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Review

Research progress on polysaccharides from medicine and food homology materials in functional foods

Dejun Hu[Δ], Yifan Zhang[Δ], Boyao Li, Chongjiang Cao[*]

Department of Food Quality and Safety/National R&D Center for Chinese Herbal Medicine Processing, College of Engineering, China Pharmaceutical University, Nanjing 211198, China

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ABSTRACT

Polysaccharides, a class of complex macromolecules, are distinguished by their diverse biological functions and essential role in functional foods. The distinctive biological activities of polysaccharides from medicine and food homology materials (MFPs), including immunomodulation, carbohydrate metabolism regulation, and lipid metabolism regulation properties, have attracted considerable scientific attention. The relationship between polysaccharides and gut microbiota is fundamental to human health, as polysaccharides demonstrate efficacy in ameliorating various conditions—from inflammatory bowel disease (IBD) to obesity and diabetes—through their influence on intestinal flora composition and diversity. Although polysaccharide research and applications show promise, significant challenges persist, particularly regarding extraction and purification methodologies, and the complete understanding of their biological mechanisms. Future investigations should prioritize understanding the correlation between polysaccharide structure and function, advancing large-scale production and application technologies, and establishing productive interdisciplinary collaborations. MFPs demonstrate significant potential for advancing sustainable development and human health, building upon current research findings. This paper presents a comprehensive review of global developments in the extraction, purification, structural characterization, biological activities, and applications of MFPs, emphasizing opportunities for scientific and technological innovations in specialized dietary food development.

1. Introduction

In contemporary society's increasing focus on health and sustainable development, polysaccharides have garnered substantial attention from both scientific research and industry due to their distinctive biological activity and safety profile [1]. These complex carbohydrates, classified as natural polysaccharides, are prevalent in plant cell walls and storage tissues [2]. Consisting of more than 10 monosaccharides connected through glycosidic bonds in linear or branched arrangements, polysaccharides demonstrate diverse molecular weights, structural configurations, and biological functions [3]. Analogous to proteins and nucleotides, polysaccharides from medicine and food homology materials (MFPs) constitute fundamental macromolecules in biological processes, performing crucial functions in intercellular communication, cell adhesion, and immune system molecular recognition [4]. These compounds serve as essential structural components for plant growth and development while maintaining significant relevance in medicine, food science, agriculture, and environmental protection due to their unique biological activities and diverse functions.

MFPs are listed in the "Catalog of Food & Medicine Homology", published jointly by the State Administration for Market Regulation and National Health Commission of China. These materials contain various active components, with polysaccharides being particularly significant due to their extensive applications. While research and application of small molecule natural products in disease treatment has been extensive, large molecule polysaccharides have received relatively less attention [5-7]. MFPs demonstrate significant biological activities, including immunomodulation, anti-bacterial effects, anti-viral properties, anti-oxidant capabilities, and anti-tumor functions [8-10] (Fig. 1). These bioactivities have led to increased interest in specific polysaccharides, such as *Astragalus* polysaccharides, which have undergone extensive research and clinical application in immune enhancement and disease treatment, contributing significantly to drug development [11].

Furthermore, MFPs are increasingly prominent in the food industry. These compounds function as natural thickeners, stabilizers, and emulsifiers, enhancing food texture and flavor while providing dietary fiber benefits. Such fiber components assist in regulating intestinal flora, enhancing digestion, and preventing chronic diseases. MFPs are incorporated into infant formulas [12] and utilized as personalized active biomaterials in various functional foods [13]. The increasing recognition of dietary health has led to growing market demand for MFPs. These compounds serve both as direct raw materials and as carriers for other nutrients.

* Corresponding author.
E-mail address: ccj33@163.com
Δ These authors contributed equally to this work.

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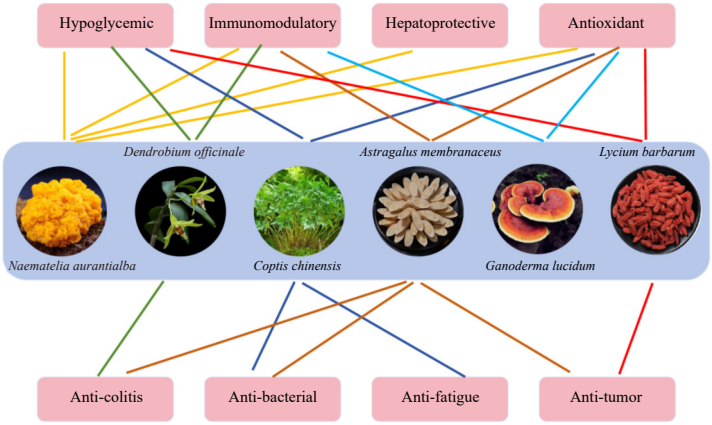

Fig. 1 Biological activities of MFPs.

As functional food components, MFPs are widely incorporated into specialized dietary products. Beyond enhancing nutritional content and palatability, these polysaccharides provide various physiological benefits, including immune regulation and metabolic improvement. They play a vital role in nutritional support and treatment assistance for patients with specific conditions. Consequently, MFP research has become a central focus in both domestic and international scientific communities [14]. This review aims to provide a comprehensive analysis of recent international developments in MFP extraction, purification, and structural characterization techniques (Fig. 2), examining their role in functional foods through the lens of gut microbiota. The review also addresses current challenges and future research directions

2. Extraction of MFPs

Polysaccharide extraction involves the systematic breakdown of plant cell walls through specific technical methods to facilitate the dissolution of intracellular polysaccharides. This process encompasses multiple stages, including solvent infiltration, polysaccharide dissolution, and diffusion [15]. The extraction methodology significantly influences the structural characteristics of the extracted polysaccharides, which subsequently affects their biological activity [16]. Therefore, various techniques including high temperature and pressure, acid and alkali treatments, ultrasonication, microwave irradiation, and enzymatic digestion are employed to optimize yield, enhance activity, and improve extraction efficiency.

The hot water extraction (HWE) method is widely employed, either independently or in combination with other auxiliary techniques, during polysaccharide extraction processes. Li et al. [17] extracted crude polysaccharides from *Radix Adenophorae* (100 g) using this method. Tang et al. [8] applied HWE to obtain polysaccharides for studying their effects on ulcerative colitis in mice, while Jiao et al. [18] utilized this method to extract polysaccharides from three varieties of *sea urchin* shells. Du et al. [19] extracted β-glucan from barley bran using high-pressure extraction under optimized conditions: 10 MPa pressure, 70 °C temperature, and 9 min extraction time, achieving a 16.39% β-glucan yield. Xu *et al.* [20] obtained polysaccharides from *Eucommia ulmoides* Oliver leaf through microwave extraction, reaching a 12.31% yield at 74 °C, with a solid-liquid ratio of 1∶29 (W/V), and a 15 min reaction time. Lu et al. [21] extracted pectin from *Premna microphylla* Turcz leaves under conditions of 1∶50 (W/V) solid-liquid ratio, 90 °C temperature, pH 2, and 2 h extraction time, yielding 18.25%.

The deep eutectic solvent (DES) extraction method represents an innovative green extraction technology showing considerable promise in polysaccharide extraction and separation. DESs comprise two or more components, primarily hydrogen bond donors (HBDs) and hydrogen bond acceptors (HBAs), as initially proposed by Abbott et al. in 2003. Common HBDs include urea, ethylene glycol, glycerol, butanediol, and glucose, while HBAs, though fewer in number, primarily consist of choline chloride and betaine. Chen et al. [22] implemented a three-phase partitioning approach using DESs to extract grape seed polysaccharides (GSP), achieving an optimal extraction yield of 98.04 mg·g^{-1}. This yield demonstrates a marked improvement over conventional three-phase partitioning methods. Additionally, Xia et al. [23] repor-

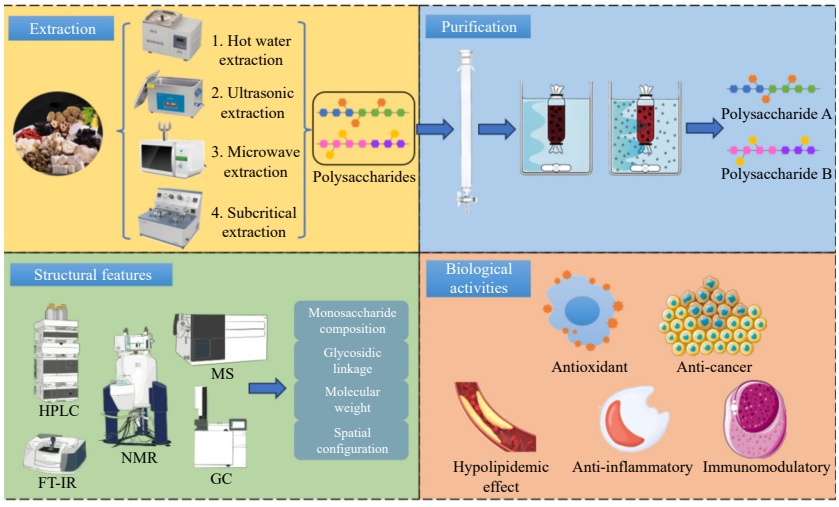

Fig. 2 Schematic diagram of research process for MFPs.

ted a 19.18% extraction rate for Anji White Tea polysaccharides using ultrasound-assisted DESs extraction, substantially higher than the 5.50% yield obtained through traditional HWE.

Different extraction methodologies can substantially affect polysaccharide yield, purity, chemical composition, structure, and particularly their weight-average molecular weight [24]. Polysaccharides extracted from *Ganoderma lucidum* [25] and *Camellia sinensis* [26] through HWE demonstrate enhanced anti-oxidant and anti-diabetic properties compared to those obtained *via* ultrasonic-assisted extraction (UAE). This increased activity potentially relates to the higher weight-average molecular weight and D-glucuronic acid content found in HWE-derived polysaccharides. Subcritical water extraction (SWE) has demonstrated superior polysaccharide yields from *Lycium barbarum* [27] and *Chimonobambusa quadrangularis* [28] compared to HWE, while maintaining identical physicochemical and bioactive properties. The selection of an appropriate polysaccharide extraction method necessitates thorough evaluation and comparison for process optimization. Sometimes, multiple methods may be required for optimal results. Wang et al. [29] extracted *Ginkgo* polysaccharides using combined parameters: 1∶50 solid-liquid ratio, 55 °C temperature, 30 min ultrasonication time, and 40 min cellulase (0.8%) hydrolysis time. This ultrasonication and enzymatic extraction combination yielded 12.85% *Ginkgo* polysaccharides. Comparing SWE, using UAE and HWE methods revealed that SWE-UAE produced *Lentinus edodes* polysaccharides with enhanced anti-oxidant activity [30]. During okra polysaccharide extraction, viscozyme treatment led to degradation, reducing anti-microbial activity, weight-average molecular weight, methyl esterification degree, and total uronic acid content, while increasing acetylation degree. However, ultrasound assistance significantly improved the extracts' radical scavenging capacity and anti-microbial activity [31].

3. Purification of MFPs

Purification represents a fundamental step in polysaccharide research, facilitating the enrichment of polysaccharide substances and separation of their components. This process encompasses the elimination of impurities including proteins, lipids, monosaccharides, oligosaccharides, and inorganic salts from polysaccharide-containing raw materials through multiple steps such as deproteinization, decolorization, salting out, and chromatographic separation, resulting in high-purity polysaccharides [32].

Various techniques are utilized for protein removal from crude polysaccharides, including trichloroacetic acid (TCA) precipitation, $CaCl_2$ salting-out, and the Sevag method, though these may result in polysaccharide loss [33, 34]. As a result, enzymatic methods, either independently or combined with other approaches, have become increasingly prevalent for protein removal [35, 36]. Novel, environmentally friendly, and efficient protein removal techniques are under investigation, such as freeze-thaw treatment [38] and high-speed counter-current chromatography [37]. For pigment elimination from polysaccharides, methods include hydrogen peroxide (H_2O_2) treatment, anion exchange macroporous resin, sequential rinsing with organic solvents, and activated carbon. However, activated carbon adsorption is less preferred due to its inefficiency [38] and residual effects [39]. The macroporous AB-8 resin has demonstrated effectiveness in removing pigments from *Toona sinensis* (A. Juss) Roem [40] and *Ganoderma lucidum* [41] polysaccharides. The elimination of small molecule materials, including inorganic salts, monosaccharides, and oligosaccharides, typically occurs through dialysis and ultrafiltration [42]. Purification of polysaccharide fractions requires more precise handling than impurity removal, generally conducted based on molecular weight distribution, affinity properties, and additional factors [43].

For instance, Li et al. [17] implemented deproteinization using the Sevag method and decolorization using an ADS-7 macroporous adsorption column. The purified polysaccharide RAPS (191.2 mg) with an average molecular weight of 1.8×10^4 Da was obtained through a cellulose DEAE-52 column and Sephacryl S-300 HR gel-filtration column. These purification techniques have been successfully applied to various polysaccharides, including *Porphyra yezoensis* polysaccharide (PPS) [44], *Artemisia annua* polysaccharides (AAP) [45], Chinese Truffle (*Tuber sinense*) polysaccharides [48], Red Ginseng polysaccharides (RGP) [46], and *Hedyotis diffusa* polysaccharides [47], each requiring specific procedural steps. Li et al. [48] extracted crude polysaccharide from jujube using aqueous extraction combined with alcohol precipitation, followed by separation through ultrafiltration and a DEAE-Sepharose CL-6B column. The single jujube polysaccharide (ZSP3c) underwent further purification after elution with a Sepharose CL-6B gel column.

The purification process remains fundamental to polysaccharide research, as purified polysaccharides demonstrate superior suitability for structural analysis, functional studies, and application as source materials for pharmaceuticals or nutraceuticals. Thus, polysaccharide purification requires comprehensive consideration of structural information and focuses on three progressive stages: polysaccharides in raw materials, polysaccharides in the extraction process, and crude polysaccharides, with appropriate purification methods selected accordingly.

4. Structural characteristics of MFPs

The complex and diverse structures of MFPs are significantly influenced by the various extraction and purification methods applied to selected polysaccharides [49]. These structural variations contribute to distinct biological activities in polysaccharides [50]. The summarized MFPs structures have been categorized into six groups based on monosaccharide composition and glycosidic bond types [51]: glucan, glucomannan, xyloglucan, arabinoxylan, rhamngalacturonan II and heteropolysaccharides (Table 1). Research demonstrates that MFPs functionalities are substantially determined by their molecular characteristics, particularly their structural and compositional features. These encompass the quantity and type of monosaccharide units, glycosidic linkage patterns, weight-average molecular weight, and three-dimensional spatial arrangement [52]. The chemical complexity and structural heterogeneity of MFPs make complete structural elucidation at all levels particularly challenging. Thus, polysaccharide structural analysis remains among the most demanding tasks within glycoscience [53].

Currently, structural characterization is primarily conducted through a combination of instrumental and chemical analysis [54], including hydrolysis, Smith degradation, methylation analysis, periodate oxidation (HIO^4), gas chromatography-mass spectrometry (GC-MS), high-performance liquid chromatography (HPLC), size exclusion chromatography coupled with multi-angle laser light scattering and refractive index detection (SEC-MALLS-RI), Fourier-transform infrared spectroscopy (FTIR), and nuclear magnetic resonance (NMR) [55]. Despite these sophisticated methods, they frequently provide only tentative conclusions about polysaccharide structure, rather than definitive determinations of absolute configuration. The biological activities of polysaccharides correlate strongly with their weight-average molecular weight, chemical compositions, and monosaccharide profiles. For example, ginger pomace polysaccharides extracted by hot water (HW-GPPs) demonstrate higher weight-average molecular weight and protein content, along with lower total uronic acid content [56]. However, their monosaccharide compositions and sulfate contents remain similar to those of ginger pomace polysaccharides extracted using ultrasonic assistance (UA-GPPs). Significantly, UA-GPPs fractions contain higher levels of glucuronic acid and sulfate. The anti-oxidant activities of UA-extracted GPPs fractions

Table 1 The structural characterization and biological activities of MFPs.

Polysaccharide types	Source	Monosaccharide compositions (mass percentage or molar ratio)	*Mw* (Da)	Main chain composition	Bioactivities	Ref.
Glucan	Chinese Truffle *Tuber sinense*	Glc	7.3×10^5	*α*-1,6-Glu	Antioxidant	68
	Strongylocentrotus nudus Eggs	Glc	2.0×10^6	*α*-1,4-Glc	Immunomodulation	69
Xyloglucan	*Lycium barbarum* L.	Rha : Ara : Xyl : Glc : Gal in the ratio of 1.61 : 3.82 : 3.44 : 7.54 : 1.00	4.9×10^4	1,4-Gal, 1,3,6-Gal, T-Gal, T-Ara	Immunomodulation	70
	Mulberry leaf	Ara, Xyl, Glc, Rha, Man in ratio of 1 : 2.13 : 6.53 : 1.04 : 8.73	8×10^3	No mention	Antidiabetic, hypoglycemic and hypolipidemic	71
Glucomannan	*Mortierella hepiali*	Man : Gal : Glc in the ratio of 5 : 2 : 3	8.8×10^3	*β*-D-Manp, *β*-D-Glcp	Antitumor, immunomodulation	72
	Artemisia annua AAP01-1	Man : Rha : GlcA : Gla : Glu : Gal : Ara in the ratio of 1.2 : 1.6 : 0.6 : 0.8 : 1.4 : 3.1 : 1.3	2.0×10^5	1-Manp, 1-Araf	Antocomplement	45
	Hedyotis diffusa	Glc : Gal : Ara : Rha : GlcA : Man in the ratio of 2.7 : 9.4 : 5.0 : 1.3 : 1.0 : 4.6	7.4×10^5	1,4,6-Glcp, 1,3,4-Glcp, 1,4-Galp	Anti-complement	47
	Lycium barbarum	Ara : Rha : Xyl : Man : Gal : Glc in the ratio of 0.18 : 0.81 : 0.07 : 2.17 : 0.23 : 6.52	No mention	No mention	Prebiotic, immunomodulation,	73
Rhamngalacturonan II	*Ziziphus jujuba*	GalA and Rha in molar ratio of 8.1 : 1	2.0×10^6	No mention	Immunomodulation	74
	Panax ginseng C. A. Meyer	Gal : Ara : Rha : GalA in ratio of 13 : 7 : 4 : 76	7.2×10^5	*α*-1,4-Gal	Antitumor, immunomodulation, antioxidant	75
	Artemisia annua AAP01-2	Man : Rha : GalA : Glc : Gal : Glu in the ratio of 1.1 : 1.8 : 2.5 : 0.9 : 1.4 : 1.1	1.4×10^5	1-Glcp, 1,3-Rhap	Antocomplement	45
	Artemisia annua AAP01-3	Man : Rha : GalA : Glc : Gal : Glu in the ratio of 1.5 : 1.4 : 1.3 : 1.0 : 2.3 : 1.3	4.9×10^4	1-Glcp, 1- Araf	Antocomplement	45
Arabinoxylan	*Plantago asiatica* L.	Rha : Ara : Xyl : Man : Glc : Gal in the ratio of 0.05 : 1.00 : 1.90 : 0.05 : 0.06 : 0.10	1.8×10^6	*β*-1,4-Xylp	Anti-complementary	76
Heteropolysaccharide	Red ginseng	Glc : Gal in the ratio of 94.26 : 4.92	5.7×10^3	*α*-1,4-Glcp, *α*-1,4-Galp	Antioxidant, anti-inflammatory	46
	Lysimachia christinae Hance	Man : Rha : GlcA : Glc : Gal : Ara in the ratio of 1.00 : 3.00 : 11.62 : 1.31 : 1.64 : 5.24	2.1×10^4	1,4-*α*-GlcpA, 1,4-*α*-Glcp, 1,4-*β*-Rha, 1,3,5-*α*-Araf	Anti-complement, antioxidant	77
	Alhagi honey	Ara : Gal : Rha : Glu : Man in the ratio of 40 : 34 : 12.5 : 9.5 : 4.0	8.7×10^5	No mention	Hepatoprotective, anti-inflammatory, antioxidant	78

exceed those of HW-extracted variants. From *A. annua*, three homogeneous polysaccharides were purified (AAP01-1, AAP01-2, and AAP01-3) [45]. The varying anti-complementary effects of these three acidic heteropolysaccharides likely stem from differences in the quantity of galacturonic acid (GalA) present in their monosaccharide compositions.

Furthermore, the crude polysaccharides ILPS and ILPS-4, extracted from wintergreen, contained glyoxylate at 21.8% and 23.2%, respectively. These polysaccharides demonstrate significant hepatoprotective effects, with the elevated glyoxylate content potentially contributing to their strong hydroxyl radical scavenging activity [57]. Research indicates that polysaccharides rich in Ara (arabinose) and Gal (galactose) in their monosaccharide composition exhibit potent anti-oxidant properties [58]. Studies demonstrate that *Hovenia dulcis* polysaccharides (HDPS), which contain high levels of Gal and Ara, show strong anti-oxidant and hepatoprotective effects [59]. Additionally, polysaccharides with high Rha (rhamnose) content, such as MZPs isolated from *Pleurotus djamor* mycelium, demonstrate substantial anti-oxidant potential. These findings emphasize the direct relationship between polysaccharides' biological activities and their structural composition. The fine structures of typical MFPs are illustrated in Fig. 3.

To enhance polysaccharide bioactivity, researchers frequently employ chemical modifications including acetylation, sulfation, and carboxymethylation [60, 61]. For instance, the carboxymethylation of polysaccharides from the medicinal fungus Ganoderma applanatum significantly enhances anti-tumor activity against sarcoma *in vivo*, surpassing the effectiveness of native polysaccharides extracted from the fruiting bodies and submerged fermentation of *G. applanatum* [62]. Similarly, *Cyclocarya paliurus* polysaccharide, a representative plant-derived polysaccharide, demonstrates strong anti-oxidant activity in assays in-

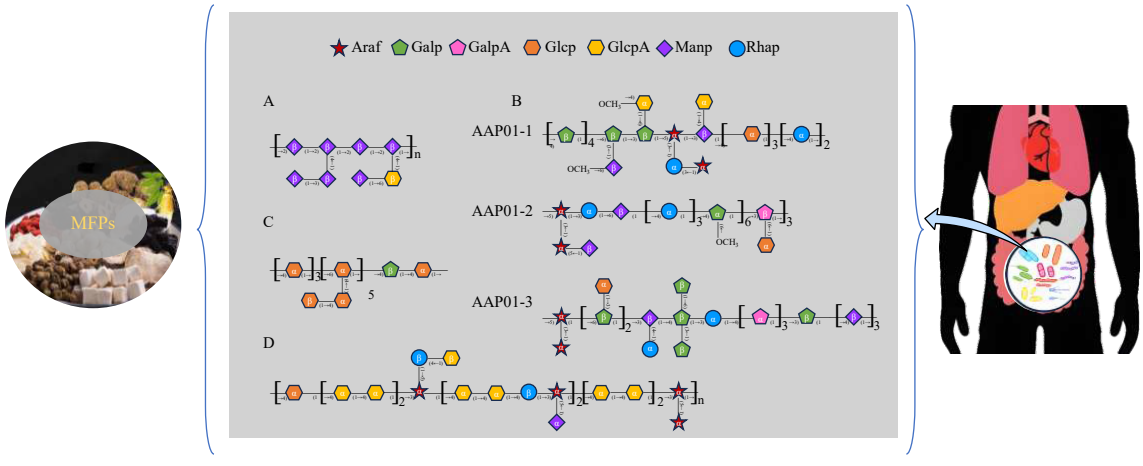

Fig. 3 The typical chemical structures of MFPs.

volving superoxide, hydroxyl, β-carotene linoleic acid, and DPPH radicals, with its sulfated form showing particularly enhanced effects [63, 64]. Compared to Chinese yam polysaccharides (CYP), sulfated Chinese yam polysaccharides (SCYP) demonstrate greater efficacy in reducing inflammatory factor secretion. Additionally, CYP associates with increased *Prevotella*, while SCYP correlates with increased *Coprococcus*. These distinct effects on intestinal flora regulation result from structural modifications following sulfation [65].

Furthermore, processing methods significantly affect polysaccharide structure and bioactivity [66]. Gu *et al.* investigated the changes in physicochemical properties and immunomodulatory capabilities of polysaccharides during the processing of *Polygonum multiflorum* Thunb (PM). Their analysis revealed marked differences in yield, weight-average molecular weight, and molar ratios of glucose to galacturonic acid (Glc/GalA) between processed PM polysaccharides (PPMPs) and raw PM polysaccharides (RPMPs). Notably, PPMPs with lower weight-average molecular weights demonstrated enhanced immunomodulatory effects compared to their unprocessed counterparts, illustrating the impact of processing on therapeutic efficacy [67].

5. Biological activities and applications of MFPs

Polysaccharides represent the most abundant macromolecular polymers in nature, occurring in various medicinal plants [79]. Extensive research has established the diverse biological activities of polysaccharides, which constitute primary bioactive components of natural plants. These activities include immunomodulation, anti-oxidant properties, anti-tumor effects, anti-inflammatory actions, anti-fungal capabilities, and intestinal flora regulation [80].

Research indicates that immunomodulation, inflammatory mechanism control, and oxidative stress reduction are fundamental therapeutic approaches for numerous diseases [81, 82]. Polysaccharides have attracted considerable attention in pharmaceutical development due to their diverse bioactivities. A growing number of MFPs are being developed into specialized healthcare products or cosmetics to address specific demographic needs, or are being utilized in chronic disease management. As a major class of biopolymers, polysaccharides play essential roles in various physiological processes, including tumor metastasis [80], immune system function, coagulation, fertilization, pathogenesis prevention, therapeutic efficacy, and intestinal barrier maintenance [83, 84]. This discussion examines MFPs as functional food components for disease treatment and prevention, emphasizing their interaction with gut microbiota. Table 2 provides a comprehensive overview of gut microbiota regulation by MFPs. The mechanism through which MFPs significantly influence host health and disease primarily relates to their interaction with gut microbiota, predominantly through stimulating microbial production of corresponding metabolites and generating related functional effects (Fig. 4).

5.1. Hypoglycemia

Diabetes, characterized by hyperglycemia, is a metabolic disorder resulting from inadequate insulin action or production [94, 95]. Type I and type II diabetes mellitus are the primary forms, with type II accounting for approximately 90% of cases [96]. Contemporary clinical diabetes treatments primarily utilize synthetic drugs, including sulfonylureas, thiazolidinediones, bisphosphonates, and α-glucosidase inhibitors, which frequently present various adverse effects [97, 98]. Additionally, newer medications targeting alternative pathways, such as DPP-4 inhibitors, SGLT-2 inhibitors, GPR 119 agonists, and GLP-1 analogs [99, 100], see limited clinical application due to cost and safety considerations. Research has demonstrated natural products' efficacy in diabetes management [101, 102]. The utilization of functional foods and supplements as synthetic drug alternatives for diabetes patients continues to increase. In China, several polysaccharides, including ginseng, pumpkin, astragalus, and konjac glucomannan, have been clinically implemented as drug alternatives for diabetes treatment. Fig. 5 illustrates the mechanisms through which polysaccharides contribute to diabetes treatment.

Diabetes exhibits strong associations with free radical accumulation, oxidative stress, and reactive oxygen species [103]. Oxidative stress can impair pancreatic β-cell function, induce insulin resistance, and reduce glucose tolerance. Peripheral tissues utilize oxidative stress-related enzymes, including glutathione peroxidase (GSH-PX), catalase (CAT), and superoxide dismutase (SOD), to combat oxidative stress damage. These enzymes additionally serve as ROS scavengers. Sun et al. [104] isolated and purified a novel polysaccharide, NAP-3, from *Naematelia aurantialba*. NAP-3 combined with metformin demonstrated therapeutic effects in treating diabetes in high-fat diet/streptozotocin-induced diabetic mice and insulin-resistant HepG2 cells, suggesting potential applications for *Naematelia aurantialba* polysaccharides as diabetes adjuvant therapy. While type II diabetes research predominates, Yang et al. [105, 106] established that *Astragalus* polysaccharide alleviates type I diabetes through intestinal microbiota regulation in mice, providing theoretical support for type I diabetes treatment. RGP demonstrates significant anti-inflammatory effects in diabetic rats, indicating potential as an insulin production stimulant and diabetes treatment option. Wang *et al.* isolated GPP polysaccharide from *Gynostemma pentaphyllum*, which at 200, 400, and 800 $\mu g \cdot mL^{-1}$ concentrations, elevated pro-inflammatory factors TNF-α and IL-6 while reducing anti-inflammatory factors IL-4 and IL-10 [107]. Furthermore, GPP enhanced GSH-PX, CAT, and SOD activities, contributing to its hypoglycem-

Table 2 Effects of MFPs on intestinal flora.

Origin of polysaccharide	Polysaccharide name	Disease treated	Changes in intestinal flora	Ref.
Cordyceps cicadae	CH-P	Diabetic	*Bacteroides*↑, *Odoribacter*↑, *Alloprevotella*↑, *Parabacteroides*↑, *Mucispirillum*↑, *Helicobacter*↓, *Lactobacillus*↓	85
Auricularia auricula	AAP	Hyperlipidemia	*Flavonifractor*↑, *Clostridium IV*↑	86
Asparagus officinalis	ASDF	Hyperlipidemia	*Muribaculaceae*↑, *Bacteroides*↑, *Alloprevotella*↑, *Desulfobacterota*↓, *Proteobacteria*↓, *Actinobacteriota*↓	87
Hericium erinaceus	HEP10	Colitis	*Akkermansia muciniphila*↑, the phylum *Proteobacteria*↓	88
Lonicerae flos	LP	Immunosuppression	*Muribaculaceae*↑, *Lachnospiracea*↑, *Ruminococcus_2*↑	89
Tibetan tea	GTTE	Type 1 diabetes	*Bacteroidetes* ↑, *Actinobacteria* ↓	90
Glycyrrhiza Uralensis	GCP	Tumor	*Enterorhabdus*↑, *Odoribacter*↑, *Enterococcus*↑, *Ruminiclostridium_5*↑, *Ruminococcaceae_UCG_014*↑, *Ruminococcaceae_UCG_010*↑, *Parasutterella*↓, *Clostridium_sensu_stricto_1*↓, *Blautia*↓	91
Mulberry leaf	MLO 2-1	Type 2 diabetes	*L. murinus*↑, *Aerococcus urinaeequi*↑	92
Lycium barbarum	LBPs	Immunosuppression	*Lachnospiraceae*↑, *Ruminococcaceae*↑, *Enterobacteriaceae*↑, *Rikenellaceae*↓, *Bacteroidaceae*↓, *Prevotellaceae*↓	93

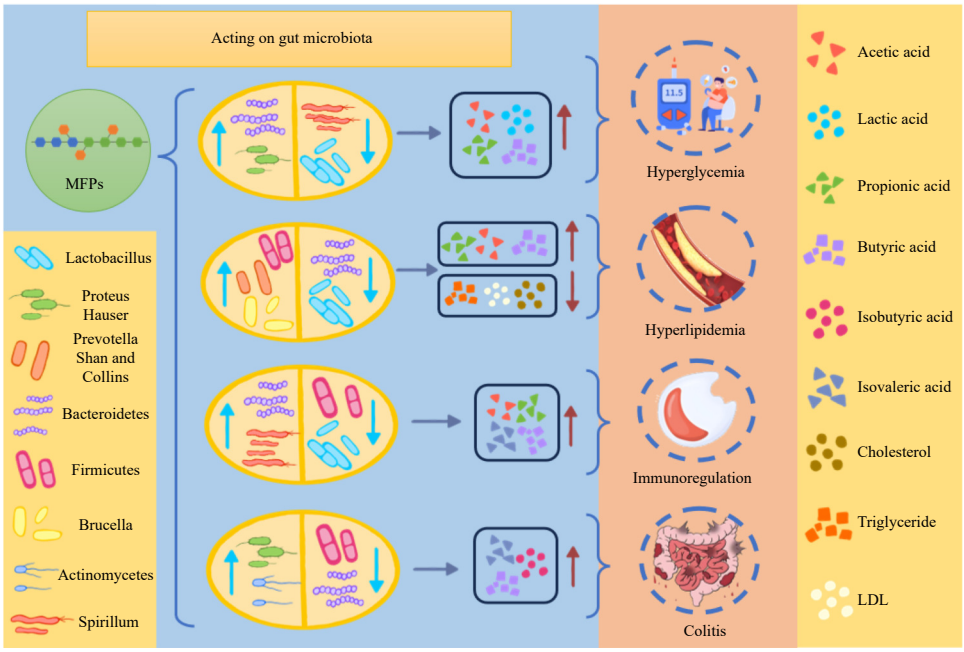

Fig. 4 MFPs regulate gut microbiota and its related metabolites.

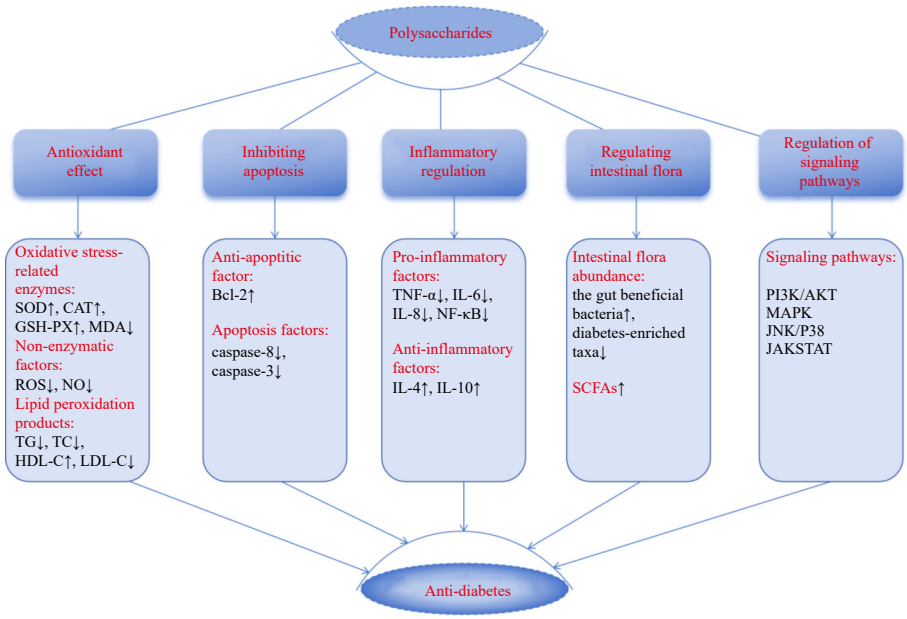

Fig. 5 Mechanisms associated with the treatment of diabetes by MFPs.

ic effects.

Disruption of gut flora balance can compromise intestinal barrier function and contribute to metabolic diseases such as diabetes by modifying the composition or quantity of microflora and disturbing the organism's internal and external environment [108]. *Grifola frondosa* polysaccharide (GFP) demonstrates the capacity to modify intestinal flora composition and enhance the survival environment of intestinal microorganisms [109]. Daily administration of 900 mg·kg^{-1} of GFP substantially decreased the relative abundance of *Alistococcus*, *Staphylococcus*, *Enterococcus*, and *Streptococcus*, while elevating the relative abundance of *Alistipes*. Therefore, GFP may improve hyperglycemia and hyperlipidemia through intestinal flora modulation. *Lycium barbarum* polysaccharide (LBP) enhanced the abundance of *Bacteroidetes* and *Cyanobacteria*, while reducing the abundance of *Firmicutes*, *Deferribacteres*, and *Tenericutes* at a dose of 400 mg·kg^{-1}·d^{-1} [110]. This modification may enhance diabetes-associated gut microbiota through toll-like receptor 2 (TLR2) in the gut barrier. *Apocynum venetum* polysaccharide (AVP) elevated the abundance of *Enterococcus*, *Bacteroides*, and *Parabacteroides*, regulated the abundance of two novel intestinal flora, *Aerocuccus* and *Klebsiella*, and improved insulin resistance and diabetes, thus alleviating metabolic disorders induced by insulin resistance and inflammation in the gut flora [111].

Diabetes commonly presents with various complications, including non-alcoholic fatty liver disease (NAFLD) and diabetic nephropathy [112]. Research has demonstrated that quercetin alleviates NAFLD induced by diabetes [113,114]. In diabetic mice models, the triterpenic acid fraction from *Cyclocarya paliurus* has been shown to reduce kidney damage through the AMPK-mTOR-regulated autophagy pathway [101]. These findings highlight the substantial potential of natural products in addressing diabetic complications. Nevertheless, research regarding the therapeutic application of medicinal polysaccharides for these conditions re-

mains limited, indicating an emerging and important direction for future research.

5.2. Hypolipidemic

Blood lipids comprise various fatty substances circulating in the bloodstream, primarily including cholesterol, triglycerides (TG), phospholipids, and free fatty acids. The term "hypolipidemic" refers to the reduction of blood lipid levels, particularly harmful components such as cholesterol and TG, through interventions including dietary modifications, lifestyle changes, or pharmacological treatments. Hyperlipidemia represents a major risk factor for atherosclerosis and cardiovascular diseases, including coronary heart disease, myocardial infarction, and stroke, and correlates with certain metabolic disorders and inflammatory responses within the body [115]. Therefore, effective blood lipid management is essential for optimizing metabolic health. Patients with hyperlipidemia often present with gut microbiota dysbiosis, which may exacerbate lipid metabolism disorders, potentially creating a detrimental cycle of increasing dysbiosis and metabolic dysfunction [116].

Inonotus obliquus polysaccharide (IOP) has been shown to effectively reduce the levels of TC, TG, and low-density lipoprotein cholesterol (LDL-C) in hyperlipidemic rats, while significantly increasing high-density lipoprotein cholesterol (HDL-C) levels [117]. Additionally, IOP treatment resulted in increased *Verrucomicrobia* and *Bacteroidetes*, decreased *Firmicutes*, and reduced *Firmicutes*/*Bacteroidetes* ratio compared to the model group (MG). Similarly, polysaccharides from *Tibetan Brassica* rapa L. have demonstrated improvement in intestinal barrier function integrity, reduction of intestinal mucosal damage, and modulation of gut microbiota by promoting beneficial bacteria growth associated with hyperlipidemia management, suppressing harmful bacteria proliferation, and facilitating short-chain fatty acid (SCFA) metabolism [118]. Moreover, studies indicate that polysaccharides can act as prebiotics, selectively modulating gut microbiota structure and function. This modulation enhances SCFA production, reduces inflammatory cytokine levels, and consequently improves the host's physiological condition [119].

5.3. Immunity function

External factors frequently trigger immune diseases, highlighting the essential role of immune system regulation in human health. While chemical drugs are employed for immune regulation, they frequently demonstrate limited effectiveness, substantial side effects, and insufficient therapeutic benefits for immunosuppressive and viral infectious diseases [120]. Traditional Chinese medicine, however, incorporates various bioactive components, including flavonoids, polysaccharides, glycosides, and alkaloids, which demonstrate immunomodulatory properties. These natural compounds effectively enhance immune function and reduce viral damage within the body [121]. Notably, polysaccharides have been extensively studied for their immunomodulatory effects. The immunological activity of *Lonicerae Flos* polysaccharide appears to function through enriching beneficial gut bacteria, subsequently increasing SCFA levels, particularly butyric acid. This enhancement regulates the differentiation and function of both innate and adaptive immune cells, stimulating cytokine and immunoglobulin expression [89].

Studies have demonstrated that LBP administration modulates gut microbiota in mice, enhancing the abundance of *Aspergillus phylum* and *thick-walled phylum* while decreasing *Anaplasma phylum* proportions. At 400 mg·mL^{-1}, LBP notably increased serum TGF-β and IL-6 levels, along with colonic secretory IgA (sIgA) content in mice. These results indicate LBP's potential as a prebiotic, capable of enhancing gut microbiota, increasing beneficial bacteria populations, and modulating innate immune responses [73]. Research indicates that polysaccharides can modify the immunological environment of small intestinal mucosa, affecting intestinal flora distribution and TLR/NF-κB signaling pathway activity, subsequently influencing small intestinal paracellular absorption [50, 122]. Galli Gigeriae Endothelium Corneum (GGEC), containing abundant proteins and polysaccharides, demonstrates gastrointestinal barrier protection by strengthening intercellular connections and reducing inflammatory responses, without compromising RAW264.7 cells [123]. Huo et al. [45] isolated three homogeneous polysaccharides from *Astragalus*, named AAP01-1, AAP01-2, and AAP01-3, containing GalA contents of 8%, 28%, and 15%, respectively. These branched-chain acidic heteropolysaccharides exhibit potent anticomplementary activity, with AAP01-2's effectiveness potentially linked to its high GalA content. Furthermore, Zhang et al. [47] revealed that *Hedyotis diffusa* polysaccharides demonstrate anticomplement activity, possibly through inhibiting neutrophil recruitment, complement activation, and extracellular matrix (NET) production. Polysaccharides from *Lysimachia christinae* Hance have similarly demonstrated anti-complement activity [77].

5.4. Anti-colitis

Chronic, non-specific inflammatory bowel disease (IBD) patients typically present with symptoms including diarrhea, hematochezia (blood in the stool), abdominal pain, and mucopurulent toxins. When the condition progresses without timely treatment, complications may develop, including anemia, cachexia, hypoproteinemia, and water-electrolyte imbalances [124]. The intestinal microbiota maintains a complex relationship with IBD's multifactorial etiology and pathogenesis, which includes immune system dysfunction, genetic factors, environmental influences, and psychological stressors [125-127]. A critical factor in colitis development involves the disruption of intestinal immune homeostasis, characterized by an imbalance between immune response and tolerance, resulting in excessive and uncontrolled immune reactions. Traditional IBD treatments, including corticosteroids, monoclonal antibodies, aminosalicylic acid derivatives, and immunomodulators, frequently result in adverse effects and inadequate clinical outcomes [128, 129].

In recent years, polysaccharides derived from various natural sources, including plants, animals, and microorganisms, have emerged as safe, effective, non-toxic, economical, and biocompatible agents. These compounds provide a non-invasive oral administration route, minimizing patient discomfort and improving compliance. Polysaccharides influence IBD through multiple mechanisms, including modulation of inflammatory cytokines, immune system function, intestinal microbiota, and adhesion to colonic ulcerative lesions. For instance, garlic polysaccharides regulate intestinal flora by increasing the population of *Lactobacillus* and *Lachnospiraceae* and decreasing that of *Facklamia* and *Firmicutes* at a dosage of 400 mg·kg^{-1} [130]. Similarly, yam polysaccharides and inulin modulate intestinal microbiota composition and reduce oxidative stress, thereby ameliorating colitis in rats induced by 2,4,6-trinitrobenzenesulfonic acid (TNBS) [131]. Research has demonstrated that intestinal microbiota can ferment dietary fiber, a common plant polysaccharide, into gas and SCFAs, which inhibit pathogenic microbe growth [132]. At a concentration of 1% (*W/V*), potato fiber exhibits prebiotic properties, protecting probiotic *Lactobacillus* strains and maintaining gut flora balance [133]. The mucosal layer covering the colon's surface contains polysaccharides that adhere to mucosal tissues, extending their local retention time [134] and maintaining therapeutic efficacy, thus facilitating ulcer surface healing. Medicine and food paired (MFP) polysaccharides create an environment unfavorable for potentially pathogenic Gram-negative bacteria by increasing intestinal

pH and enhancing SCFA production, including acetic, butyric, and propionic acids [135]. Tang et al. [11] examined the effects of combined *Astragalus* and *Codonopsis* polysaccharides (AERP 600 mg·kg^{-1}·d^{-1} + CERP 300 mg·kg^{-1}·d^{-1}) on ulcerative colitis in mice. Their findings, obtained through histo-immunology, ELISA assays, and bacterial colony analysis, demonstrated significant impact on colitis. This research provided additional insights into the mechanism of action, regulation of fecal SCFA production, changes in gut microbiota structural presentation, and effects on intestinal microbiota abundance.

6. Conclusions and outlook

Polysaccharides, recognized for their diverse and potent biological activities, have attracted considerable attention in functional food development. However, a comprehensive review of research on MFPs remains insufficient. MFPs demonstrate various biological effects, including anti-oxidant properties, immunomodulation, hypoglycemia, hepatoprotection, anti-aging capabilities, and radioprotection. These multiple activities present numerous opportunities for incorporating MFPs into functional food products. This review presents a thorough analysis of MFPs research advancements, encompassing extraction and purification techniques, structural characterization, and biological activities. The oral consumption of polysaccharides as food components particularly highlights the essential role of gut microbiota in their functional efficacy. The mechanisms through which MFPs exert their effects have been substantially elucidated from immune response modulation, inflammatory mechanism control, oxidative stress mitigation, and their interaction with gut microbiota, illuminating their role in modulating host health and disease (Fig. 6).

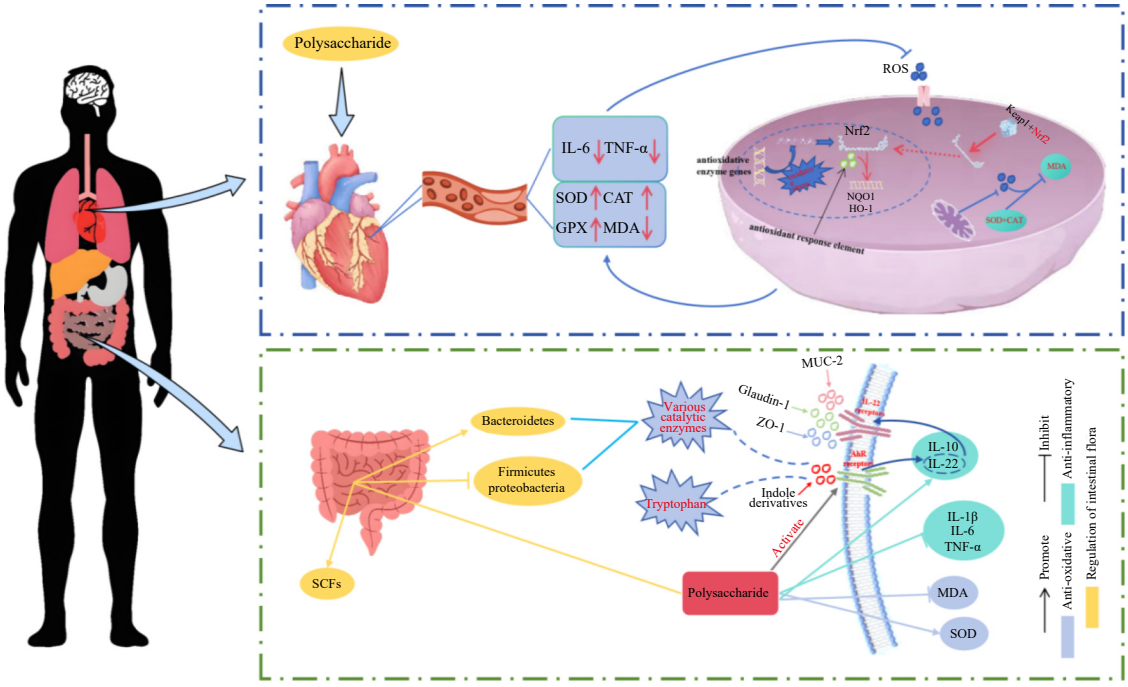

Fig. 6 Mechanisms associated with the treatment of diseases by MFPs.

The gut microbiome, comprising a complex community of microorganisms in mammalian intestines, substantially influences human health and disease by regulating various physiological processes, including essential nutrient biosynthesis, dietary fiber digestion, gut-brain axis regulation, and host immune system modulation. Gut microbiota metabolites serve as key mediators in regulating these biological pathways, frequently through specific host receptor engagement. This interaction is fundamental for understanding how polysaccharides, as dietary components, influence host health through gut microbiota modulation. The investigation of MFPs' effects on gut microbiota and their subsequent impact on immune function and other biological activities represents a promising research direction, providing insights into their therapeutic potential and functional food applications. Understanding these mechanisms is crucial for developing prophylactics and therapeutics for treating numerous inflammatory diseases affected by gut microbiota. The research on MFPs continues to advance significantly in understanding their multifaceted roles in health and disease. The exploration of MFPs' effects on gut microbiota and their consequent impact on immune function and other biological activities offers valuable insights into their therapeutic potential and applications in functional foods.

Despite the extensive potential applications of MFPs, their research and practical utilization face several significant challenges [136]. A primary concern involves the innovation and advancement of extraction and purification technologies. Polysaccharides, characterized by their complex structures, high weight-average molecular weights, and heterogeneous distributions, present significant extraction challenges using conventional methods such as acid-base or HWE, which may compromise their structural integrity. Contemporary extraction techniques, including UAE, microwave-assisted extraction, and enzymatic extraction, offer promising approaches to enhance extraction efficiency and polysaccharide purity. However, these methods require additional optimization and broader implementation in practical applications. Furthermore, a comprehensive understanding of the biological activities and mechanisms of action of medicinal polysaccharides remains incomplete. While numerous studies have established their diverse biological functions, the underlying mechanisms require thorough elucidation. Understanding the molecular mechanisms of action of plant polysaccharides is essential for maximizing their medicinal potential and developing targeted therapeutic strategies.

The trajectory of research and development for MFPs should focus on several critical areas. Primary emphasis should be placed on investigating the structure-function relationship of

these polysaccharides [137]. The molecular structure of polysaccharides correlates directly with their biological activity, with significant variations observed in structure and function across different sources and extraction techniques. Through advanced separation and purification techniques and analytical methods such as high-resolution MS and NMR, detailed analysis of polysaccharide fine structure and exploration of functional relationships will establish a theoretical foundation for targeted modification and functional optimization. Additionally, promoting large-scale production of medicinal and food polysaccharides and advancing application technology research represents a crucial developmental direction. Currently, the high production costs of natural plant polysaccharides limit their widespread application. Future efforts must focus on developing efficient, cost-effective production processes and establishing standardized procedures to ensure consistent product quality. Simultaneously, research should accelerate the application of polysaccharides in medicine, food, agriculture, and environmental protection, promoting the transformation and industrialization of scientific achievements. Finally, emphasis should be placed on multidisciplinary cross and synergistic innovation [138]. The research of medicinal and food polysaccharides encompasses multiple disciplines including botany, chemistry, biology, and medicine, necessitating interdisciplinary collaboration. For instance, utilizing bioinformatics and artificial intelligence to construct molecular network mappings of polysaccharide action reveals deeper biological regulatory mechanisms, while integration with nanotechnology enables development of polysaccharide-based nanomedicine carriers to enhance drug targeting and bioavailability.

As a vital natural resource, medicinal polysaccharides demonstrate extensive application potential and research value. Through innovative extraction and purification techniques, comprehensive research on biological activities and mechanisms, advancement of large-scale production and application technology, and multidisciplinary synergistic innovation, future research on plant polysaccharides will achieve new breakthroughs and deliver significant contributions to human health and sustainable development.

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Declaration of competing interest

These authors have no conflict of interest to declare.

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