Food & Medicine Homology

ISSN 3006-6867 (print); 3006-4252 (online)
https://doi.org/10.26599/FMH.2025.9420040

Review Article

Research progress on structural characterization and bioactivities of *Poria cocos* and *Ganoderma* polysaccharides

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Received: 27 July 2024 / **Revised:** 2 August 2024 / **Accepted:** 3 August 2024

Abstract: *Poria cocos*, *Ganoderma lucidum*, and *Ganoderma sinense*, as the famous medicine and food homologous fungal, has been used as traditional Chinese medicine for a long history. Polysaccharide is one of the most important bioactive ingredients of *P. cocos* and *Ganoderma,* which possess a wide range of biological activities including immunomodulation, anti-tumor, anti-inflammation, antioxidative stress, modulation of gut microbiota properties, etc. This review systematically recapitulates the recent advances in the extraction and purification methods, structural characterization, biological activities, synthesis of derivates, and potential application of polysaccharides derived from *P. cocos* and *Ganoderma*. Therefore, the information provides a reference point for the in-depth development of medicinal value and health functions of medicine and food homologous fungal polysaccharides and their resource utilization.

Keywords: *Poria cocos*; *Ganoderma lucidum*; *Ganoderma sinense*; polysaccharides; structural characterization; bioactivities

Citation: 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: 9420040. https://doi.org/10.26599/FMH.2025.9420040

1 Introduction

Poria cocos and *Ganoderma* belong to Polyporales, having a long history of medicinal use in China[1,2]. According to the traditional Chinese medicine theory, *P. cocos* and *Ganoderma* can maintain homeostasis of the internal environment, reduce the occurrence of diseases, and prolong life by regulating the physiological functions of various organs in the human body[3-5]. Besides, *P. cocos* and *Ganoderma* are widely integrated into the daily diet, reflecting the concept of "medicine and food homology". *P. cocos* was recorded in the directory of medicinal and edible homology in China in 2002, while *Ganoderma*, including *G. lucidum* and *G. sinense*, was recorded in 2023. *P. cocos* and *Ganoderma* both exhibit a similar morphology, characterized by the presence of mycelium and fruiting bodies. Instead, the mycelium of *P. cocos* forms dense sclerotia used to store nutrients[6].

Through the progress of science and technology, researchers have discovered that polysaccharides, the primary constituents of *P. cocos* and *Ganoderma* (account for 70%~80%)[1,2], exhibit a wide range of biological activities (Fig. 1), such as immunomodulation and anti-tumor activity, anti-inflammation activity, antioxidative stress activity, and modulation of gut microbiota[7-10]. The potential role of *P. cocos* and *Ganoderma* polysaccharides in the application of various diseases has been continuously developing, providing the possibility for disease therapy. The structure of *P. cocos* polysaccharides is mainly 1,3-linked glucan. The monosaccharide analysis shows that *P. cocos* polysaccharides are also composed of fucose[1]. Similarly, the polysaccharide from *Ganoderma* comprises 1,3-glucans as a backbone with the terminal fucose residues[2]. It is worth noting that the bioactivity of *P. cocos* and *Ganoderma* polysaccharides is proportional to the water solubility, and the greater the water solubility, the more significant the bioactivity[3-5]. The anti-tumor effect of *P. cocos* polysaccharides is more closely related to its solubility in water. Therefore, the anti-tumor effect of *P. cocos* polysaccharides can be further increased by the derivation into insoluble *P. cocos* polysaccharides and connecting with hydrophilic groups[4]. The 1,3-glucan from *Ganoderma* possess significant bioactivities, relating to its spatial structure. The *Ganoderma* polysaccharides with a three-strand helical structure has a significant anti-tumor effect on tumor cells[3]. At the same time, as medicine and food homologous fungal polysaccharides, its development in nutritious food (or functional food) is also hot. This paper reviews the chemical structure, biological activity, and structure-activity relationship of medicinal and edible homologous fungal polysaccharides (mainly *P. cocos* polysaccharides and *Ganoderma* polysaccharides) in the past five years to provide some

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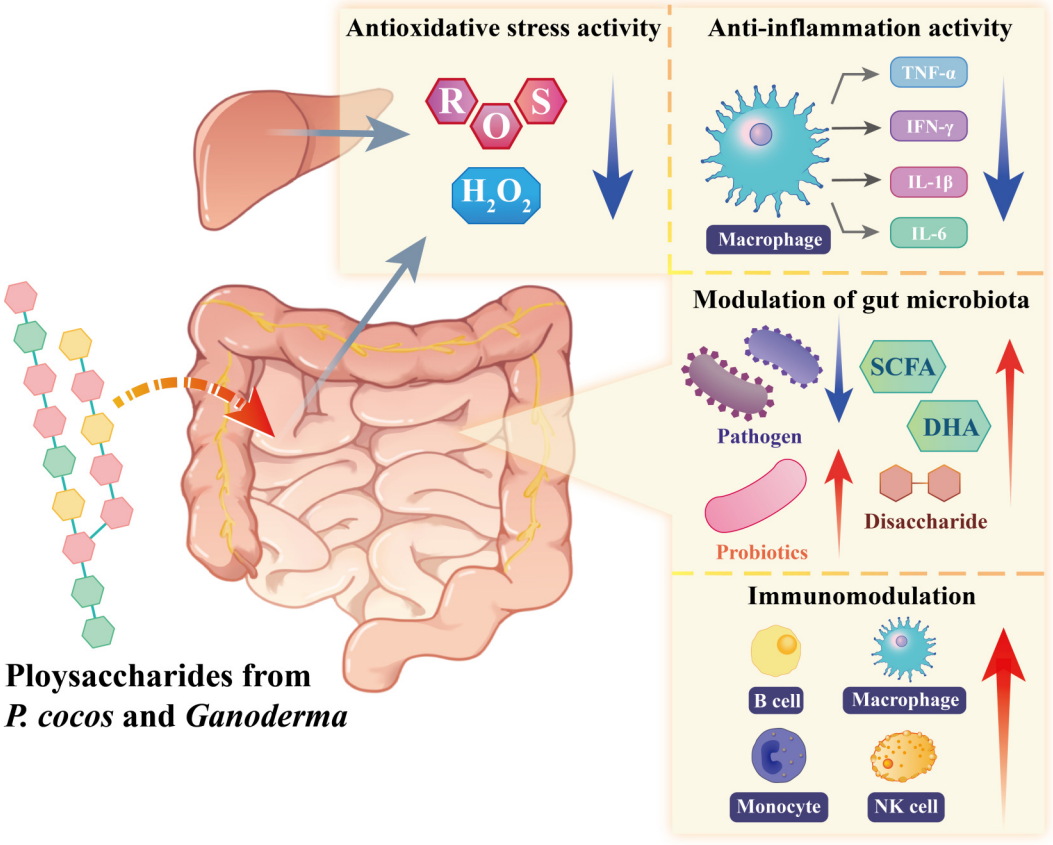

Figure 1 Diversified bioactivities of polysaccharides from *P. cocos* and *Ganoderma*. DHA: docosahexaenoic acid, ROS: reactive oxygen species, SCFA: short-chain fatty acids.

guidance for future research. The review hopes to promote the wide application and dissemination of medicinal and food homologous fungal polysaccharides such as *P. cocos* and *Ganoderma* in the health, pharmaceutical, food, and other industries, and to attract more emerging scholars to pay attention to the industrial development and pharmacological activities of general practitioners.

2 Extraction and purification of polysaccharides from *P. cocos* and *Ganoderma*

Currently, the polysaccharide extraction techniques including hot water extraction, alkali extraction, acid extraction, supercritical fluid CO_2 extraction, microwave-assisted extraction, ultrasound-assisted extraction, enzyme extraction, ultrahigh pressure extraction, etc. The hot water extraction is a classic and extensively applied in laboratories, but the yield is low[4]. The procedures for extraction of polysaccharide are summarized as follows: defatting is commonly performed using ethanol, the plant was soaked in 95% ethanol to remove lipid-soluble substances. After pretreatment the residues further extracted by different extraction methods. The extraction solutions were concentrated by vacuum rotary evaporation, which was followed with different concentrations of ethanol to precipitate the polysaccharides at 4 °C for 24-48 h. After the precipitate was collected by centrifugation, deproteinized by the Sevag method for several times, and followed by lyophilization, the crude polysaccharides were obtained.

Following deproteinization, crude polysaccharides require further separation and purification process to gain a homogenous polysaccharide for structural analysis. Ion exchange chromatography and gel filtration chromatography as an efficient isolated technique for purifying polysaccharides. The ion exchange chromatography (DEAE-52, DEAE-Cellulose, DEAE-Sepharose, DEAE-Sephadex, etc.) is utilized to differentiate between neutral and acidic polysaccharides from crude polysaccharides based on the reversible charge interaction. The gradient elution is deionized water and a series of sodium chloride (NaCl) solutions, and monitor by the phenol sulfuric acid colorimetric method, and the absorbance at 490 nm was measured[11]. The gel filtration chromatography (Sephadex G-75, Sephacry S-100, Sepharose GL-4B, etc.) is utilized for isolation based on the molecular sieve principle. Table 1 lists the extraction and purification of polysaccharides from *P. cocos* and *Ganoderma*.

P. cocos powder was extracted with distilled water at 95 °C, followed by precipitation with four volumes of 95% ethanol at 4 °C for 24 h (yield 1.1 ± 0.2%). Subsequently, the main fraction *P. cocos* polysaccharide was isolated through DEAE-52 chromatography and further purified by Sephacryl S-100 HR to obtain PCP-1 (yield ≈ 0.11%) and PCP-2 (yield ≈ 0.11%)[12]. The crude water-soluble polysaccharides (GLSP) were extracted from *G. luciduma* spore by hot water and the yield was calculated to be 2.02 ± 0.15%. The leading polysaccharide fraction (GLSP-I) was collected after purification by DEAE Sepharose Fast Flow column and Sephadex G100 column[13]. The crude polysaccharide was isolated from *G. sinense* by 0.5 mol/L sodium hydroxide solution. Following ethanol precipitation, deproteinization, dialysis and freeze-drying, GSPB70-S was obtained on a DEAD Sepharose Fase Flow column by anion-exchange chromatography[14]. A schematic diagram of the extraction and purification of process of polysaccharides from *P. cocos* and *Ganoderma* is shown in Fig. 2.

Table 1 Extraction, separation, and purification of polysaccharides from *P. cocos* and *Ganoderma*

Name	Source	Extraction method	Temperature (°C)	Deproteinization	Purification method	Yield	References
Poria cocos							
PCP-2	Sclerotium	Water extraction and alcohol precipitation	95	Sevag method	Cellulose DEAE-52 and Sephacryl S-100HR column	0.32%	[12]
PCP	Sclerotium	Water extraction and alcohol precipitation	100	Sevag method	DEAE-cellulose and Sephacryl S-400HR column	ND	[9]
CMP33	ND	Alkali extraction and ethanol precipitation	Room temperature	ND	DEAE-52 and Saphadex-G200+ Saphdex-G150 column	ND	[15]
EPS-0M EPS-0.1M IPS-0M IPS-0.1M	Culture Supernatant and mycelium	Water extraction and alcohol precipitation	80	ND	DEAE-650M and Saphadex-G100 column	ND	[16]
FMGP	Mycelia	0.1 mol/L sodium acetate, containing cysteine, papain, and EDTA and ethanol precipitation	60	ND	Column of Fractogel BioSec 10^3×1.3 cm (Merck)	ND	[17]
PCWPW PCWPS	ND	Water extraction and alcohol precipitation	ND	ND	DEAE-52 cellulose column	ND	[18]
PCP-1	ND	Deep eutectic solcent and alcohol precipitation	100	Sevag method	Sephadex G-15 column	ND	[19]
PCP-1C	Sclerotium	Water extraction and alcohol precipitation	65	Sevag method	Cellulose DEAE-52 and Sephacryl S-500 column	ND	[20]
PCP1C	Sclerotium	Water extraction and alcohol precipitation	65	Sevag method	Cellulose DEAE-52 and Sephacryl S-500 column	ND	[21]
WIP	Sclerotium	Extracted with 0.75 mol/L NaOH and alcohol precipitation	100	ND	ND	39.8%	[22]
PCP-W1	Sclerotium	Water extraction and alcohol precipitation	60	Sevag method	Cellulose DEAE-52 and Sephacryl S-300HR column	ND	[23]
Ganoderma lucidum							
WSG	ND	Purchased from Wynlife Healthcare Inc.	ND	ND	ND	ND	[24]
MPN	Mycelia	Water extraction	Room temperature	ND	DEAE-Sepharose Fast Flow and Sephadex G-100 column	4.0%	[25]
GLSP-Ⅰ	Spore	Water extraction and alcohol precipitation	100	ND	DEAE Sepharose Fast Flow and Sephadex G100 column	2.02±0.15%	[13]
GLP70-1-2	Dried fruiting body	Water extract and alcohol precipitation	90	Sevag method	DEAE-52 Cellulose and Sephacryl S-100 column	1.14	[26]
FXM	Dried fruiting body	Alkaline extract	100	ND	Treated with cationic resin	ND	[27]
GLP100 GLP10 GLP1	Fruiting body	Extracted by hot water and graded by 100 kDa, 10 kDa and 1 kDa ultrafiltration membranes	ND	Sevag method	DEAE Sepharose fast flow chromatography	ND	[28]
Ganoderma sinense							
GSBP-2	Fruiting bodies	Extracted with 0.3 mol/L NaOH solution and alcohol precipitation	Room temperature	Sevag method	DEAE-cellulose 52 and sephacryl S-100 column	4.78%	[29]
GSPB70-S	ND	Extracted in 0.5 mol/L NaOH solution and alcohol precipitation	Room temperature	Sevag method	DEAE Sephrose Fast Flow column	ND	[14]

3 Structural characterization of polysaccharides from *P. cocos* and *Ganoderma*

The structural characteristics of polysaccharides are including primary and advanced structure, commonly contains molecular weight, monosaccharide composition, the pattern and locations of glycosidic linkages, backbone and branch structure, spatial configuration, etc. The analysis of polysaccharide structures by analytical equipment such as high performance gel permeation chromatography (HPGPC), high performance liquid chromatography (HPLC), UV-visible spectroscopy (UV), fourier transform infrared spectroscopy (FT-IR), gas chromatography-mass spectrometer (GC-MS), nuclear magnetic resonance (NMR), scanning electron microscopy (SEM), atomic force microscopy (AFM), and circular dichroism (CD). Table 2 list the structural characterization of polysaccharides from *P. cocos* and *Ganoderma*.

3.1 Molecular weight

Molecular weight (Mw) analysis plays an important structural information and was used to determine by HPGPC, high performance size exclusion chromatography (HPSEC), matrix-assisted laser desorption (MALDI), and multi-angle laser light scattering (MALS). Mw is represented by the weight average molecular weight, number-average molecular weight (Mn) is represented by the number average molecular weight, and polydispersity index (PI) is represented by the ratio of Mw to Mn (Mw/Mn). Generally, pure polysaccharides usually shows a single symmetrical narrow peak in the HPGPC spectrum diagram and PI is close to HPGPC was used to detect its molecular weight with dextran of different molecular weights as standards. The equation of the standard curve was obtained with the retention time as the abscissa and the logarithm of the average molecular weight as the ordinate. PCP-1 had a homopolysaccharide isolated from *P. cocos*

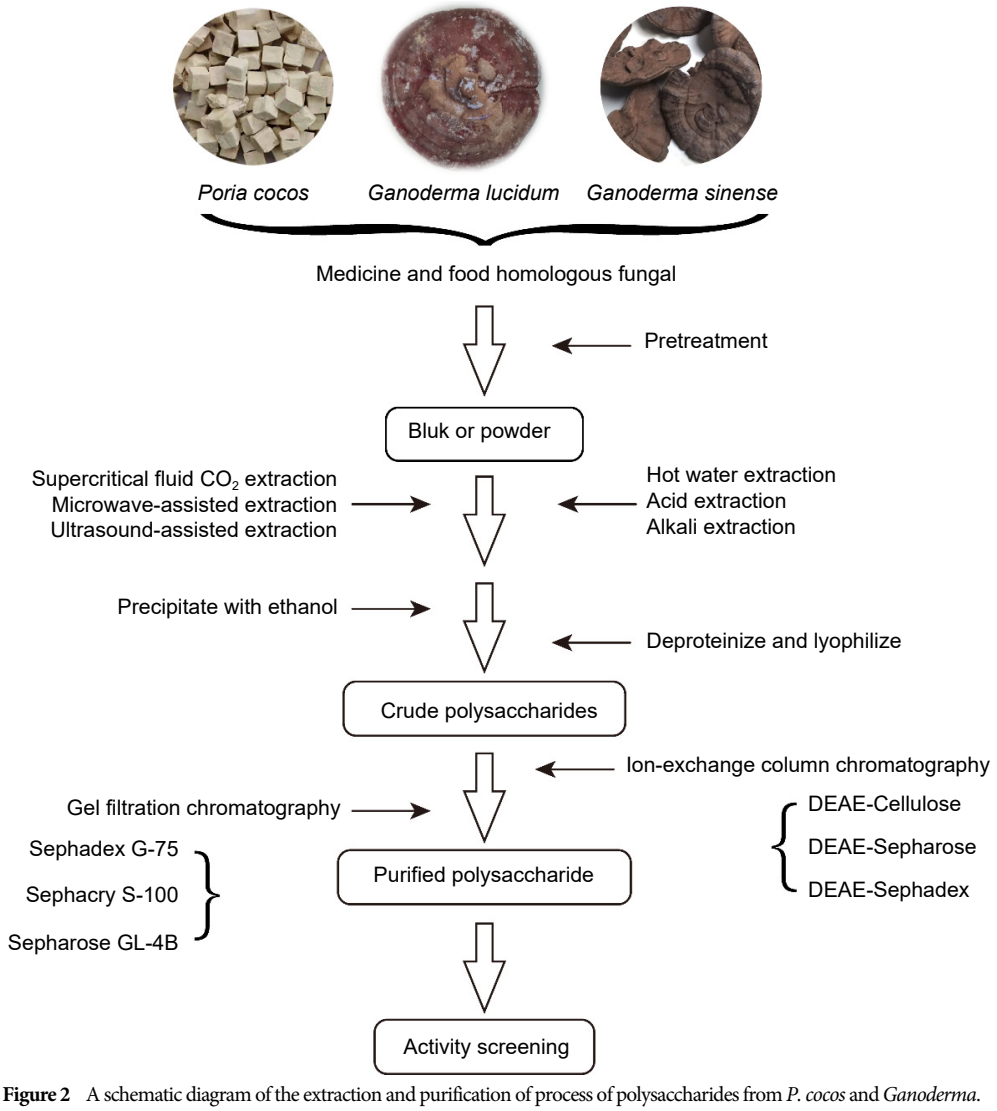

Figure 2 A schematic diagram of the extraction and purification of process of polysaccharides from *P. cocos* and *Ganoderma*.

powder. The equation was $y = -1.2237x + 14.685$, $R^2 = 0.9967$, the retention time of PCP-1 was about 11.44 min, and its molecular weight was 3.2 kDa calculated based on the above regression equation[19]. WSG, a water soluble glucose-rich polysaccharides, was isolated from the raw material of *G. lucidum* polysaccharides solution (named GLPs: F3). WSG was separated by HPSEC to give one major fraction, and Mw value of WSG was determined to be approximately 1,000 kDa[24].

3.2 Monosaccharide compositions

At present, HPLC, GC, and high performance anion exchange chromatography (HPAEC) are one of the main methods for the analysis of monosaccharide compositions of polysaccharides. In general, the HPLC using 1-phenyl-3-methyl-5-pyrazolone (PMP) as a pre-column derivatization reagent has been widely used for the monosaccharide compositions analysis[30]. The standard monosaccharide was contained of mannose (Man), rhamnose (Rha), glucuronic acid (GlcA), galactocuronic acid (GalA), glucose (Glc), galactose (Gal), xylose (Xyl), arabinose (Ara), ribcose (Rib), glucosamine (GlcN), fucose (Fuc), galactosamine (GalN), acetylglucosamine (GlcNAc), mannuronic acid (ManA), etc. A galactoglucan (PCP-1C) was purified from *P. cocos* sclerotium. The monosaccharide composition of PCP-1C was determined by the ion chromatographic (IC) method. PCP-1C was a heteropolysaccharide containing of Man: Gal: Glc: Fuc with molar percentages of 17.4: 43.5: 24.4: 14.6[20]. A novel homogeneous heteropolyasccharide (GSPB70-S) was isolated from *G. sinense*. Monosaccharide composition analysis showed that GSPB70-S was composed of Glc, GlcN, Man, and Gal with ratio of 12.90: 3.70: 2.26: 1.00 via HPAEC[14]. A mannoglucan (GSBP-2) was extracted and purified from *G. sinense* fruiting bodies. The monosaccharide composition of GSBP-2 was determined by HPLC using the pre-column derivatization method with PMP. HPLC analysis of GSBP-2 revealed a composition of Man, GlcA, Glc, Gal, and Fuc at a ratio of 9.1: 2.2: 12.2: 3.7: 1.0[29].

3.3 Structural characteristics

Methylation, partial acid hydrolysis, and NMR analysis are the common method, and they are suitable to characterize the primary structure of polysaccharide. NMR spectroscopy is a powerful technique used to investigate the order of connection of each glycosyl residue in polysaccharide. The possible primary structures of polysaccharides from *P. cocos* and *Ganoderma* were shown in Fig. 3-5.

A water soluble polysaccharide (PCP) isolated and purified from *P. cocos*. The PCP with Mw of 20.112 kDa, was composed of Gal, Glc, Fuc, and Man with molar percentages of 34.79%, 39.34%, 13.25%, and 12.63%. The PCP was primarily consisted of →6)-*α*-*D*-

Table 2 Structural characteristics of polysaccharides from *P. cocos and Ganoderma*

Name	Molecular weight (kDa)	Monosaccharide composition	Main chain	Conformation	References
			Poria cocos		
PCP-2	2.35	Glc: Gal: Man: Fuc = 42.0: 35.0: 13.9: 9.1	→3)-*β*-*D*-Glc*p*-(1→, →6)-*β*-*D*-Glc*p*-(1→, →6)-*α*-*D*-Gal*p*-(1→	ND	[12]
PCP	20.11	Gal: Glc: Fuc: Man = 34.79: 39.34: 13.25: 12.62	→6)-*α*-*D*-Gal*p*-(1→, →3)-*β*-*D*-Glc*p*-(1→, →4)-*β*-*D*-Glc*p*-(1→	ND	[9]
CMP33	152.3	Glc	→3)-*β*-*D*-Glc*p*-(1→	Congo red: triple-helix structure	[15]
EPS-0M	1.77	Glc: Man: Gal: Fuc: Rha = 17.3: 46.3: 19.9: 8.7: 5.0	ND	SEM: loose fragmentary aggregation with an amorphous spherical structure	[16]
EPS-0.1M	2.01	Glc: Man: Gal: Fuc: Rha = 11.5: 46.5: 21.9: 10.7: 5.6			
IPS-0M	0.03	Glc: Man: Gal: Fuc: Rha = 79.7: 8.9: 5.5: 1.7: 3.1			
IPS-0.1M	4.97	Glc: Man: Gal: Fuc: Rha = 50.3: 20.9: 16.1: 6.0: 4.0			
FMGP	31.7	Glc: Gal: Man: Fuc = 16: 7: 3: 2	→4)-*β*-*D*-Man*p*-(1→, →3)-*β*-*D*-Glc*p*-(1→	ND	[17]
PCWPW	37.15	Man: Glc: Gal: Fuc	→3)-*β*-*D*-Glc*p*-(1→	ND	[18]
PCWPS	186.2	Man: Glc: Gal: Fuc			
PCP-1	3.2	Glc	→3)-*β*-*D*-Glc*p*-(1→	Congo red: triple-helix structure	[19]
PCP-1C	17	Gal: Glu: Man: Fuc = 43.5: 24.4: 17.4: 14.6	→6)-*α*-*D*-Gal*p*-(1→	ND	[20]
PCP1C	ND	ND	ND	SEM: loose network structure similar to honeycomb	[21]
WIP	4,486	ND	→3)-*β*-*D*-Glc*p*-(1→	ND	[22]
PCP-W1	18.38	Gal: Glu: Fuc: Man = 35.87: 28.56: 21.77: 13.64	→3)-*β*-*D*-Glc*p*-(1→, →3,6)-*β*-*D*-Glc*p*-(1→, →6)-*β*-*D*-Glc*p*-(1→, →6)-*α*-*D*-Gal*p*-(1→, →2,6)-*α*-*D*-Gal*p*-(1→	CD: random coil conformation. SEM: rough globular packing structure. AFM: multiple sugar chains coiled and wound	[23]
			Ganoderma lucidum		
WSG	1,000	Glc: Gal: Man: GlcN: Fuc = 20: 4: 4: 3: 2	ND	ND	[24]
MPN	10.26	ND	*α*-*D*-Glc*p*-(1→, →4)-*α*-*D*-Glc*p*-(1→, →4,6)-*β*-*D*-Glc*p*-(1→	ND	[25]
GLSP-Ⅰ	128.0	Glc	→3)-*β*-*D*-Glc*p*-(1→	ND	[13]
GL70-1-2	6.2	Man: Gal: Glu: Fuc	→6)-*α*-*D*-Glc*p*-(1→, →6)-*β*-*D*-Glc*p*-(1→, →6)-*β*-*D*-Man*p*-(1→, →4)-*α*-*D*-Glc*p*-(1→, →2)- *β*-*D*-Gal*p*-(1→, →4,6)-*β*-*D*-Glc*p*-(1→	SEM: relatively smooth surface with a lamellar structure and irregular edges	[26]
FXM	35.9	Fuc: Xyl: Man: Glc = 24: 25: 48.3: 2.7	→4)-*α*-*D*-Man*p*-(1→	ND	[27]
GLP100	322.0				
GLP10	18.8	Fuc: Ara: Gal: Glc: Xyl: Man	ND	ND	[28]
GLP1	6.4				
			Ganoderma sinense		
GSBP-2	11.5	Man: GlcA: Glc: Gal: Fuc = 9.1: 2.2: 12.2: 3.7: 1.0	→3)-*β*-*D*-Glc*p*-(1→, →6)-*β*-*D*-Man*p*-(1→, →3,6)-*β*-*D*-Glc*p*-(1→, →6)-*β*-*D*-Man*p*-(1→	SEM: rough and uneven surface	[29]
GSPB70-S	2.87	Glc: GlcN: Man: Gal = 12.90: 3.70: 2.26: 1.00	→3)-*β*-*D*-Glc*p*-(1→, →4)-*α*-*D*-Glc*p*NAc-(1→, →4)-*α*-*D*-Man*p*-(1→	AFM: there may be branches in structure. SEM: long strip shape with different thicknesses	[14]

Gal*p*-(1→, with a small amount of →3)-*β*-*D*-Glc*p*-(1→ and →4)-*β*-*D*-Glc*p*-(1→, which were connected to form the main chain[9]. A galactoglucomannan (GLP70-1-2) was isolated from the dried fruiting body of *G. lucidum*. GLP70-1-1 with Mw of 6.2 kDa, was identified as a heteropolysaccharide consisting of Man, Glc, Gal, and Fuc. The backbone of GLP70-1-2 was →6)-*α*-*D*-Glc*p*-(1→6)-*β*-*D*-Gal*p*-(1→[6)-*β*-*D*-Man*p*-(1]$_3$→4)-*α*-*D*-Glc*p*-(1→6)-*α*-*D*-Glc*p*-(1→2)-*β*-*D*-Gal*p*-(1→[4)-*α*-*D*-Glc*p*-(1→6)-*β*-*D*-Man*p*-(1→2)-*β*-*D*-Gal*p*-(1]$_2$→6)-*β*-*D*-Glc*p*-(1→6)-*β*-*D*-Glc*p*-(1→ with two side chains attached to *O*-4 of →6)-*β*-*D*-Gal*p*-(1→ and *O*-3 of →6)-*β*-*D*-Glc*p*-(1→, respectively[26]. GSBP-2 was extracted from *G. sinense* with a molecular weight of 11.5 kDa. The backbone of GSBP-2 was composed of →3)-*β*-*D*-Glc*p*-(1→6)-*β*-*D*-Man*p*-(1→, →6)-*β*-*D*-Man*p*-(1→3)-*β*-*D*-Glc*p*-(1→, and →6)- *β*-*D*-Man*p*-(1→3)-*β*-*D*-Glc*p*-(6,1→, respectively[29].

3.4 Advanced structure

The morphological features and spatial configuration of

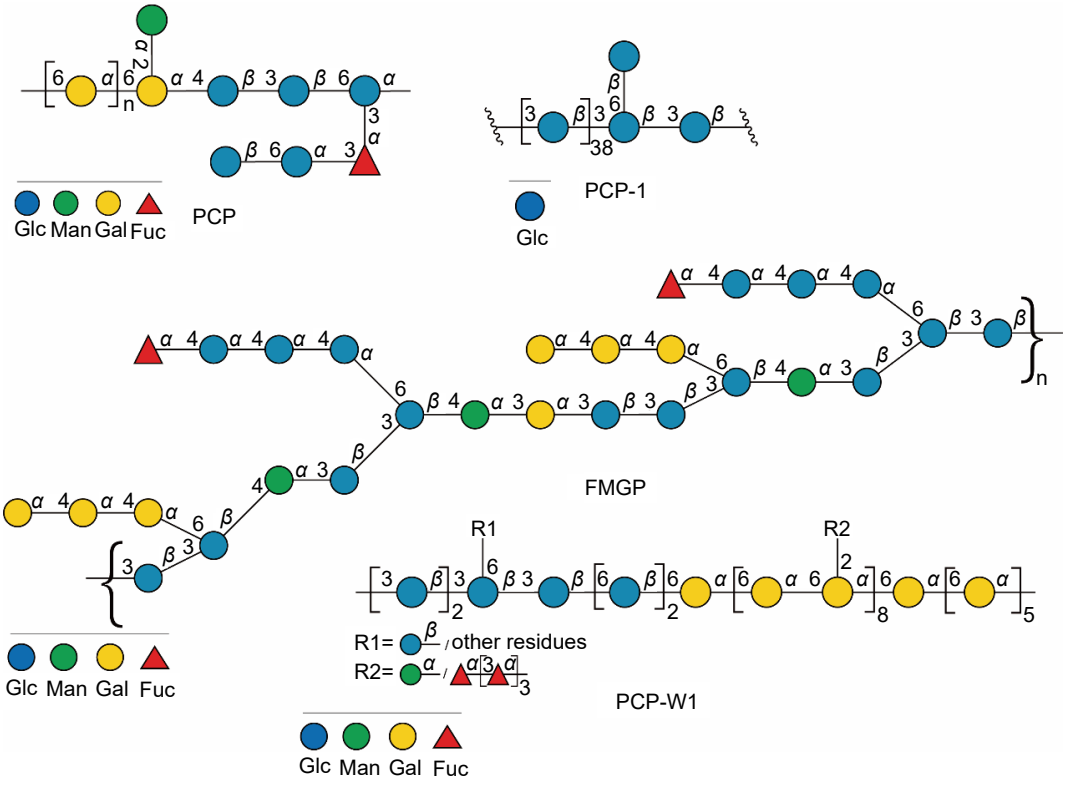

Figure 3 The possible primary structures of polysaccharides from *P. cocos*.

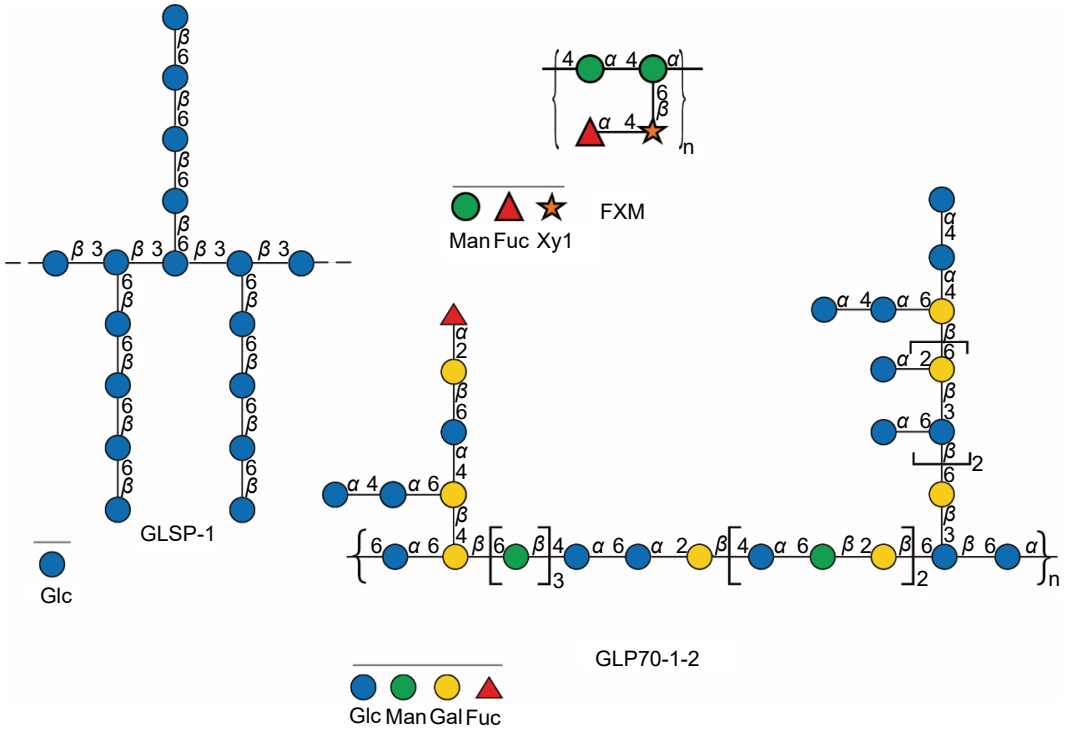

Figure 4 The possible primary structures of polysaccharides from *G. lucidum*.

polysaccharide are analyzed by congo red, SEM, AFM, and CD.

A carboxymethyl polysaccharide (CMP33) was isolated from edible and pharmaceutical mushroom *P. cocos*. Congo red analysis displayed that CMP33 possessed triple-helix structure[15]. A homogeneous polysaccharide (PCP1C) was extracted and purified from *P. cocos*. The scaning electron microscopy-energy dispersive spectrometer (SEM-EDS) analysis displayed that surface morphology of PCP1C had a loose network structure similar to honeycomb, with different particle sizes[21]. A polysaccharide PCP-W1 was isolated from *P. cocos*. CD spectrum indicated that PCP-W1 with a random coil conformation and the absence of residual protein. Congo red test showed that PCP-W1 may not have a triple helix structure, but mainly exists in the form of random coiled like glucan. SEM showed that PCP-W1 exhibited a rough

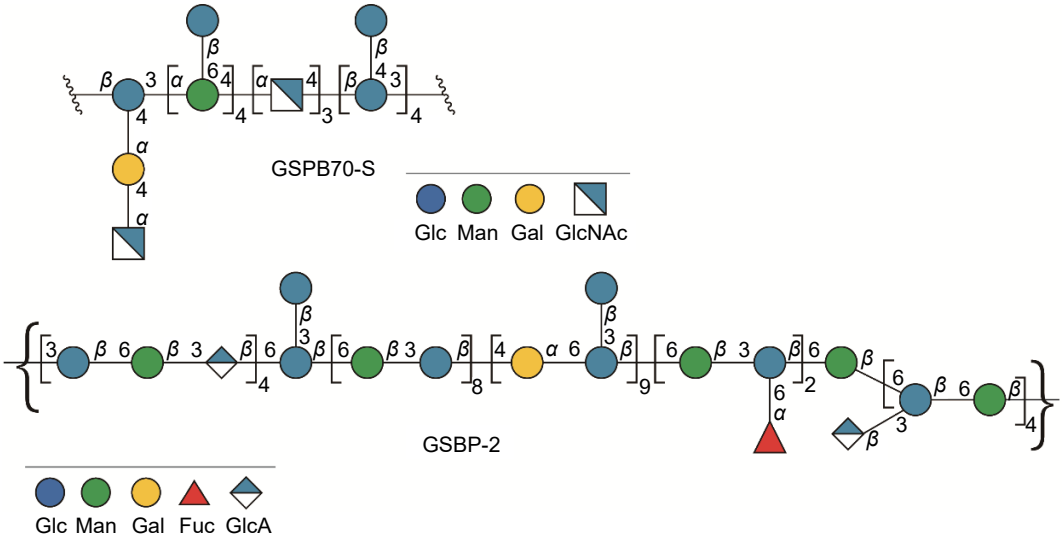

Figure 5 The possible primary structures of polysaccharides from *G. sinense*.

globular packing structure, AFM showed that the molecular chain of PCP-W1 was not a single chain structure but was composed of multiple sugar chains coiled and wound. Combined with the results of conformation and morphological characterization, PCP-W1 is a kind of polysaccharide with random coil spatial conformation[23]. A novel homogeneous heteropolysaccharide (GSPB70-S) was isolated from *G. sinense*. Congo red test showed that GSPB70-S was not present in a triple helix structure in solution. AFM showed that GSPB70-S was approximately 2.6 nm, which was distributed in sharp peaks in space. This indicated that there may be branches in the polysaccharide structure. SEM observed that GSPB70-S presented a long strip shape with different thicknesses, and there were many lamellar substances on the surface[14].

4 Bioactivities of polysaccharides from *P. cocos* and *Ganoderma*

4.1 Immunomodulation and anti-tumor activity

Numerous researches suggested that *P. cocos* and *Ganoderma* polysaccharides could regulate immunity in both directions[31-35]. On the one hand, polysaccharides could activate immune effector cells, promote the production and secretion of various growth factors and cytokines, up-regulate the expression of antibodies, enhance innate and specific immunity, eliminate damage factors, and promote health. On the other hand, uncontrolled immune response would damage tissues and organs, aggravate pathological conditions, and induce autoimmune diseases. Polysaccharides could alleviate the inflammation by inhibiting the over-activation of immune effector cells to avoid further damaging tissues and organs. Overall, polysaccharides derived from *P. cocos* and *Ganoderma* not only directly activate immune cells, but also coordinate the complicated signal transduction process among various immune cells. This coordination helps to maintain the balance of immune homeostasis in the human body.

Li *et al.*[16] isolated *P. cocos* polysaccharides into extracellular polysaccharides (EPS-0M and EPS-0.1M) and intracellular polysaccharides (IPS-0M and IPS-0.1M). It was reported that EPS-0M, EPS-0.1M, and IPS-0.1M could promote the secretion of NO, interleukin (IL)-6, and tumor necrosis factor-α (TNF-α) from macrophages at a dose of 50 μg/mL. Interestingly, EPS-0M and EPS-0.1M could inhibit the excessive secretion of inflammatory factors when lipopolysaccharide (LPS) activated macrophages. GP-1, a polysaccharide from *G. lucidum*, was shown to effectively improve the spleen and thymus injury induced by cyclophosphamide (CTX) *in vivo*, promote hematopoiesis, and increase the serum level of IgA[36].

Ying *et al.*[37] minutely demonstrated that *G. lucidum* polysaccharides could restore intestinal immune dysfunction induced by CTX by promoting the formation and maturation of IgA secretory cells, regulating the secretion of immunoglobulin, improving the expression of toll-like receptors (TLRs) and increasing the number of $CD4^+$ and $CD8^+$ T cells. Meanwhile, *G. lucidum* polysaccharides not only increase the number of goblet cells and up-regulate the expression of tight junction proteins ZO-1, occludin, and claudin-1, but also enhance the function of the intestinal tight junction barrier by up-regulating autophagy. Accordingly, in the chemistry therapy, *G. lucidum* polysaccharides could alleviate the immune dysfunction and toxic adverse reactions. Analogously, Tan *et al.*[38] reported that carboxymethylated polysaccharides from *P. cocos* could significantly reduce the inflammatory response of colitis induced by dextran sulfate sodium (DSS), decrease the expression of pro-inflammatory factors (IL-1β, IL-6, and TNF-α), and myeloperoxidase in serum, and increase the expression of anti-inflammatory factors IL-4 and superoxide dismutase. The above results have proved that polysaccharides from *P. cocos* and *Ganoderma* possessed dual-directional regulation in immunity.

There was a variety of pattern recognition receptors (PRRs) on the surface of immune cells, such as TLR4, mannose receptor (MR), scavenger receptor (SR), cluster of differentiation 14 (CD14), and Decin-1[39, 40]. *P. cocos* and *Ganoderma* polysaccharides could exploit immunomodulatory function by activating these PRRs (shown as Fig. 6). TLR4 was essential for the interaction between innate immunity and polysaccharides to activate the immune responses[41, 42]. Tian *et al.*[43] found that after feeding C57BL/10J ($TLR4^{+/+}$ wild-type) mice with *P. cocos* polysaccharides of 200 mg/kg/d for 25 days, the organ immune activity index of C57BL/10J mice increased, while in C57BL/10ScNJ (TLR4-deficient) mice or addition feed of TAK-242 (TLR4 inhibitor) in C57BL/10J mice, the index was significantly decreased when evaluated. The results indicated that *P. cocos* polysaccharide might bind with TLR4, which was crucial

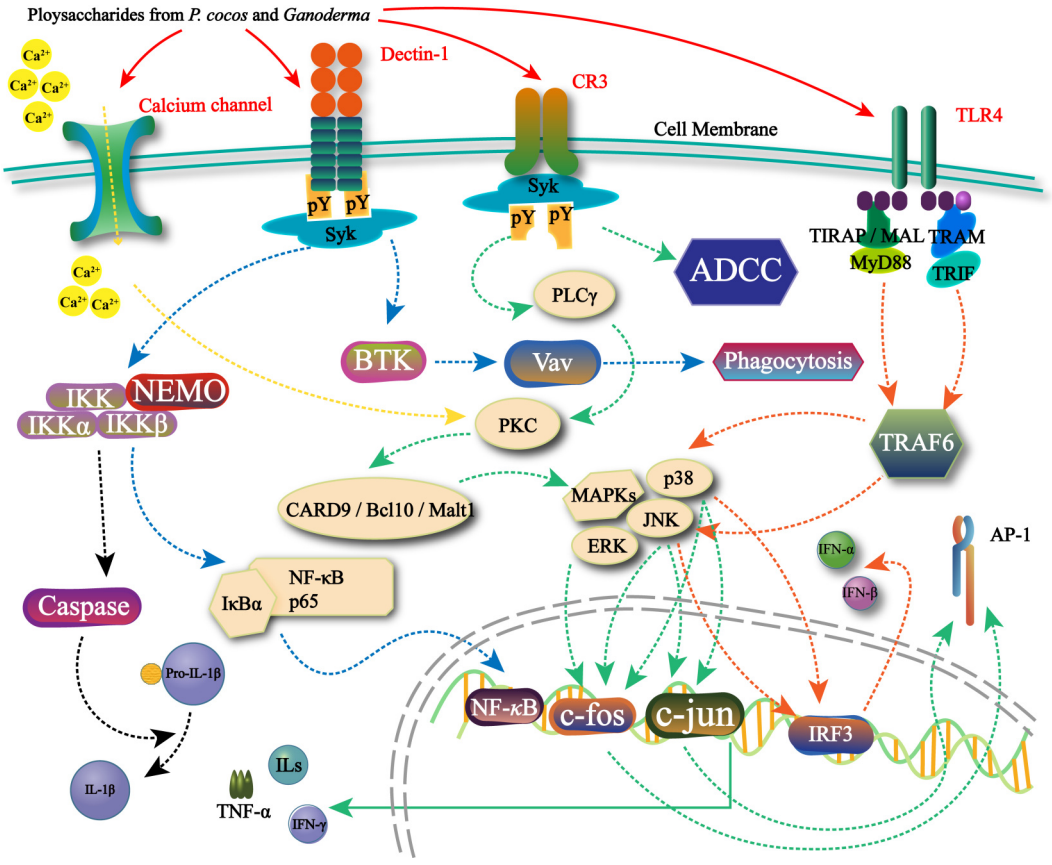

Figure 6 Molecular mechanism for the immunomodulation of polysaccharides from *P. cocos* and *Ganoderma*. ADCC: antibody-dependent cell-mediated cytotoxicity; Bcl10: B-cell lymphoma 10; BTK: Bruton's tyrosine kinase; CARD9: caspase recruitment domain family member 9; c-fos: proto-oncogene c-Fos; ERK: extracellular regulated protein kinases; IKK: inhibitor of κB kinase; IRF3: interferon regulatory factor 3; JNK: c-Jun N-terminal kinase; MAL: MyD88-adaptor like protein; Malt1: mucosa-associated lymphoid tissue lymphoma translocation protein 1; MyD88: myeloid differentiation factor 88; NEMO: NF-κB essential modulator; PKC: protein kinase C; PLC: phospholipase C; Syk: spleen tyrosine kinase; TIRAP: toll-IL-1R domain-containing adaptor protein; TRAF6: TNF receptor-associated factor 6; TRAM: TRIF-related adaptor molecule; TRIF: toll-IL-1R domain-containing adapter-inducing interferon-β; Vav: proto-oncogene Vav protein.

to activate the downstream signal pathway of immunity. In addition, after incubating with 200 μg/mL *P. cocos* polysaccharides for 24 h, the secretion of NO, IL-2, IL-6, IL-17A, TNF-α, and interferon-γ (IFN-γ) produced from RAW264.7 cells were significantly increased. These cytokines could promote the phenotypic differentiation of helper T cells (Th), like Th1 cells (IL-2, TNF-α, and IFN-γ), Th2 cells (IL-6) and Th17 cells (IL-17A), which would enhance immune responses.

Furthermore, polysaccharides could also orchestrate the expression of TLR4. Liu *et al.*[44] reported that in immunodeficient mice induced by CTX, *P. cocos* polysaccharides (CMP-1 and CMP-2) could up-regulate the gene expression of TLR4, MyD88, p65, and nuclear factor-kappa B (NF-κB) in the impaired spleen. Meanwhile, both CMP-1 and CMP-2 could reduce spleen damage and increase serum levels of TNF-α, IL-2, IL-6, IFN-γ, IgA, and IgG with an administration of 200 mg/kg/d. TLR2 was considered to be another significant kind of polysaccharide receptors that modulated immunity as well as TLR4[45]. Gao *et al.*[46] found that GLP-3, a *G. leucocontextum* polysaccharide, was capable of being recognized by TLR2 distributed on macrophages RAW264.7, and activating mitogen-activated protein kinase (MAPK), phosphatidylinositol-3-kinase (PI3K)/AKT and NF-κB signal pathways. Simultaneously, GLP-3 would significantly up-regulate the secretion of NO, TNF-α, and IL-6. However, with the addition of anti-TLR2 preparation, the up-regulation was reversed. The results indicated that polysaccharides could mediate immune response by TLR2 indeed.

Pu *et al.*[47] demonstrated that *P. cocos* polysaccharide PCP enhanced the production of cytokines in RAW264.7 cells, while concurrently elevated intracellular calcium levels. These effects were significantly decreased by the addition of calcium channel antagonist $NiCl_2$ and p38 inhibitor SB203580, indicating that calcium and p38 were indispensable in the immunomodulatory of PCP. Moreover, after the application of $NiCl_2$ and SB203580, the up-regulation of PKC and NF-κB genes improved by PCP was significantly decreased. These findings suggested that the involvement of Ca^{2+} was crucial in the immune regulation facilitated by the PKC/p38/NF-κB signaling pathway.

Polysaccharides derived from *P. cocos* and *Ganoderma* not only directly stimulate immune effector cells to carry out immune functions but also modulate the function of immune cells by regulating the expression of immune cell maturation-related factors. Dong *et al.*[48] found that *P. cocos* polysaccharide could significantly up-regulate the expression of MHCII, CD40, CD80, and CD86, and promote mature dendritic cells to produce and secrete IL-6 and IL-12p40. IL-12, as a pivotal Th-1 immunostimulatory factor, facilitates the mediation of the Th1 immune response and bolsters overall immunity[49,50].

Macrophages were a vital component of the inflammatory microenvironment. Upon activation, these cells exhibit either anti-inflammatory or pro-inflammatory properties, potentially influencing local tissue damage or cellular regeneration[51]. M1 macrophages, one of the phenotypes from macrophages, demonstrate a robust capacity for antigen presentation under

stress conditions and are capable of secreting a substantial quantity of pro-inflammatory cytokines, including TNF-α, IL-6, and IL-12, which would exhibit cytotoxic effects on tumor cells.[52]. Hu *et al.*[53] found that different concentrations of *P. cocos* polysaccharide PCP-1C (50, 100, and 200 μg/mL) were mixed with LPS (2 μg/mL) to incubate with RAW264.7 cells, respectively. Compared with the control group and LPS group, PCP-1C could induce the expression of TNF-α, IL-6, and IL-12 among macrophages in a dose-dependent manner. While the level of IL-10, a marker of M2 macrophages, decreased. At the same time, PCP-1C induced the increase of CD86 (M1 marker)/CD206 (M2 marker) . Furthermore, the expression of NOTCH1, ligand Jagged1, and Hes1 were improved with the incubation of PCP-1C, indicating that *P. cocos* polysaccharide mediated the M1 macrophages polarization through the Notch signaling pathway.

Tumor immune escape is the process by which malignant tumor cells evade recognition and attack by the immune system, thereby facilitating growth and metastasis[54, 55]. This phenomenon involves the aggregation of immunosuppressive cells around the tumor, which could secrete factors that hinder the immune system's surveillance and response to the tumor cells[56, 57]. Wang *et al.*[58] found that *G. lucidum* polysaccharides (GLP) could increase the percentage of CD^{4+} and CD^{8+} T cells and the production of Th1 cytokines in the spleen of tumor-bearing mice (Lewis lung cancer, LLC) to enhance immune recognition and immune clearance. Meanwhile, GLP (25 and 100 mg/kg) could increase the protein levels of CARD9, p-Syk, and p65 and decrease IDO protein levels in myeloid-derived suppressor cells (MDSCs) of LLC-bearing mice. CARD9, the crucial downstream junction between Syk-coupled receptor and NF-κB pathway, contributes to adapter protein in innate immunity[59]. Abnormal activation of CARD9 usually leads to a series of inflammatory diseases or cancers. Studies have shown that CARD9 inhibits the development of lung cancer by inhibiting the production of immunosuppressive cell MDSCs and its downstream product IDO in LLC[60]. These results indicated that GLP exerted anti-tumor activity by inhibiting MDSCs through the CARD9-NF-κB-IDO pathway. Song *et al.*[61] reported that *Ganoderma lucidum* polysaccharides could promote the M1 polarization of macrophages and increase the secretion of inflammatory factors and cytokines, reshaping the tumor microenvironment. *G. lucidum* polysaccharides could still block H22 tumor cells into the G2/M phase by activating macrophages, activating the PI3K/AKT signal pathway, affecting the mitochondrial apoptosis pathway, and promoting tumor cell apoptosis.

P. cocos and *Ganoderma* polysaccharides could directly inhibit the proliferation of tumor cells[62, 63]. Lin *et al.*[17] was demonstrated that FMGP, a fucose-containing mannan polysaccharide from *P. cocos*, could effectively inhibit the migration of lung cancer CL1-5 cells. Mechanically, FMGP could significantly down-regulate the expression of the transforming growth factor beta receptor and inhibit its phosphorylation. In addition, FMGP decreased the expression of metastasis-related protein Slug. Xie *et al.*[29] reported that *G. sinense* polysaccharide GSBP-2 could selectively inhibit the proliferation of triple-negative breast cancer MDA-MB-231 cells and down-regulate the expression of specific genes (such as *Snail*, *ZEB1*, *VIM*, *CDH2*, and *MMP9*) and proteins (such as E-cadherin and N-cadherin) by inhibiting the PI3K/AKT signaling pathway, to restrict the migration mediated by EMT of MDA-MB-231 cells. In addition, GSBP-2 also inhibited the angiogenesis of human umbilical vein endothelial cells, suggesting that GSBP-2 might inhibit tumorigenesis by reducing the invasion of micro-vessels in the tumor.

In synopsis, *P. cocos* and *Ganoderma* polysaccharides exhibit a broad spectrum of immunomodulatory effects, encompassing the activation of immune cells to fortify the immune response against tumors, bacteria, and viruses. Further investigation is warranted to comprehend the correspondence between the target response and signal pathway in the context of the medicinal and nutritional synergy of fungal polysaccharides when employed as an adjuvant therapy.

4.2 Anti-inflammation activity

Inflammation is a component of immune regulation, whereby the dynamic equilibrium of inflammatory factors assists in eliminating harmful agents from the body to maintain normal bodily functions[64, 65]. However, an overabundance of inflammatory factor secretion can disrupt the body's equilibrium and impair its functionality[66, 67].

Studies have shown that *P. cocos* and *Ganoderma* polysaccharides could decrease the level of inflammatory factors and alleviate inflammatory injury[68, 69]. Tan *et al.*[70] found that *P. cocos* polysaccharide PCP could decrease the expression of TLR4, TNF-α, and NF-κB in the liver of nonalcoholic steatohepatitis (NASH) mice, indicating that PCP down-regulated the NF-κB signaling pathways to alleviate the inflammatory response of NASH. Meanwhile, the expression of chemokine (C-C motif) ligand 3 (CCL3) and C-C motif receptor 1 (CCR1) was decreased by PCP. CCL3 was induced by macrophages and recruited macrophages to the inflammatory site[71]. In addition, the NF-κB can up-regulate CCL3 expression, and CCR1 is the receptor of CCL3[72]. Inhibiting the expression of CCL3 and CCR1 can alleviate inflammatory diseases. The results suggested that PCP could improve NASH through the NF-κB/CCL3-CCR1 axis.

Due to the lack of carbohydrate-active enzymes, polysaccharides cannot be directly digested and absorbed by the human body. The anti-inflammatory effect of polysaccharides between intestinal epithelial cells and immune cells cannot be elucidated simply by the monolayer cell culture model. Hu *et al.*[73] used the a co-culture model of RAW264.7 macrophages and intestinal-like Caco-2 to explore the direct and indirect effects of endotoxin-induced inflammation. It was shown that *G. atrum* polysaccharide PSG-1 could inhibit the secretion of TNF-α, IL-6, and IL-1β induced by LPS. The expression of cyclooxygenase-2 (COX-2) in LPS-stimulated RAW264.7 cells and the Caco-2/RAW264.7 co-culture model decreased by PSG-1. COX-2 contributes to inflammation and converts arachidonic acid into prostaglandins, leading to acute and chronic inflammation, including intestinal inflammation[74]. In addition, compared with the LPS group, PSG-1 significantly inhibited the phosphorylation of ERK1/2, JNK, and p38 induced by LPS, suggesting that PSG-1 exerted anti-inflammatory effects by inhibiting the activation of the MAPKs signal pathway. The Caco-2/RAW264.7 co-culture model did the same. Thus, PSG-1 could directly reduce inflammation in LPS-induced RAW264.7 cells and indirectly reduce inflammation in the Caco-2/RAW264.7 co-culture model.

4.3 Antioxidative stress activity

ROS, including superoxide anion, hydrogen peroxide, and hydroxyl radical, lead to oxidative stress in organisms. It is now well-established that numerous diseases are intricately linked to oxidative stress, influencing their onset and progression[75, 76]. *P. cocos* and *G. lucidum* polysaccharides may have antioxidant and

free radical scavenging effects in animal models[77-79], possibly linked to immune regulation and pharmacological actions such as anti-tumor, anti-inflammatory, liver protection, and anti-aging effects.

Oxidized low-density lipoprotein (ox-LDL) is considered a crucial stimulant of vascular smooth muscle cell (VSMC) proliferation and the progression of atherosclerosis[80]. Uncontrolled uptake of ox-LDL by VSMCs and macrophages would lead to the formation of foam cells, which goes with inflammation[81]. Heme oxygenase-1 (HO-1) is a protective factor that regulates the level of intracellular ROS and it is regulated by Nrf2[82]. Zhao *et al.*[83] reported that *P. cocos* polysaccharides exerted their protective effect on oxidative stress and inflammation through the myd/Nrf2/HO-1 signal pathway. *P. cocos* polysaccharides could significantly reduce the oxidative stress induced by ox-LDL, along with the decrease of ROS and malondialdehyde in VSMCs, while the activity of superoxide dismutase increased. In addition, the research has shown that ERK inhibitor PD98059 could reverse the up-regulation of ERK1/2 signal pathway by *P. cocos* polysaccharides, reduce the translocation of Nrf2 from cytoplasm to nucleus, and down-regulate the expression of HO-1.

Jiang *et al.*[84] also found that *P. cocos* polysaccharide PCP-1C attenuated liver inflammation by inhibiting the TLR4/NF-κB signal pathway and protected hepatocytes by inhibiting the CYP2E1/ROS/MAPKs signal pathway. Li *et al.*[85] reported that *G. lucidum* polysaccharide GDLP could significantly reduce food/water intake, body weight, fasting blood glucose, blood lipids, urine biomarkers, liver lipid accumulation, and TNF-α in *db/db* mice. In addition, GDLP increased the expression of many antioxidant enzymes, including superoxide dismutase, catalase, and glutathione peroxidase, while decreased the level of malondialdehyde. Meanwhile, GDLP could significantly increase the protein level of Nrf2 and its downstream target gene HO-1 and reduce the expression of TNF-α. These results suggested that GDLP antagonized hepatic steatosis, oxidative stress, and inflammation induced by type 2 diabetes mellitus by improving the Nrf2/HO-1 signaling pathway.

4.4 Modulation of gut microbiota

Gut microflora is essential to human health[86]. Many chronic diseases, such as hypertension, diabetes mellitus, inflammatory intestine disease, and tumorigenesis, are closely related to the changes in gut microflora[87]. Polysaccharides could reach the large intestine without degradation by the digestive system. Hence, polysaccharides demonstrate potential for use as probiotics within the gut microflora, thus contributing to the maintenance of human health through their involvement in regulating internal environmental signaling molecules[88-90].

Yu *et al.*[91] discovered that *P. cocos* polysaccharide significantly enriched beneficial bacteria such as *Parabacteroides* and *Fusicatenibacter* and increased salutary metabolites such as 7-ketodeoxycholic acid and haloperidol glucuronic acid. However, metabolites could inhibit inflammation of prostate cancer by reducing the expression of Cyp1a1 and Hsd17b7 and increasing the expression of Alox15 and Pla2g2f, suggesting that *P. cocos* polysaccharide was involved in probiotic metabolism to promote the secretion of 7-ketodeoxycholic acid and haloperidol glucuronide to achieve the "intestinal-prostate" axis for the treatment of prostatitis. Zhang *et al.*[92] reported that *P. cocos* polysaccharide could protect against skin damage caused by acute ultraviolet irradiation through the microflora axis of skin-intestinal-intestinal microorganisms. Local application and oral administration of *P. cocos* polysaccharide could significantly improve the fecal bacteria related to energy metabolism, propionic acid metabolism, and butyric acid metabolism and eventually reduce inflammation and oxidative stress, improve intestinal morphology, and reduce the symptoms of skin damage in ICR mice under intense ultraviolet radiation.

Guo *et al.*[93] reported that *G. lucidum* polysaccharide GLP improved the microflora imbalance induced by azoxymethane/DSS and significantly reduced the disease activity (body weight loss, diarrhea, and blood stool), increased the production of SCFAs, and reduced endotoxemia by inhibiting TLR4/MyD88/NF-κB signal pathway. GLP attenuated the infiltration of macrophages and the over-expression of IL-1β, iNOS, and COX-2. Moreover, GLP could significantly increase the number of goblet cells, increase the secretion of Mucin2, and up-regulate the expression of tight junction protein to reduce intestinal inflammation and improve intestinal barrier function. These results suggest that GLP could regulate the function of intestinal microbiota and immune cells and inhibit colonic inflammation and tumorigenesis. In addition, Shao *et al.*[94] demonstrated that *G. lucidum* polysaccharides could alleviate insulin resistance and improve related inflammation by reducing intestinal endotoxin release and fermentating carbohydrate and activating the intestinal brain axis to restore the diversity of intestinal flora, such as enriching the contents of *Lactobacillus*, *Bacteroides*, *Ruminants*, and SCFAs in the intestine of diabetic mice.

The effectiveness of antibiotics in treating infections is readily apparent[95]. However, long-term and inappropriate use of antibiotics against infection would induce complications of antibiotic-associated diarrhea and affect the distribution of intestinal flora[96]. Therefore, maintaining the balance of gut microorganisms and reversing the imbalance of intestinal flora caused by antibiotics is an inevitable hot issue in clinical practice[87]. Lai *et al.*[97] discovered that *P. cocos* polysaccharide PCY could significantly improve the intestinal mucosal defects of mice induced by lincomycin, reduce inflammatory cell infiltration, and reduce submucosal edema. At the same time, PCY increased the content of SCFAs, reduced the level of inflammatory cytokines, and changed the structure of intestinal microflora by increasing relative abundance, promoting the growth of probiotics.

Above all, gut microbiota could degrade the polysaccharides of *P. cocos* and *Ganoderma* to produce various beneficial secondary metabolites. Various metabolites are enriched in the gut and play a local regulatory role in improving the species and proportion of probiotics. Through the intestinal mucosa of metabolites, metabolites act as a messenger, and the environment adjusts the tissue and organ function.

4.5 Others bio-activities

Based on the pharmacological mechanisms of immunomodulation, anti-inflammatory and antioxidant stress, and regulation of intestinal flora, polysaccharides from *P. cocos* and *Ganoderma* have been extensively utilized for other diseases, such as neuroprotection[26,98,99] and hepatoprotection[100,101]. Wu *et al.*[102] reported that *P. cocos* polysaccharides could reduce the inflammatory cytokines and oxidative stress in plasma and spleen tissue of mice with fecal-induced peritonitis (FIP), reduce the number of Treg cells, and improve the resistance to FIP. Ye *et al.*[103] have studied that *P. cocos* polysaccharide PCP could slow down weight gain, hyperlipidemia, and liver steatosis induced by a

high-fat diet in mice. More importantly, PCP could reduce the destruction of the intestinal vascular barrier and endotoxin translocation caused by a high-fat diet. Wu *et al.*[104] demonstrated that *G. lucidum* polysaccharides promoted the upregulation of core clock genes and proteins and restored the co-localized expression of clock and Aquaporins (AQPs) AQP5 during aging, which helped reduce weight loss, decreased saliva secretion, and structural and functional damage caused by aging.

5 Correlation of structures and bio-activities of polysaccharides from *P. cocos* and *Ganoderma*

The biological activities of polysaccharides were largely influenced by factors such as their molecular weight, monosaccharide composition, conformation, and physical properties, including solubility, molecular size, and branches[105-108].

P. cocos and *Ganoderma* polysaccharides, which contain glucose and mannose, could reduce the risk of cancer progression, this is mainly recognized and mediated by these specific cell surface receptors, such as Dectin-1, MR, TLR4, TLR2, complement receptor 3, etc.[40]. Zhang *et al.*[18] discovered that *P. cocos* polysaccharides PCWPW and PCWPS played an immunomodulatory role by binding to MR and activating the NF-κB/MAPK signal pathway to regulate the expression of TNF-α.

Numerous studies have shown that the polysaccharide with the most immunomodulatory activity is *β*-(1,3) glucans. The *β*-(1,3) linkages with relatively variable *β*-(1,6) branches in the main chain of the most abundant proportion of glucans among polysaccharides from *P. cocos* and *Ganoderma* show high anti-tumor and immunomodulatory activity[20, 109]. Fu *et al.*[110] demonstrated that *G. lucidum* polysaccharide WGLP is consisted of *β*-(1,3)-*D*-glucopyranose residues backbone with an average repeat unit of six sugars, to which the side chain connected by the terminal and *β*-(1,6)-*D*-glucopyranose residues to the *O*-6 position of the branch residue. WGLP could significantly inhibit the growth of S180 tumors in mice. Most importantly, *β*-glucans are absent in mammalian cells and thus identified as a pathogen-associated molecular pattern by the PRRs.

In addition, the *β*-glucans in *P. cocos* have poor solubility but possess good anticancer activity[111]. However, the solubility and anticancer activity would improve through different chemical modifications, such as sulfation, carboxymethylation, and sulfation[12, 112]. Liu *et al.*[15] reported carboxymethyl *P. cocos* polysaccharides CMP33 for the first time. CMP33 has a triple helix structure, and the backbone was (1→3)-linked glucose residues, while the side chain was composed of (1→6) and (1→2)-linked glucose residues. The inhibitory effect of CMP33 on four kinds of cancer cells (HepG-2, MCF7, SGC7901, and A549) was dose-dependent in the range of 31.25~100 μg/mL.

The continuous advancement in structural analysis of polysaccharides has led to endeavors in synthesizing complex polysaccharides and investigating the relationship between their structure and bioactivity. This exploration aims to identify and cultivate new carbohydrate-based treatments. Chen *et al.*[113] for the first time used GSPB70-S, a *G. lucidum* polysaccharides with different biological activities, as raw materials, to synthesize nine-decosaccharide motifs by using one-pot stereoselective glycosylation strategy based on glycosyl ortho-(1-phenyvinyl) benzoates, which not only accelerated the synthesis of carbohydrates but also reduced chemical waste and avoided the problem of aglycone transfer inherent in one-pot glycosylation of glucosinolates. The study offers the opportunity to elucidate the potential biological activity and structure-activity relationship of polysaccharides.

In addition, polysaccharides, because of the advantages of safety and environmental friendliness, are also used to develop new carrier materials. PCPA, extracted by diluted sodium hydroxide at low temperature from *P. cocos*, was characterized as a liner *β*-glucan with 1,3-linked glycosidic bonds[114]. Due to the abundance of hydroxyl groups, PCPA possessed good thermal stability, water retention, and swelling properties after being constructed successfully into hydrogels, promising applications in the food, pharmaceutical, and cosmetic fields. *G. lucidum* fermentation incorporating pullulan and sodium hyaluronate was fabricated by electrospinning as a facial healthcare mask with good water retention capacity, and the high concentration of *G. lucidum* fermentation could scavenge 79% of DPPH[115]. This work could shed light on the development of polysaccharides in skincare products and provide a green development direction for the natural macromolecule ingredients.

6 Conclusion and prospect

P. cocos and *Ganoderma* are traditional Chinese medicine and food homologous fungi with a long medicinal history and are used to prevent and treat various diseases. With the development of the theory and technology of modern pharmacy and related pharmacy disciplines, more and more pharmacological activities of traditional Chinese medicine have been gradually discovered and used in clinical practice. Polysaccharides are significant bioactive components of *P. cocos* and *Ganoderma*, which have unique pharmacological activities in immunomodulatory and anti-tumor, liver protection, hypoglycemic and anti-diabetes, neuroprotection, cardiovascular protection, and antioxidant stress. It has become a research hotspot with a broad development prospect. Recent studies have shown that glucan with *β*-(1→3) bond as the main backbone and with a relatively variable number of *β*-(1→6) branch chains is the most bioactive among polysaccharides of *P. cocos* and *Ganoderma*. This kind of glucan exhibits outstanding anti-tumor activity and immunomodulatory activities. Although it has a good anti-tumor activity, the water solubility of *β*-glucan of *P. cocos* is relatively poor. Therefore, the derivatization of hydrophilic groups to improve the water-insoluble *P. cocos* glucan would improve the anti-tumor activity, becoming one of the application aspects of polysaccharide derivatization. On the other hand, by group derivatization of polysaccharides from *P. cocos* and *Ganoderma*, researchers can improve their physical properties to become biocompatible and environmentally friendly carriers in application among food, beauty, and medical industries. Due to the complex structure of polysaccharides, there are still enormous challenges to elucidate advanced structures. The bio-activity and structure-function relationship of *P. cocos* and *Ganoderma* polysaccharides remain to be clarified. There are still bottlenecks in pharmacokinetics, and the molecular mechanisms of many targets still need to be further discussed. Therefore, further study on the structural characteristics, pharmacological activity, and structure-function relationship of medicine and food homologous fungi polysaccharides will provide a theoretical and practical basis for the development and utilization of polysaccharides. Furthermore, this review was hope to shed light on the development of medicine and food homologous fungi polysaccharides from as potential adjuvants in clinic therapy. Due to their high nutritional value, *P. cocos* and *Ganoderma* polysaccharides may also be developed as

nutraceuticals or functional foods.

Conflicts of interest

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

Acknowledgements

This study was funded by the Open Project of State Key Laboratory of Chemistry and Molecular Engineering of Medicinal Resources (No. CMEMR2020-B10) and Anhui Province Innovation Team of Authentic Medicinal Materials Development and High Value Utilization (No. 2022AH010080).

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