazie. 2009;64(472-476).doi.org/10.1691/ph.2009.8806

[102.] Dong, K, Wang, J, Tang, F, et al. A polysaccharide with a triple helix structure from *Agaricus bisporus*: Characterization and anti-colon cancer activity. Int J Biol Macromol. 2024;281(Pt 4):136521.doi.org/10.1016/j.ijbiomac.2024.136521

[103.] Chen, J, Seviour, R. Medicinal importance of fungal beta-(1-->3), (1-->6)-glucans. Mycol Res. 2007;111(Pt 6):635-52.doi.org/10.1016/j.mycres.2007.02.011

[104.] Wasser, SP. Medicinal mushrooms as a source of antitumor and immunomodulating polysaccharides. Appl Microbiol Biotechnol. 2002;60(3):258-74.doi.org/10.1007/s00253-002-1076-7

[105.] Chen, R, Xu, J, Wu, W, et al. Structure-immunomodulatory activity relationships of dietary polysaccharides. Curr Res Food Sci. 2022;5:1330-41.doi.org/10.1016/j.crfs.2022.08.016

[106.] Hetland, G, Tangen, JM, Mahmood, F, et al. Antitumor, Anti-Inflammatory and Antiallergic Effects of *Agaricus blazei* Mushroom Extract and the Related Medicinal Basidiomycetes Mushrooms, Hericium erinaceus and Grifola frondosa: A Review of Preclinical and Clinical Studies. Nutrients. 2020;12(5).doi.org/10.3390/nu12051339

[107.] Liu. A low molecular weight polysaccharide isolated from *Agaricus blazei* suppresses tumor growth and angiogenesis in vivo. Oncology Reports. 2009.doi.org/10.3892/or_00000201

[108.] Chen, N, Hu, M, Jiang, T, et al. Insights into the molecular mechanisms, structure-activity relationships and application prospects of polysaccharides by regulating Nrf2-mediated antioxidant response. Carbohydr Polym. 2024;333:122003.doi.org/10.1016/j.carbpol.2024.122003

[109.] Bai, L, Xu, D, Zhou, YM, et al. Antioxidant Activities of Natural Polysaccharides and Their Derivatives for Biomedical and Medicinal Applications. Antioxidants. 2022;11(12).doi.org/10.3390/antiox11122491

[110.] Harikrishnan, R, Devi, G, Van Doan, H, et al. Effect of diet enriched with *Agaricus bisporus* polysaccharides (ABPs) on antioxidant property, innate-adaptive immune response and pro-anti inflammatory genes expression in Ctenopharyngodon idella against Aeromonas hydrophila. Fish Shellfish Immunol. 2021;114:238-52.doi.org/10.1016/j.fsi.2021.04.025

[111.] Fang, YZ, Yang, S, Wu, G. Free radicals, antioxidants, and nutrition. Nutrition. 2002;18(10):872-9.doi.org/10.1016/s0899-9007(02)00916-4

[112.] El-Aal, MA, Hassan, HA. Lipid Peroxidation End-Products as a Key of Oxidative Stress: Effect of Antioxidant on Their Production and Transfer of Free Radicals. Lipid Peroxidation2012.

[113.] Tan, BL, Norhaizan, ME, Liew, WP, et al. Antioxidant and Oxidative Stress: A Mutual Interplay in Age-Related Diseases. Front Pharmacol. 2018;9:1162.doi.org/10.3389/fphar.2018.01162

[114.] Li, Y, Lu, X, Li, X, et al. Effects of *Agaricus blazei* Murrill polysaccharides on hyperlipidemic rats by regulation of intestinal microflora. Food Sci Nutr. 2020;8(6):2758-72.doi.org/10.1002/fsn3.1568

[115.] Hao, Z, Dai, S, Tan, J, et al. Modification, Structural Characterizations, and Biological Activities of Sulfated Polysaccharides: A Review. Starch-Starke. 2023;76(5-6).doi.org/10.1002/star.202300116

[116.] Zhao, Y, Tian, N, Wang, H, et al. Chemically Sulfated Polysaccharides from *Agaricus blazei* Murill: Synthesis, Characterization and Anti-HIV Activity. Chem Biodivers. 2021;18(9):e2100338.doi.org/10.1002/cbdv.202100338

[117.] Xu, Bw, Li, Ss, Ding, Wl, et al. From structure to function: A comprehensive overview of polysaccharide roles and applications. Food Frontiers. 2024:1-25.doi.org/10.1002/fft2.490

[118.] Morin, E, Kohler, A, Baker, AR, et al. Genome sequence of the button mushroom *Agaricus bisporu*s reveals mechanisms governing adaptation to a humic-rich ecological niche. PNAS. 2012;109(43):17501-6.doi.org/10.1073/pnas.1206847109

[119.] Zhao, C, Feng, X-l, Wang, Z-x, et al. The First Whole Genome Sequencing of *Agaricus bitorquis* and Its Metabolite Profiling. J Fungi. 2023;9(4):485

[120.] Liu, T, Ren, Q, Wang, S, et al. Chemical Modification of Polysaccharides: A Review of Synthetic Approaches, Biological Activity and the Structure-Activity Relationship. Molecules. 2023;28(16).doi.org/10.3390/molecules28166073

[121.] Zhao, T, Yang, M, Ma, L, et al. Structural Modification and Biological Activity of Polysaccharides. Molecules. 2023;28(14).doi.org/10.3390/molecules28145416

[122.] Miao, T, Wang, J, Zeng, Y, et al. Polysaccharide-Based Controlled Release Systems for Therapeutics Delivery and Tissue Engineering: From Bench to Bedside. Adv Sci. 2018;5(4):1700513.doi.org/10.1002/advs.201700513

[123.] Zhang, J, Zhan, P, Tian, H. Recent updates in the polysaccharides-based Nano-biocarriers for drugs delivery and its application in diseases treatment: A review. Int J Biol Macromol. 2021;182:115-28.doi.org/10.1016/j.ijbiomac.2021.04.009

[124.] Zhang, Y, Cui, Z, Mei, H, et al. Angelica sinensis polysaccharide nanoparticles as a targeted drug delivery system for enhanced therapy of liver cancer. Carbohydr Polym. 2019;219:143-54.doi.org/10.1016/j.carbpol.2019.04.041

[125.] Ding, C, Liu, X, Zhang, S, et al. Multifunctional hydrogel bioscaffolds based on polysaccharide to promote wound healing: A review. Int J Biol Macromol. 2024;259(Pt 2):129356.doi.org/10.1016/j.ijbiomac.2024.129356

[126.] Manal, GM, Abeer, YI, Mohsen, MSA, et al. Therapeutic potential and structural elucidation of a water-soluble polysaccharide of a wild edible mushroom *Agaricus bisporus* against neurodegenerative disease, Alzheimer. World Journal of Pharmaceutical Sciences. 2014;2(10):1136-45