CHAPTER SEVENTEEN

The structures and biological functions of polysaccharides from traditional Chinese herbs

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Contents

Abstract

Most of traditional Chinese medicine substances come from herbal plants. The medicinal quality of herbal plants varies with the locations of cultivation, the parts of the herb collected, the season of the herb collected, and the herb processing method. Polysaccharides are major components of the herb plants and their biosynthesis is partly controlled by the genes but mostly influenced by the availability of the nutrition and determined by the various environmental factors. In recent decades, polysaccharides isolated from different kinds of Chinese herbs have received much attention due to their important biological activities, such as anti-tumor, anti-oxidant, anti-diabetic, radiation protecting, antiviral, hypolipidemic, and immunomodulatory activities. Interestingly, different batches of the same herb can obtain different polysaccharide fractions with

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subtle differences in molecular weight, monosaccharide compositions, glycosidic linkages, and biological functions. Even with these variations, a large number of bioactive polysaccharides from different kinds of traditional Chinese herbs have been purified, characterized, and reported. This review provides a comprehensive summary of the latest polysaccharide extraction methods and the strategies used for monosaccharide compositional analysis plus polysaccharide structural characterization. Most importantly, the reported chemical characteristics and biological activities of the polysaccharides from the famous traditional Chinese herbs including *Astragalus membranaceus*, *Ginseng*, *Lycium barbarum*, *Angelica sinensis*, *Cordyceps sinensis*, and *Ophiopogon japonicus* will be reviewed and discussed. The published studies provide evidence that polysaccharides from traditional Chinese herbs play an important role in their medical applications, which forms the basis for future research, development, and application of these polysaccharides as functional foods and therapeutics in modern medicine.

1. Introduction

The biological information flows from DNA to RNA to protein with template-based precision.[1] However, thorough understanding the information residing in DNAs, RNAs, and proteins cannot explain the makeup of cells, tissues, and organs as well as the pathophysiological and physiological processes because the environment is in charge of both the building materials and waste management to keep the organisms alive. Moreover, polysaccharides/glycans and lipids are constantly synthesized and metabolized by concerted effort of at least hundreds of proteins from inorganic elements and small organic molecules without a template in living organisms. Furthermore, polysaccharides are heterogeneous biomolecules containing far more structural information than that are carried by protein-, nucleic acid-, and lipid-combined.[2,3] Such paradigm is applicable to all living systems including animals, plants, fungi, and microbes.[4–7] Thus, polysaccharides are positioned to serve important energy, structural, and biological functions in all living organisms.

Traditional Chinese medicine is one of the oldest medical systems in the world. Most traditional Chinese medicine substances come from herbal plants. The individual plant cell makes a cell wall enriched in cellulose, non-cellulosic polysaccharides and lignin. The non-cellulosic polysaccharides are heterogeneous.[4] Spatially and temporally controlled heterogeneity in the physicochemical properties of cell wall non-cellulosic polysaccharides is observed at the tissue and individual cell levels, which plays important role in defensing and survival of the plants. It has been found that the herb polysaccharides have important biological activities such as anti-tumor, anti-oxidant, anti-diabetic, radiation protecting, antiviral, hypolipidemic, immunomodulatory, and other activities[8–19] with lower toxicity and side effects. Therefore, the isolation, characterization, and biological activity testing of polysaccharides in herbs have become a hot research field in China.[20]

This review provides a comprehensive summary of the extraction, isolation, identification, structural analysis and biological activity from many important traditional Chinese Herbs, such as *Astragalus membranaceus*, *Ginseng*, *Lycium barbarum*, *Angelica sinensis*, *Cordyceps sinensis*, and *Ophiopogon japonicus*. The published studies provide solid evidence that polysaccharides from traditional Chinese herbs play an important role in their medical applications, which forms the basis for future research, development, and application of these polysaccharides as functional foods and therapeutics in modern medicine.

2. Extraction, separation, purification and structural analysis method of polysaccharide

The most common method for preparing herbal medicine is to boil the herb in hot water and the liquid is then taken as the medicine. Most of the non-cellulosic polysaccharides are polar macromolecules that are readily soluble in water. Thus, the traditional polysaccharide extraction method is a water leaching extraction method, which is usually extracted by hot water leaching, and the polar macromolecular compound polysaccharide is dissolved in a polar solvent such as water to extract by using the principle of "similar compatibility." In addition, according to the structure and properties of polysaccharides, some auxiliary means are introduced.[20] On the basis of traditional water extraction, acid–base extraction method, enzymatic extraction method, microwave-assisted extraction method, ultrasonic assisted extraction method and ultrahigh-pressure extraction method have been developed.[20–28] Then the separation and purification process of the polysaccharide is generally carried out from the water extracted materials by removing the non-polysaccharide components first. Common methods for polysaccharide purification include precipitation, gel chromatography, anion exchange chromatography, macro porous resin column chromatography, ultrafiltration, and other methods alike.[29–34] Most of the polysaccharides obtained by the extraction, separation and purification techniques at this stage are still crude products because the quality of polysaccharides is difficult to control. First, the medicinal quality of herbal plants varies with the locations of cultivation, the parts of the herb collected, the season of the herb collected, and the herb processing method. Second, the extraction methods used vary from lab to lab. Third, unlike DNA, RNA, and proteins, the non-template synthesized polysaccharides are never pure compounds no matter how many procedures have been used for purification. The obtained polysaccharides are always associated with either narrow or wide molecular weight ranges. The biological activities of the polysaccharides purified by the same starting materials vary as well. Therefore, special attention has to be paid during the extraction, separation and purification of herb polysaccharides.[35–38] The advantages and disadvantages of each method are shown in Table 1.

The structure of polysaccharides is more complex than that of proteins and DNAs. From a chemical point of view, the complexity of the polysaccharides undoubtedly brings great difficulties to its structural analysis. The structural classification of polysaccharides follows the suit of proteins and DNAs, i.e., the structure of polysaccharides can be divided into primary, secondary, tertiary and quaternary structures.[39]

Like other biomolecules, the higher structure of the polysaccharide chain is based on its primary structure. The difference is that primary structure of the polysaccharide chain having much more “meaning” than the protein or DNAs. To determine the primary structure of a polysaccharide chain, the

Table 1 Polysaccharide extraction, separation and purification methods from traditional Chinese herbs.

Contents	Methods	Features
Extraction	Acid–base or water	Prevent glycosidic bond break
	Enzymatic	Mild conditions, lower damage, higher yield, avoiding changes in physiological activity
	Microwave-assisted	High yield, shorter extraction time and lower cost
	Ultrasound-assisted	Faster, energy-saving, higher yield
	Ultra high pressure	Shorter time and high efficiency

Table 1 Polysaccharide extraction, separation and purification methods from traditional Chinese herbs.—cont'd

Contents			**Methods**	**Features**
Isolation and purification	Miscellaneous	Removing proteins	Sevage method	Troublesome, time-consuming, large amount of reagents, structural damage, and large losses
			Trichloroacetic acid	Effect but destroying structure
			Protease	Mild and efficient
		Decolorization	Activated carbon adsorption	Stronger affinity adsorption, larger loss
			Hydrogen peroxide	Pigment containing unsaturated double bonds, hydroxyl groups and aromatic rings
			Ion exchange	High decolorization and retention rate
		Small molecule impurities	Dialysis	–
	Fractional purification		Precipitation	Polysaccharides with differences in solubility
			Gel chromatography	–
			Anion exchange chromatography	Crude purification of polysaccharide
			Macroporous resin column chromatography	Have no effect on the biological activity
			Ultrafiltration	High separation efficiency, low energy consumption, no pollution and no damage to polysaccharide activity, easy to be contaminated

Modified from Xie MY, Nie SP. A review about the research of structure and function of polysaccharides from natural products. J Chin Inst Food Sci Technol 2010;10(02):1–11.

following problems have to be solved: (1) relative molecular mass; (2) monosaccharide compositions of the polysaccharide chain; (3) presence or absence of uronic acid and specific uronic acid type and ratio; (4) D- or L-configuration of each monosaccharide residue, pyran ring or furan ring form; (5) sequence of linkage between individual monosaccharide residues; the α- or β-anomeric form of each glycosidic bond; (7) the substitution of a hydroxyl group on each monosaccharide residue; (8) the attachment of a polysaccharide chain to a non-polysaccharide moiety; (9) the backbone of the polysaccharide chain and the branch linkage site; and (10) a polysaccharide residue may be modified by a sulfate group, an acetyl group, a phosphate group, a methyl group, or the like. There are many analytical methods for polysaccharide structural characterization,[40,41] not only instrumental analysis methods such as infrared, nuclear magnetic resonance, mass spectrometry, etc., but also chemical methods such as partial acid hydrolysis, complete acid hydrolysis, periodic acid oxidation, Smith degradation, etc., as well as biological methods such as specific glycosidase digestion, immunological methods, etc. Polysaccharide extraction, separation and purification methods from traditional Chinese herbs are shown in Table 1.[39]

3. Overview of biological activities of polysaccharides purified from traditional Chinese herbs

3.1 *Astragalus membranaceus*

Astragalus membranaceus (*A. membranaceus*) (Table 3) belongs to the family *Leguminosae* and is widely distributed in Asia, Europe and North America.[43,79] According to reports, there are >3000 different types of *A. membranaceus*, and the roots are collected and dried for use. It has been known for centuries as a treatment for various diseases in traditional Chinese medicine. Such as in wound healing, diabetes, leukemia, hypertension, eye disease, nephritis, cirrhosis, uterine cancer.[80] In recent years, many phytochemistry and pharmacological studies show that the polysaccharide part is one of the major bioactive components of *A. membranaceus*. It has a variety of health benefits, including immune regulation, anti-inflammatory, anti-oxidation, anti-glomerulonephritis, anti-atherosclerosis, anti-diabetes and anti-tumor ability.[42]

A number of polysaccharides are isolated from the roots and aerial parts of *A. membranaceus*. Jin et al. listed 24 polysaccharides isolated from the roots of *A. membranaceus*, and most of them are heteropolysaccharides.[42] These heteropolysaccharides have molecular weights ranging from 8.7

to 4800 kDa, with different proportions of the monosaccharides, including arabinose, fructose, fucose, galactose, glucose, mannose, rhamnose, ribose and xylose. Kiyohara et al. separated 13 different types of polysaccharides from the aerial part of *A. membranaceus*, 9 of which consist of arabinogalactans and pectic acid arabinogalactan or pectin.[44]

Structural analysis of the water-soluble heteropolysaccharide (APSID3) isolated from *A. membranaceus* showed that the minimal repeat unit consists of one terminal arabinose, one 1,5-linked arabinose, one 1,3-linked rhamnose, one 1,3,4-linked rhamnose, six 1,4-linked glcuronic acid and five 1,4-linked galacturonic acid residues, with the backbone of which consists of 1,4-linked galacturonic acid, 1,4-linked glcuronic acid and a small amount of 1,3-linked rhamnose is attached and the side chain consists of a 1,5-linked arabinose on the C-4 of the 1,3-linked rhamnose.[45]

The immunomodulatory activity of the APS polysaccharide has been extensively studied both in vitro and in vivo. APS has been reported to improve the function of T cells, B cells, macrophages, lymphocytes and dendritic cells[42] (Fig. 1). Abuelsaad[46] studied the immunomodulatory effects of APS treatment on mice infected with *Aeromonas hydrophila* and found that APS treatment reduces ROS production, downregulates neutrophil activity and the proportion of CD4+/CD8+ T cells is increased. Yang et al.[47]

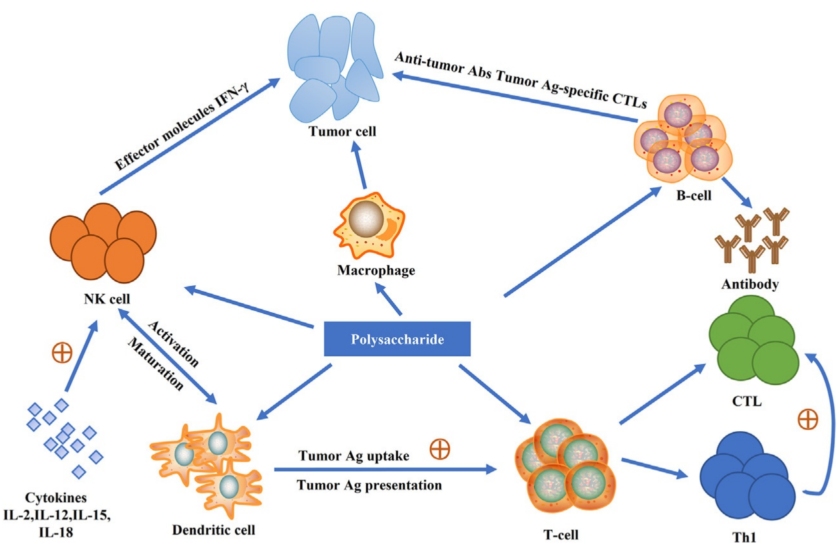

Fig. 1 Immune regulatory mechanisms of herb polysaccharides. *Modified from Jin M, Zhao K, Huang Q, Shang P. Structural features and biological activities of the polysaccharides from Astragalus membranaceus. Int J Biol Macromol 2014;64:257–266.*

reported the immunomodulatory activity of APS in experimental rat model of colitis induced by trinitrobenzene sulfonic acid. It is reported that APS can significantly improve experiment rat TNBS-induced colitis by regulating the expression of TNF-α, IL-1β and NFATc4.[47]

3.2 *Ginseng*

Ginseng (Table 3) has a long history of use as a traditional herb in many Eastern countries including Korea, China and Japan. There are two main types of ginseng: *Panax ginseng* and *Panax quinquefolius*. The common medicinal "ginseng" is mainly derived from the roots. It has been found to play a role in the improvement of various injuries and diseases from the central nervous system, the cardiovascular system to endocrine secretion and the reproductive and immune systems.[52] The main active compound *ginseng* is ginsenoside, which is a steroidal saponin conjugated to different sugar moieties and polysaccharides (10–20% by weight).

To date, several components of ginseng polysaccharides have been identified and studied, including arabinogalactan, pectin and acidic polysaccharides, which are mainly composed of monosaccharides such as L-arabinose, D-galactose, L-rhamnose, D-galacturonic acid and D-glucuronic acid.[53] Molecular weights are ranged from 3.2 to 1900 kDa.[48] However, there is a lack of detailed information on the actual structural characteristics and heterogeneity of these polysaccharide components. Many studies have shown that ginseng polysaccharides have antibacterial, anti-oxidant, anti-inflammatory, anti-depressant, anti-tumor and immunomodulatory properties both in vitro and in vivo.[48]

Anti-tumor and chemical protective effects of ginseng polysaccharide have received a lot of attention in the past decade. In a tumor-bearing mouse model, a sublethal dose of cyclophosphamide (CP) after treatment with 100 mg/kg Ganshan injection significantly reduced mortality and promoted recovery.[49] Ginseng polysaccharide is also found to inhibit cell proliferation and to induce apoptosis in HCT116 human colon cancer cells through the cyclin inhibitor protein p21.[50] And in both sexes of mice, a 100 mg/kg dose of Ginsan (the polysaccharide fraction of ginseng) significantly enhances liver endogenous anti-oxidant levels with no significant hepatotoxicity.[51] In a mouse model of γ-radiation-induced spleen injury, Ginsan (100 mg/kg) can be used to restore endogenous anti-oxidant enzymes heme oxygenase-1 (HO-1), SOD and GPx by the action of cytokines.[54,81]

3.3 *Lycium barbarum*

Lycium barbarum (Table 3) polysaccharide (LBP) is derived from the *Lycium barbarum* (wolfberry) fruit in the *Solanaceae* family. LBP is a well-known traditional Chinese herbal formula that has been used in China for >2300 years.[55] The Chinese believe that it can nourish the eyes, liver and kidneys, and balance the "yin" and "yang" in the human body.[56] Today, it has become a popular food or food supplement in East and West. Recent studies have confirmed the beneficial effects of wolfberry on human health, including anti-oxidative stress, anti-tumor, anti-radiation, anti-fatigue, anti-aging, anti-inflammatory and immunomodulatory properties.[57]

Under optimized extraction conditions, the polysaccharide component is 23% of the cognac mass.[58] Up to 95% of the LBP consists of glycans including glucose, arabinose, galactose, mannose, xylose, rhamnose, and fucose.[59] Recent studies have found that water-soluble polysaccharides derived from hydrazine have an average molecular weight of 49.1 kDa and an average protein content of 3.75%. The molar ratio of arabinose to galactose is 5.6:1. In addition, LBP is a highly branched polysaccharide with a backbone of $(1\rightarrow6)$ Galp linked galactose replaced by galactosyl or arabinose at O-3.[82]

Studies have confirmed LBP's beneficial effects on various diseases such as acute liver injury,[60] alcoholic liver injury,[83] and nonalcoholic fatty liver disease,[60,84] performance impairment,[85] brain I/R injury,[86] retinal degeneration,[82] stroke[87] and Alzheimer's disease.[55,88]

3.4 *Angelica sinensis*

Angelica sinensis (*A. sinensis*) (Table 3) is a well-known Chinese herbal medicine that has been used as a nourishing and hematopoietic agent for the treatment of gynecological diseases[61] for thousands of years. Recent studies have shown that polysaccharides in *A. sinensis* (APS) are the main bioactive components with various biological activities.[62]

Many ASP polysaccharides have been identified from the roots of *A. sinensis*. Their main structural features such as the monosaccharide compositions and molecular weight ranges have been summarized.[62] Several components of ASP are mainly composed of monosaccharides such as glucose, mannose, galactose, rhamnose, arabinose, and xylose. Molecular weights range from 5.1 to 2300 kDa. Most of the polysaccharides isolated from *A. sinensis* reported in the literature are heteropolysaccharides.

Cao et al.[63] studied the structural characteristics of an anti-tumor polysaccharide named APS-1d isolated from *A. sinensis*. It was found that the backbone of APS-1d consists of α (1,4)-D-glucopyranosyl residues. Branches consist of α (1,6)-D-Glcp residues and terminating with β-L-arabinofuranose residues.

In addition, some glucans are isolated and purified from *A. sinensis*. As-IIIa with a M_w of 850 kDa from *A. sinensis* consists of α-(1→3)-glucan.[64] It is also reported that a glucan from *A. sinensis* has an M_w of 100 kDa and consists of α-(1→6)-linked glucose.[65] Cao et al.[63] studied the structural characteristics of two glucans (APS-1cI and APS-1cII) from *A. sinensis*, and found that APS-1cI is a linear α-glucan composed only of α-(1→6)-D-Glcp. And APS-1cII has a repeating unit consisting of α(1→6)-D-Glcp and α-(1→4)-D-Glcp in a molar ratio of 1:4, α-(1→4)-D-Glcp-α-(1→6)-D-Glcp-α-(1→4)-D-Glcp-α-(1→4)-D-Glcp α(1→$]_n$ is a repeating unit of APS-1cII.[47]

The immunomodulatory activity of ASP has been extensively studied both in vitro and in vivo. It has been found that ASP increases the proliferation of total spleen cells, macrophages, and T cells by primary activation of non-specific immunity and secondary activation of helper T cells. ASP also enhances the gene expressions of IL-2 and IFN-γ.[89] The anti-tumor activity of ASP is revealed in that ASP can significantly inhibit the proliferation of HeLa cells and lung cancer cells. ASP also inhibits the growth of transplanted sarcoma-180 tumors in mice.[63] Other biological activities have also been found in ASP, such as hematopoietic activity, anti-oxidant activity, hepatoprotective activity, anti-osteoarthritis activity,[60] gastrointestinal protection[66,90] and anti-diabetic activity.[47,66]

3.5 *Cordyceps sinensis*

Cordyceps sinensis (Table 3), the Chinese caterpillar fungus or Dong-ChongXiaCao (winter worm-summer grass) in Chinese or Tochukaso in Japanese, is a valuable traditional Chinese medicine. *C. sinensis* has been used in China for >700 years, mainly as a tonic for nourishing the lungs and nourishing the kidneys.[91] Modern pharmacological studies have shown that it has a therapeutic effect on a variety of diseases and conditions such as the respiratory system, kidneys, liver, nervous system and cardiovascular diseases, as well as tumors, aging, hyposexuality, and hyperlipidemia.[92–99] Since 1964, *C. sinensis* has been listed as the official Pharmacopeia of the Chinese Ministry of Health by the Pharmacopeia and the Chinese Ministry of Education's

Committee of Herbs in the Severe Acute Respiratory Syndrome (SARS) outbreak in China in 2003, with a significant increase in the use of *C. sinensis*.[100,101]

Polysaccharides have become the target of the development and quality control of *C. sinensis*. And they can be classified into two types according to their position in fungal cells, intracellular polysaccharides (IPSs) and extracellular polysaccharides (extracellular polysaccharides, EPS).[68,101–105] The monosaccharide composition is usually glucose, mannose and galactose in different molar ratios. Different molecular weights have been found under various source materials and experimental conditions of *C. sinensis*, ranging from 1 to 1000 kDa.[68,100,106–111] Recently, some water-soluble IPSs isolated from cultured *C. sinensis* are identified as glucomannan, whose backbone is mainly composed of (1→2) and (1→4)-mannose, (1→3)-galactose, (1→) and (1→3,6)-the linkage of glucose.[100,112] Wang et al.[30] reported that the chemical structure of the isolated water-soluble polysaccharide (CPS-2) is derived from cultured *C. sinensis*, which is mainly composed of α-(1→4)-D-glucose and α-(1→3)-D-mannose branched with (1→4,6)-D-glucose every 12 residues on averages.[101] We found that salinity-induced anti-angiogenesis activities and structural changes of the polysaccharides from cultured *Cordyceps militaris*.[113,114]

Based on the theory of traditional Chinese medicine, the main role of *C. sinensis* is to "enrich lung yin and yang." Its uses include treatment of chronic low back pain, colds, excessive mucus and tears, chronic cough and wheezing, and sputum caused by kidney yang (shenyangqu). According to Western medicine, *C. sinensis* also has antibacterial activity, which reduces asthma, lowers blood pressure and enhances heartbeat. According to a large number of animal and clinical studies, polysaccharides represent a large class of biologically active components of *C. sinensis*, contributing to its health and pharmacological activity. The various biological activities and health benefits of IPS and EPS are summarized in Table 3. Both IPS and EPS obtained from wild or cultured *C. sinensis* show immunomodulation, anti-tumor, anti-oxidant and hypoglycemic effects, as well as other important biological activities, including anti-fibrosis, anti-fatigue, kidney protection, increasing plasma testosterone levels, and radiation protection.[30,69–73,111,113]

3.6 *Ophiopogon japonicus*

Ophiopogon japonicus (Maidong in Chinese) (Table 3), is a widely used traditional Chinese herbal medicine (Chinese Pharmacopeia Commission, 2015). According to traditional Chinese medicine theory, *O. japonicas* can nourish yin deficiency, promote body fluid production, nourish the lungs, relieve the mind, and eliminate heart fire. *O. japonicas* is listed as an edible Chinese medicine by the Ministry of Public Health of China because of its high efficiency, high availability and safety.[112] To date, China Food and Drug Administration (CFDA) has approved patent drugs namely Shen Mai injection/granule, Xuan Mai Gan Jie capsule/granule, etc., which contain *O. japonicas* as the main medicinal ingredient.[74,115]

The polysaccharides, the main composition of *O. japonicas* with an extraction rate up to 35%.[75] The molecular weights of *O. japonicas* polysaccharides are inconsistent, ranging from 2.74 to 325 kDa. In general, *O. japonicus* polysaccharide are mainly composed of β-fructose and a small amount of α-glucose. The backbone of OJP is formed by Fru-β(2→,→2)-Fru-β(6→,→6)-Glc-α(1→ and →1,2)-Fru-β(6→), and the molar ratios were 6.8:15.8:1.0:5.8.[75]

O. japonicus is rich in polysaccharides, which are possibly responsible for its biological activities, such as anti-diabetic activity, cardiovascular protection, immunomodulatory activity, anti-oxidant activity, anti-obesity activity, therapeutic effect on Sjogren's syndrome, etc.[74,76–78,116–120]

4. Future perspectives

Bioactive polysaccharides from traditional Chinese Herbal medicines are well known. During the past few decades, considerable efforts have been dedicated to the development of bioactive polysaccharides from the traditional Chinese Herbs. The main focus of these studies has been the purification of the polysaccharides from the traditional Chinese herbs, which are followed by monosaccharide compositional analysis, structural characterization and biological activity studies (Fig. 1 and Tables 1–3). The polysaccharides from *Astragalus membranaceus*, *Ginseng*, *Lycium barbarum*, *Angelica sinensis*, *Cordyceps sinensis*, *Ophiopogon japonicus* have been systematically studied by many different research groups. Both structural and biological information obtained are plentiful and accountable.

The unique and distinctive monosaccharide compositions, structural diversity, and remarkable biological activities of polysaccharides from the traditional Chinese herbs represent rich natural sources for drug development. The information reviewed here may be helpful in the definition of structure and function relationships necessary to design biological active polysaccharides with potential for the therapeutical use or to be used as

Table 2 Analytical methods for identifying monosaccharide compositions, molecular weight distributions, and glycosidic linkages of polysaccharides.

Items	Methods
Determination of purity and relative molecular weight distributions of polysaccharides	HPGPC, osmotic pressure, viscosity method, light scattering method, polyacrylamide gel electrophoresis
Monosaccharide compositional analysis	Complete acid hydrolysis, HPLC, GC, GC–MS, ion chromatography
Glycoside ring form (pyran, furan)	Infrared spectrum
Glycosidic linkages of the polysaccharide	Methylation analysis, GC–MS, LC–MS
The anomeric forms substituted by glycosides (α- and β-)	Glycosidase hydrolysis, nuclear magnetic resonance, infrared spectroscopy, laser Raman spectroscopy, etc.
Sequence of the oligosaccharides	Elective acid hydrolysis, sequential hydrolysis by glycosidases, nuclear magnetic resonance, etc.
The hydroxyl positions in the monosaccharide	Methylation, periodate oxidation, Smith degradation, GC–MS, nuclear magnetic resonance, etc.
Polysaccharide-peptide linkage	Dilute alkali hydrolysis method, hydrazine reaction, amino acid composition analysis, etc.

ingredients in functional foods. Both advantages and disadvantages of polysaccharides as drugs rely on its complicated molecular structures, multiple biological functions, and multiple molecular targets. Thus, there is a great need for further clarifying the active ingredients in the polysaccharides and its molecular targets responsible for the observed drug effects. In addition, how to comprehend the pharmacodynamics of these polysaccharides, how to standardize the quality of polysaccharides, and how to perform reliable pharmacokinetic studies of polysaccharides also should be addressed in the near future. The relatively inexpensive polysaccharides from the traditional Chinese herbs should be useable for the development of novel therapeutic agents, functional food, or adjuvants for preventing or treating different pathological conditions as those fungal polysaccharide-based drugs approved and used in China.[6,121–126]

Table 3 Summary of structural and biological activities of polysaccharides from six traditional Chinese herbs.

Species	Glycans	Extraction methods	Major monosaccharides	Glycosidic linkage in backbone	MW (Da)	Bioactivities	References
	*Astragalus membranaceus* Polysaccharides	Hot water，ultrasonic and microwave extraction, DEAE-Sephadex A-25, Sephadex G-100	Rhamnose, arabinose, xylose, ribose, galactose, glucose, mannose, fructose, fucose	α-(1→4)-Glc; α(1→3)-Gal	8.7–4800 K	Immunomodulation	42
						Anti-inflammation	43
						Anti-oxidant	44
						Anti-glomerulonephritis	45
						Anti-atherosclerosis	46
						Anti-diabetes	47
						Anti-tumor	49
	*Ginseng* Polysaccharide	Hot water, ethanol fractionation, DEAE-Sepharose-CL-6B, Sepharose-CL-6B, Sephadex-G-75	L-arabinose, D-galactose, L-rhamnose, D-galacturonic acid, D-glucuronic acid	α-(1→3)-Ara; β-(1→3) or β-(1→4) Gal	3.2–1900 K	Antibacterial	48
						Anti-oxidant	49
						Anti-inflammatory	50
						Anti-depressant	51
						Anti-tumor	52
						Immunomodulation	53
	*Lycium Barbarum* Polysaccharide	Warm water extraction, DEAE cellulose column, Sephadex G-150	Glucose, arabinose, galactose, mannose, xylose, rhamnose, fucose, galacturonic acid, glucuronic acid	β-(1→3) or β-(1→4) Gal; α-(1→6)-Glc	Average 49.1 K	Anti-oxidant	54
						Anti-tumor	55
						Anti-radiation	56
						Anti-fatigue	57
						Anti-aging	58
						Anti-inflammation	59
						Immunomodulation	60

	*Angelica* Polysaccharide	Water extraction, SephadexG-100, DEAE-52	Glucose, mannose, galactose, rhamnose, arabinose, xylose	α(1,4)-Glc	5.1–2300 K	Immunomodulation	61,62
						Anti-tumor	63,64
						Hepatoprotective	65
						Anti-diabetic	66
						Gastrointestinal protection	66,67
	*Cordyceps sinensis* Polysacchride	Hot water extraction, DEAE-Sepharose Fast Flow, Sephadex G-75	Mannose, glucose, galactose, galacturonic acid	α(1→2) or α(1→4)-Man-α(1→4)-Glc	7.7–210 K	Immunomodulation	30,68
						Anti-tumor	69
						Anti-oxidant	70
						Anti-diabetes	71
						Anti-aging	72
						Anti-scald	73
	*Ophiopogon japonicus* Polysaccharide	Hot water, ultrasonic and enzymatic water extraction, DEAE-52, Sephadex G-100	Fructose, glucose, arabinose, mannose	Fru-β (2→,→2)-Fru-β(6→,→6)-Glc-α(1→ and →1.2)-Fru-β (6→)	3.4–48.7 K	Anti-myocardial infarction	74
						Anti-diabetes	75
						Anti-oxidant	76
						Immunomodulation	77
						Anti-thrombotic	78

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Conflict of interest

The authors declare no conflict of interest.

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