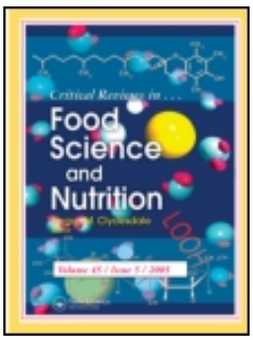

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Advances on Bioactive Polysaccharides from Medicinal Plants

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In recent decades, the polysaccharides from the medicinal plants have attracted a lot of attention due to their significant bioactivities, such as anti-tumor activity, antioxidant activity, anticoagulant activity, antidiabetic activity, radioprotection effect, anti-viral activity, hypolipidemic and immunomodulatory activities, which make them suitable for medicinal applications. Previous studies have also shown that medicinal plant polysaccharides are non-toxic and show no side effects. Based on these encouraging observations, most researches have been focusing on the isolation and identification of polysaccharides, as well as their bioactivities. A large number of bioactive polysaccharides with different structural features and biological effects from medicinal plants have been purified and characterized. This review provides a comprehensive summary of the most recent developments in physiochemical, structural features and biological activities of bioactive polysaccharides from a number of important medicinal plants, such as polysaccharides from Astragalus membranaceus, Dendrobium *plants,* Bupleurum, Cactus *fruits,* Acanthopanax senticosus, Angelica sinensis *(Oliv.) Diels,* Aloe barbadensis *Miller, and* Dimocarpus longan *Lour. Moreover, the paper has also been focused on the applications of bioactive polysaccharides for medicinal applications. Recent studies have provided evidence that polysaccharides from medicinal plants can play a vital role in bioactivities. The contents and data will serve as a useful reference material for further investigation, production, and application of these polysaccharides in functional foods and therapeutic agents.*

Keywords Medicinal plants, polysaccharides, chemical structure, physicochemical properties, biological activities

INTRODUCTION

Polysaccharides are polymeric carbohydrate macromolecules composed of long chains of monosaccharide units joined by glycosidic linkages (Delattre et al., 2011). With the development of molecular biology, the scientific community has gradually realized that polysaccharides, together with proteins and polynucleotides, are extremely important biomacromoleules which play important roles in the growth and development of living organisms (Cosgrove, 2005).

In nature, polysaccharides can be found in almost all living organisms, including in tissues of seeds, stems and leaves of herbal plants, body fluids of animals, cell walls and extra cellular fluids of bacteria, yeast and fungi (Singh et al., 2012). They range in structure from linear to highly branched. Examples include storage polysaccharides such as starch and glycogen, and structural polysaccharides such as cellulose and chitin. There are two types of polysaccharides: Homo-polysaccharides and hetero-polysaccharides. A typical homo-polysaccharide is defined to have only one type of monosaccharide repeating in the chain; whereas, a hetero-polysaccharide is

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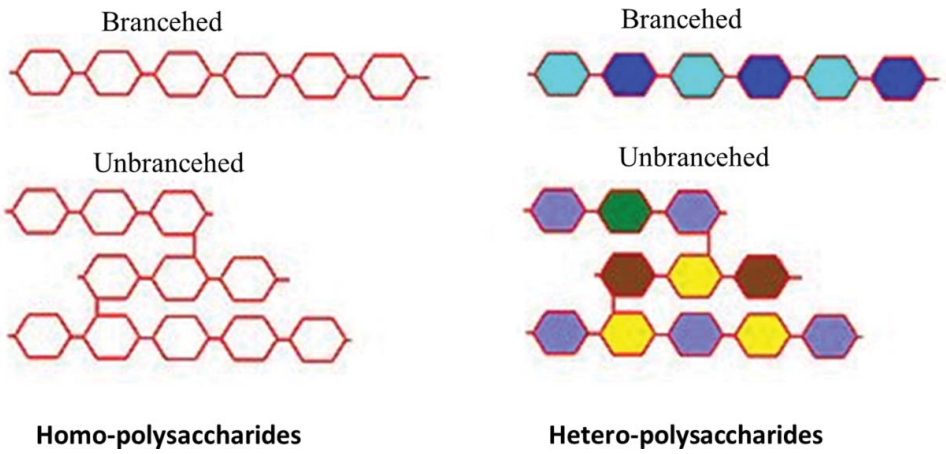

Figure 1 Two types of polysaccharides: Homo-polysaccharides and hetero-polysaccharides. The different colors represent different monosaccharides.

composed of two or more types of monosaccharides (Fig. 1). Homo-polysaccharides can be branched or unbranched as long as they all have the same monosaccharide unit. In both types of polysaccharide, the monosaccharide can link in a linear fashion or they can branch out into complex formations. It should also be noted that for a polysaccharide to be considered acidic it must contain one or more of the following groups: phosphate, sulfuric, or carboxyl.

The use of plants as food and medicinal products can be found throughout the world, particularly in the traditional medicines of China, Korea, India, Africa, Asia, and South America, and plants are also used as so-called "traditional remedies" in the Western countries. Stimpel et al. (1984) published one of the first scientific reports on potential macrophage immunomodulation activities of a pure, complex polysaccharide obtained from *Echinacea purpurea*, a plant that had a long traditional as a remedy agent for the treatment of influenza and wound-healing in the North America. Soon thereafter, more attention was devoted to the study of bioactive polysaccharides and most of these studies performed on bioactive polysaccharides took the traditional information on the use of medicinal plants and their related bioactivities as a guide to choose which plants should be studied (Paulsen and Barsett, 2005).

Recently, studies have demonstrated that polysaccharides have various types of biological effects, such as immunomodulatory activity, anti-oxidant activity, antimutant activity, antidiabetic activity, antibiotic activity, anticoagulant, and anti-inflammatory activities (Wasser, 2002; Jin et al., 2013; Xie et al., 2013a, 2013b; Xie et al., 2015a). The large number of bioactive polysaccharides with different structural features from different medicinal plants source and physiochemical properties constitutes a large source of material for applications in the future, especially medicinal applications.

In this paper, the review will focus on the physicochemical characteristics, structural features, and bioactive properties of some bioactive polysaccharides from a number of important medicinal plants. Special attention will be devoted to applications in the fields of pharmaceutical and biological medicine. It should also be noted that other types of bioactive polysaccharides, especially polysaccharides from fungal, bacterial and marine sources are also of great interest for both fundamental research and biomedical applications, however, these bioactive polysaccharides were recently extensively covered in several excellent reviews (Wasser, 2002; Zhang et al., 2007; Freitas et al., 2011; Fedorov et al., 2013; Mayakrishnan et al., 2013; Giavasis, 2014; Kozarski et al., 2014), and will not therefore be covered here.

OVERVIEW OF BIOACTIVE POLYSACCHARIDES FOR MEDICINAL APPLICATION

Polysaccharides derived from plant sources constitute a large family of biopolymers and are widely distributed in nature. Many of these polysaccharides have a long history as part of herbal ingredients that have been widely accepted in Asian countries (Guo and Cui, 2014). Several groups of polysaccharides have been studied over the last few decades with the aim of exploring their specific bioactivities towards human health. Importantly this trend has become more significant during the last 10 years as demonstrated by the number of publications in the area (Fig. 2). Both publications and citations in scientific journals related to "bioactive polysaccharides" have increased steadily particularly since 2004.

In recent years, some bioactive polysaccharides extracted and separated from plants, especially from the medicinal plants, have attracted a great deal of attention in the field of pharmacology and biochemistry due to their potential biological activities such as antitumor (Iguchi et al., 2000), anticoagulant (Cai et al., 2013), anti-oxidant (Xie et al., 2010, 2012; Yang et al., 2010b), antidiabetic (Simpson and Morris, 2014) and immunomodulatory activities (Lee et al., 2013; Tzianabos, 2002). Specifically, most polysaccharides derived from plants are relatively nontoxic and do not cause significant side effects (Xu et al., 2009; Xie et al., 2014). Many polysaccharides and their derivatives have been used in a variety of medicinal applications (Iguchi et al., 2000; Khan and Ahmad, 2013).

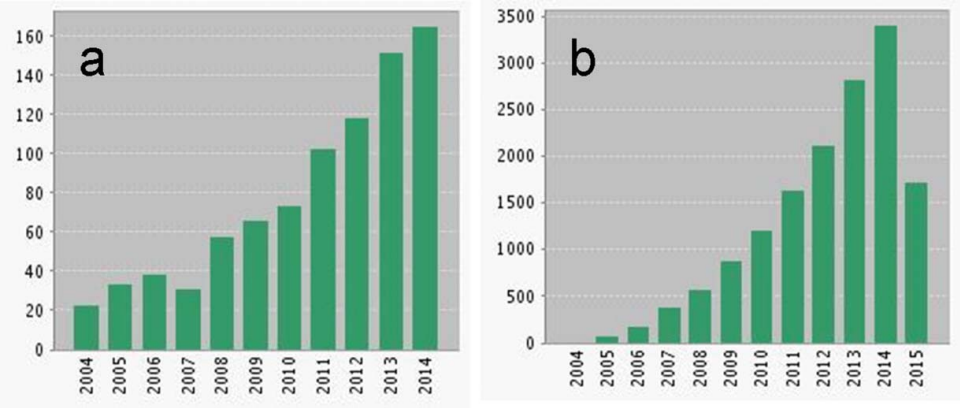

Figure 2 Number of scientific publications published on the topic of function of the Publication year. (a) Published Items in each year, and (b) Citations in each year. Taken from the database of web of science (http://apps.webofknowledge.com)**.** Topics entered: "polysaccharide" and "bioactive."

Lentinan, a β-(1→3)-D-glucan isolated from *Lentinus edodes*, has been known for its potent anti-tumor and anti-viral activities since the 1970s, and it has been widely used as an alterative medicine (Zhang et al., 2011). In Japan, lentinan injection was approved as an immunotherapeutic agent for the treatment of cancer and clinically applied in combination with chemotherapy (Bisen et al., 2010). Lentinan has also been widely employed as therapeutic agent in China in the treatment of malignant tumors for almost 20 years (Chen et al., 2013c). In clinical practice, chitosan has been proven to be beneficial in accelerating wound-healing, and can be applied as wound dressing as it does not generate irritation and allergic effects. In addition, oligosaccharides derived from the capsular polysaccharides are effective compounds for the preparation of glycoconjugate vaccines. The bioactive D-fraction (β-glucan) isolated from *G. frondosa* had been shown to have good anti-tumor activity and proposed for phase I/II clinical trials in USA and Japan (Zong et al., 2012). In Japan, polysaccharide-K (PSK) has been developed as a non-specific immunostimulant and had a long use against gastric and colorectal cancers. Clinical trials have shown that immunochemotherapies consisting of PSK and chemotherapeutic agents can improve long-term prognosis, reduce the risk of recurrence and increase the survival rates in patients with gastric and colorectal cancer (Zong et al., 2012). Finally, intravenous treatment of 30 T2DM patients with polysaccharides isolated from pumpkin significantly improved the treated patients (Shi et al., 2003). Polysaccharides isolated and identified from *A. membranaceus* (APS) has shown significant immunomodulatory effects and anti-cancer activity (Zahran et al., 2014). Thus, it is clear that polysaccharides derived from higher plants have significant therapeutic potential and represent a rich source for future discovery and development of novel compounds of medical value. Many plant-derived polysaccharides with a great deal of biological activities are found in traditional Chinese medicines, and therefore, high content of polysaccharides with proven pharmacological activities is considered to be an indicator of the medicinal status of a natural product (Wong et al., 1994).

The majority of polysaccharides are mainly used alone or in combination with other compounds. However, most of these polysaccharide-based medicines have not been scientifically investigated and there is little clinical data supporting their therapeutic use (Paterson, 2008). All in all, a summary of the main medicinal properties of these polysaccharides extracted from higher plants of their mode of action is necessary for understanding their potential for use in functional foods and nutraceuticals.

In addition, polysaccharides perform different physiological functions and hence have great potential applications in the fields of drug delivery, tissue engineering and regenerative engineering. There are numerous research and review articles that describe the applications in drug delivery, tissue engineering and regenerative engineering fields (Suh and Matthew, 2000; Shukla and Tiwari, 2012; Wang and Wang 2013; Shelke et al., 2014). However, the detailed description of these applications goes beyond the scope of this paper.

PHYTOCHEMICALS AND BIOACTIVITY OF POLYSACCHARIDES FROM MEDICINAL PLANTS

Dendrobium Plants

Dendrobium plants (Fig. 3A) belonging to *Orchidaceae* family have been used in traditional Chinese medicine for more than thousand years. It has been claimed that eating or drinking the comestibles made from *Dendrobium* plants can protect eyesight, alleviate throat inflammation, reduce fever, eliminate phlegm, and prevent cardiovascular diseases. Recent research provides evidence that polysaccharides are the primary active components exerting various pharmacological activities in these plants.

Physiochemical and Structural Features

D. officinale, also named *D. candidum* in some cases, is ranked "the first of the Chinese nine kinds of supernatural medicinal herbs" in China. In recent years, eight different polysaccharides have been obtained and characterized from this plant. Wang et al. (1988) reported three *D. officianle*

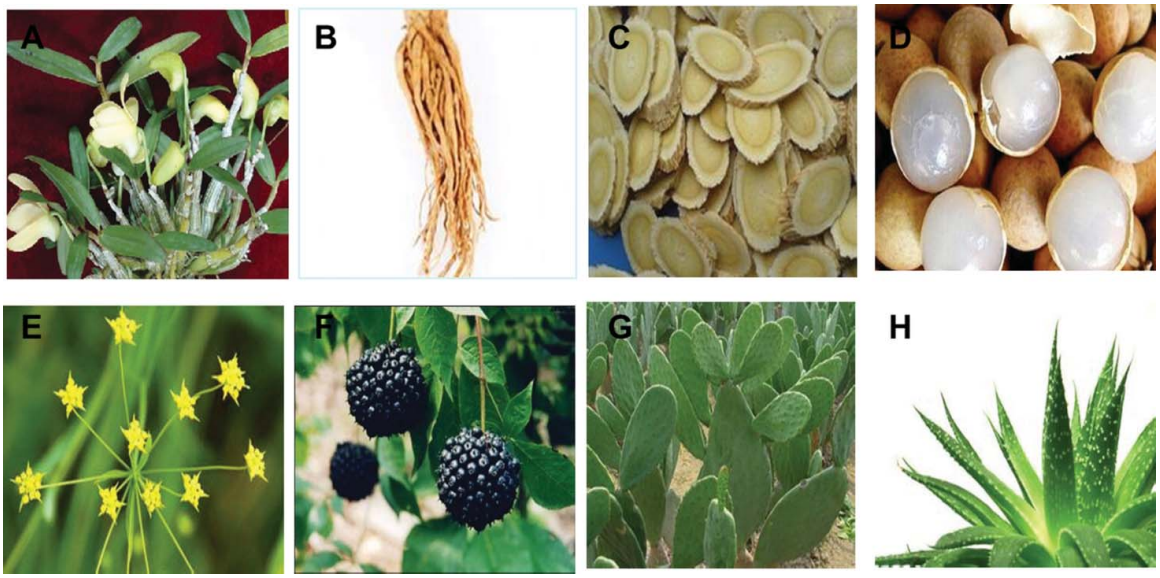

Figure 3 (A) Dendrobium plants, (B) Angelica sinensis (Oliv.) Diels, (C) Astragalus membranaceus, (D) Dimocarpus longan Lour., (E) Bupleurum plants, (F) Acanthopanax senticosus, (G) Cactus fruits, (H) Aloe barbadensis Miller.

polysaccharides with average M_ws of 1.2×10^5, 5×10^5 and 1×10^6 Da, respectively. Based on the analysis of acid hydrolysis, IR, ^{1}H and ^{13}C NMR, it is concluded that all the three polysaccharides were *O*-acetylglucomannan consisting of (1→3)-linked *β*-D-Man*p* and (1→4)-linked *β*-D-Glc*p* (Table 1). Yang et al. (2003) obtained two polysaccharides of DT2 and DT3 with the M_w of 7.4×10^5 and 5.4×10^5 Da. DT2 and DT3 were mainly composed of xylose (Xyl), arabinose (Ara), glucose (Glc), galactose (Gal), and mannose (Man), corresponding to the molar ratio of 1.0:0.8:5.9:1.0:0.5 and 1.0:0.5:7.9:1.3: 0.7, respectively. Methylation analysis and NMR spectrum revealed both DT2 and DT3 have a backbone consisting of (1→4)-linked *α*-D-Glc*p* (Table 1). A 2-*O*-acetylglucomannan (DOP-1-A1) extracted from *D. officinale* was composed of Ara, Man and Glc in a molar ratio of 1:40.2:8.4, with M_w of 1.3×10^5 Da (Hua et al., 2004). The backbone of DOP-1-A1 was shown to consist of (1→4)-linked *β*-D-Man*p* and (1→4)-linked *β*-D-Glc*p*, with branches of [*β*-D-Man*p*-(1→3)-*β*-D-Man*p*-(1→3)-*β*-D-Man*p*-(1→] at *O*-6 of (1→4)-linked *β*-D-Man*p* residue and [D-Ara*f*-(1→3)-*β*-D-Glc*p*-(1→] at *O*-6 of (1→4)-linked *β*-D-Glc*p* residue (Table 1). Glucomannan from *D. officinale* was demonstrated to be composed of Glc and Man with molar ratio of 1:6.9 and M_w of 3.12×10^5 Da. In comparison with DOP-1-A1, branches and O-acetylated glucose were not found in *Dendronan* (Xing et al., 2014). As well as *D. officinale, D. nobile* polysaccharides have also been well studied and seven different polysaccharides have been reported in recent years. Among these polysaccharides, two water-soluble fractions were extracted from the stems, named DNP-W3, DNP-W5 and DNP-W1B with the M_w of 7.1×10^5, 4.6×10^5 and 7.7×10^5 Da, respectively (Table 1). DNP-W3 was estimated to be a rhamnoarabinogalactan consisting of a backbone of (1→3)-linked *β*-D-Gal*p* with occasionally branches at *O*-4. The branches were mainly composed of (1→4)-linked *α*-L-Rha*p* and terminated with *β*-L-Ara*p* residues (Wang et al., 2010a). DNP-W5 was referred to be a pectic polysaccharide possessing a backbone of disaccharide of [→4)-*α*-GalA*p*-(1→2)-*α*-Rha*p*-(1→]. The branches were composed of galactosyl, mannosyl, glucosyl and xylosyl residues, which were attached to the position at *O*-4 of rhamnose and *O*-3 of galacturonic acid (Wang et al., 2010b). DNP-W1B was characterized to have a backbone consisting of (1→4)-linked and (1→6)-linked *β*-D-Glc*p* residues. [*α*-L-Ara*f*-(1→3)-*α*-L-Ara*f*-(1→3)-*α*-L-Ara*f*-(1→] and [1-linked *α*-D-Gal*p*] were referred to the branches attached to the *O*-4 of (1→6)-linked *β*-D-Glc*p* (Wang et al., 2013). Luo et al. (2010) also obtained four different polysaccharide fractions from *D. nobile*, named DNP1-1, DNP2-1, DNP3-1 and DNP4-2. Although there is significant difference in average M_w, the four fractions have similar monosaccharide compositions.

D. huoshanense is an endangered *Dendrobium* species and endemic to the Dabieshan mountain area of China. So far, five different polysaccharides have been found in *D. huoshanense*, three of which were extracted from the stems and two were extracted from the tissue cultures of protocorm-like bodies (PLBs, Table 1). Zha et al. (2007) reported a neutral polysaccharide HBS-1B23 with M_w 2.2×10^4 Da from the stem extracts of *D. huoshanense*, which consists of Glc, Man and Gal with molar ratio of 10:31:8. Structural characterization showed that HBS-1B23 have a backbone composed of (1→6)-linked *α*-D-Glc*p*, (1→3)-linked *α*-D-Man*p* and (1→4)-linked *α*-D-Glc*p*, with *O*-acetyl groups and *α*-D-Gal*p* residues attached to the *O*-3 position of (1→6)-linked *α*-D-Glu and (1→6)-linked *α*-D-Man, respectively. An immunostimulating polysaccharide (designated Fraction B) from the mucilage of *D. huoshanense* stem was characterized to be with a backbone

Table 1 Polysaccharides isolated from *Dendrobium* plants

Species	Compound name	Components	M_W (kDa)	Main chain composition	Branch composition	Bioactivites	References
D. candidum (D. *officinale*)	Candiduman I	Man:Glc=3.2:1	1000	→3)-β-D-Man*p*-(1→ →4)- β-D-Glc*p*-(1→	→4)-β-D-Glc*p*-(1→ β-pentose	—	Wang et al., 1988
	Candiduman II	Man:Glc:Ara:Xyl= 5.8:1:0.1:0.1	500			—	
	Candiduman III	Man:Glc:Xyl= 3.2:1:0.1	120			—	
	DT2	Glc:Gal:Xyl:Ara: Man=5.9:1.0:1. 0:0.8:0.5	740	→4)-α-D-Glc*p*-(1→	—	—	Yang et al., 2003
	DT3	Glc:Gal:Xyl:Ara: Man=7.9:1.3:1. 0:0.5:0.7	540		—	—	
	DOP-1-A1	Man:Glc:Ara=40.2:8 .4:1	130	→4)-β-D-Man*p*-(1→ →4)-β-D-Glc*p*-(1→	β-D-Man*p*-(1→ D-Ara*f*-(1→→3)-β-D-Man*p*-(1→ →3)-β-D-Glc*p*-(1→	—	Hua et al., (2004)
	Dendronan	Man:Glu=6.9:1	312	→4)-β-D-Man*p*-(→1→ 4)- β-D-Glc*p*-(→1	No branches	—	Xing et al., 2014
D.chrysotoxum	DCP-E	Ara:Glc:Man:Gal= 0.8:85.1:12.7:1.4	2010	—	—	Immunomodulation	Pan et al., 2015
	DCP-H	Ara:Glc:Man:Xyl: Gal=1.7:57.5:38. 5:0.8:1.5	2240	—	—	Immunomodulation	
	DCPP-I-a	Xyl:Glc:Gal=1.44:6. 93:12.79	122	—	—	Anti-tumor	Sun et al., 2013a
D.denneanum	DDP1-1	Ara:Xyl:Man:Glc: Gal=1.00:2.82:57. 11:140.82:7.76	51.5	—	—	Immunomodulation	Fan et al., 2009;2010
	DDP2-1	Ara:Xyl:Man:Glc: Gal=1.00:1.62:1. 18:77.5:7.79	26.1	—	—	Antioxidant	
	DDP3-1	Ara:Man:Glc:Gal= 1.00:1.03:8.84:2.00	6.95	—	—	—	
	DDP	Ara:Xyl:Man:Glc: Gal=1.00:2.66:8. 92:34.20:10.16	480	—	—	Antioxidant	Luo et al., 2011
D. fimhriatum	DFHP	Man:Glc:Gal=1.94:2. 23:1	210	—	—	Antioxidant	Luo et al., 2011
D. huoshanense	HPS-1B23	Glc:Man:Gal=31:10:8	22	→6)-α- D-Glc*p*-(1→ →3)-α-D-Man*p*-(1→ →4)-α-D-Glc*p*-(1→	α- D-Gla*p*-(1→	Immunomodulation; Prevention of liver injury and fibrosis	Pan et al., 2012; Zha et al., 2007
	Fraction B	Man:Glc=3.8:1	9.7	→4)-β-D-Man*p*-(1→ →4)-β-D-Glc*p*-(1→	No branches	Immunomodulation	Hsieh et al., 2008

(Continued on next page)

Table 1 Polysaccharides isolated from *Dendrobium* plants *(Continued)*

Species	Compound name	Components	M_W (kDa)	Main chain composition	Branch composition	Bioactivites	References
	DHP1A	Man:Glc:Gal=2.5:16.0:1.0	6.7	→4)-α-D-Glc*p*-(1→ →4,6)-α-D-Glc*p*-(1→ →6)-α-D-Glc*p*-(1→ →4)-β-D-Man*p*-(1→	β-D-Gal*p*-(1→	Antioxidant	Tian et al., 2013
	DHPD2	Gal:Glc:Ara=0.896:0.723:0.2	~8090	→5)-α-L-Ara*f*-(1→ →6)-α-D-Glc*p*-(1→ →6)-β-D-Glc*p*-(1→ →4)-β-D-Glc*p*-(1→ →3,6)-β-D-Gal*p*-(1→→6)-β-D-Gal*p*-(1→	α-D-Xly*p*-(1→β-D-Man*p*-(1→	Antiglycation	Li et al., 2014
	DHP-4A	Glc:Ara:Man:Rha=13.8:3.0:6.1:2.1	232	→6)-β-D-Glc*p*-(1→ →6)-β-D-Man*p*-(1→ →3,6)-β-D-Man*p*-(1→	β-L-Rha*p*-(1→ α-L-Ara*f*-(1→ →2)-β-L-Rha*p*-(1→ →4)-β-D-Man*p*-(1→ →3)-α-L-Ara*f*-(1→	Immunomodulation	Li et al., 2015
D. nobile	DNP-W1B	Glc:Ara:Gal=6.2:3.1:0.9	770	→4)-β-D-Glc*p*-(1→ →6)-β-D-Glc*p*-(1→	α-L-Ara*f*-(1→α-D-Gal*p*-(1→ →3)-α-L-Ara*f*-(1→	Immunomodulation	Wang et al., 2013
	DNP-W3	Gal:Rha:Ara=-3.1:1.1:1.0	710	→3)-β-D-gal*p*-(1→	β-L-Ara*p*-(1→ →4)-α-L-Rha*p*-(1→	Immunomodulation	Wang et al., 2010a
	DNP-W5	Man:Glc:Gal:Xyl:Rha:galacturonic acid=3.1:8.1:8.2:0.6:4.2:3.9.	460	→4)-α-GalA*p*-(1→ →2)-α-Rha*p*-(1→	Gal*p*, Man*p*, Glc*p*, Xyl*p*	Immunomodulation	Wang et al., 2010b
D. tosaense	DTP	Gal:Glc:Man=1:9.1:150.7	15~305	—	—	Immunomodulation	Yang et al., 2014a

Note: M_W, average molecular weight; Glc, glucose; Man, mannose; Gal, galactose; Rha, rhamnose; Ara, arabinose; Xyl, xylose; Man*p*, mannopyranosyl; Gal*p*, galactopyranosyl; Glc*p*, glucopyranosyl; Xyl*p*, xylopyranosyl; Rha*p*, rhamnopyranosyl; Ara*f*, arabinopyranosyl.

consisting of (1→4)-linked β-D-Man*p* and (1→4)-linked β-D-Glc*p* residues, and partially acetylated at *O*-2 and *O*-3 position of (1→4)-linked β-D-Man*p* residue (Hsieh et al., 2008). DHP1A is another polysaccharide with a low M_w of 6.7×10^3 Da found in the stems of this plant, of which the backbone was composed of (1→4)-linked α-D-Glcp, (1→4,6)-linked α-D-Glc*p*, (1→6)-linked α-D-Glc*p* and (1→4)-linked β-D-Man*p* in a molar ratio of 12.5:1.1:2:2.6, with a branched terminal β-D-Gal*p* attached to the *O*-6 position of (1→4,6)-linked α-D-Glc*p* residue (Tian et al., 2013). The protocorm-like bodies (PLBs) are actually somatic embryos induced from the stem segments of orchid plants. However, increasing research confirmed that polysaccharides in PLBs have distinct differences in structural features from those in the stems (Li et al., 2014, 2015) (Table 1).

Some other polysaccharides have also been extracted and purified from *D. chrysotoxum, D. denneanum, D. fimhriatum* and *D. tosaense*. Although their monosaccharide compositions have been determined, their detailed structures have not been reported (Table 1).

Biological Activities

Immunomodulatory Activity. Many studies have demonstrated that polysaccharides from *Dendrobium* plants have potent immnomodulatory activities both in vivo and in vitro (Table 1). *Dendrobium aphyllum* polysaccharides have been reported to stimulate the proliferation of plague forming cell (PFC), T lymphocytes and B lymphocytes in ICR mice at dosage of 25 mg/kg (Zhao et al., 1993). *D. candidum* polysaccharides could significantly increase the number of peripheral white blood cells, enhance lymph cells to produce moving inhibition factor, and eliminate the side effects of immunological inhibitor in vivo. Using the transplantable model of in mice, polysaccharides from *D. denneanum* at 1.25 mg/mL/day exhibited high immunomodulatory actions in S180 mice by increasing the serum levels of TNF-α, IL-2 and IFN-γ (Fan et al., 2010). The water soluble polysaccharides from the stem of *D. tosaense* enhanced the population of splenic natural killer (NK) cells, NK cytotoxicity, macrophage phagocytosis and cytokine induction in splenocytes (Yang et al., 2014a). The polysaccharide fraction of DCP-E and DCP-H of *Dendrobium chrysotoxum* polysaccharides stimulated the proliferation of BALB/C mice splenocytes in a dose-dependent manner (Pan et al., 2015).

The in vitro immunostimulating activity of *D. huoshanense* polysaccharides have been well studied in recent years. Hsieh et al. (2008) reported that the mucilage polysaccharides extracted from the stems of *D. huoshanense* exhibited specific functions in activating murine splenocytes to produce several cytokines including interleukin-6 (IL-6), interleukin-10 (IL-10), interferon-γ (IFN-γ) and interleukin-1α (IL-1α). Li et al. (2015) found *D. huoshanense* polysaccharide DHP-4A had the potential to stimulate RAW264.7 cells to release tumor necrosis factor-α (TNF-α), IL-6, nitric oxide (NO) and IL-10 via activation of NF-κB and MAPK signaling pathways.

Beside these, *D. moniliforme* and *D. nobile* polysaccharides have also demonstrated immunomodulatory activity via in vitro tests (Wang et al., 2010a, 2010b; Wang et al., 2013).

Antioxidant Activity. Bao et al. (2009) compared the in vitro antioxidant properties of *D. candidum* polysaccharide fractions with different M_w. Results showed that DSP1 (1.48×10^4 Da) had the strongest capability for eliminating DPPH (1,1-diphenyl-2 picrylhydrazyl) radical, inhibiting lipid peroxidation induced by Fe^{2+}-V_C and erythrocyte hemolysis induced by H_2O_2. *D. chrysotoxum* polysaccharide has strong antioxidant activities as demonstrated by the scavenging hydroxyl radicals, eliminating superoxide anions and chelating iron ions (Zhao et al., 2007). Among *D. denneanum* polysaccharide fractions, DDP2-1 exhibited powerful DPPH and hydroxyl radicals scavenging effects, and while DDP1-1 and DDP3-1 have no obvious effects (Fan et al., 2009). The in vitro radical-scavenging of DNP4-2 from *D. nobile* had better potential scavenging activity of ABTS, DPPH and hydroxyl radicals than the other polysaccharide fractions (Luo et al., 2010). The in vitro tests also showed that a water-soluble polysaccharide from *D. denneanum* (DDP) has excellent scavenging ability on DPPH and hydroxyl radicals. Meanwhile, DDP exhibited the ability to enhance the levels of antioxidant enzymes (e.g., SOD) and to decrease the serum MDA content by the in vivo assay (Luo et al., 2011).

Antitumor Activity. The anti-tumor activities of some *Dendrobium* polysaccharides have been evaluated in vitro and in vivo (Table 1). Wang et al. (2010c) obtained six different polysaccharide fractions (DNP-W1, DNP-W2, DNP-W3, DNP-W4, DNP-W5 and DNP-W6) purified from *D. nobile*. Results indicated that DNP-W1 and DNP-W3 exhibited high antitumor activities against sarcoma 180 in vivo, with the inhibition ratio of 65.3% and 61.2%, respectively. In agreement with this finding, DNP-W1 and DNP-W3 have also shown better protection against the growth of HL-60 cells than the other fractions. Jin et al. (2010) reported that mice sarcoma 180 was seriously inhibited by *D. candidum* polysaccharide (DP). Moreover, the index of thymus and spleen were significantly enhanced as well as the levels of IL-2 and TNF-α in mice serum by DP. The in vitro test showed that the growth of human hepatoma SMMC27721 cells was also restricted by DP in a dose-dependent manner. Two polysaccharide fractions (DCPP-I-a and DCPP-II) from the *D. chrysotoxum* exhibited prominent inhibitory activity against the proliferation of SPC-A-1 cells, suggesting the potential prospects of *D. chrysotoxum* polysaccharides as functional ingredient to prevent lung cancer (Sun et al., 2013a).

Other Biological Activities. A galactoglucomannan (GGM) extracted from *D. huoshanense* was reported to prevent selenite-induced liver injury and fibrosis by reducing the expression of

transforming growth factor-1 and type I collagen (Pan et al., 2012). Li et al. (2014) also reported the antiglycation activity of *D. huoshanense* polysaccharides. Lin et al. (2010) showed that administration of *D. officinale* polysaccharides could reverse the changes in body weight and water intake induced by immunization with SG autoantigen and protecting cells from apoptosis.

Angelica Sinensis *(Oliv.) Diels*

Angelica sinensis (Oliv.) Diels (*A. sinensis*) (Fig. 3B), a well-known Chinese herbal medicine, has been used as a tonic and hematopoietic agent for the treatment of gynecological disease (Cao et al., 2010a) for thousands of years. Recent research has shown that polysaccharides in *A. sinensis* are the major active components exerting various bioactivities (Jin et al., 2012).

Physiochemical and Structural Features

Numerous polysaccharides (ASP) have been identified from the root of *A. sinensis*. Their primary structural features such as monosaccharide composition and M_w have been summarized (Jin et al., 2012). The published literature mainly focused on M_w and monosaccharide components, and little structural information about *A. sinensis* polysaccharides have been reported (Table 2). Most of the polysaccharides isolated from *A. sinensis* reported in literature are heteropolysaccharides. Cao et al. (2006b) investigated the structural features of an antitumor polysaccharide named as APS-1d isolated from *A. sinensis*, and it was found that the backbone of APS-1d was composed of 1,4-α-D-glucopyranosyl residues, with branches, which were composed of 1,6-α-D-Glc*p* residues and terminated with β-L-arabinofuranose residues. The heteropolysaccharide isolated from *A. sinensis* had a backbone composed of (1→2)-linked-Rha and (1→4)-linked-Gal, with branches composed of (1→5)-linked-Ara terminated with Ara residues, and (1→4)-linked-Xyl terminated with Man residues (Wang et al., 2007). Sun et al. (2010b) reported that the polysaccharide isolated from *A. sinensis* named as ASP3 had a backbone composed of linear homogalacturonan fragments as smooth regions, and rhamnogalacturonan fragments with repeating unit of [→4)-α-D-Gal*p*A-(1→2)-α-L-Rha*p*-(1→] formed ramified parts as hairy regions. The side chains mainly contained short α-1,5-arabinofuranan possessing 3,5-substituted α-L-arabinofuranose residues as branching points. It also found that two homogeneous polysaccharides, APS-1a and APS-3a, isolated from *A. sinensis* mainly consisted of 1,3,6-linked Gal, 1,4-linked Gal, Ara and Gal (Zhao et al., 2012a).

In addition, some glucans have been isolated and purified from *A. sinensis*. A glucan (As-IIIa) with M_w of 8.5×10^4 Da from *A. sinensis* was composed of α-(1→3)-glucan (Zhang and Huang, 1999). It also reported that the polysaccharide from *A. sinensis* with the M_w of 1.0×10^5 Da was composed of α-(1→6)-glucan (Chen et al., 2001). Cao et al. (2006a) investigated the structural features of two glucans (APS-1cI and APS-1cII) from *A. sinensis*, and it was found that APS-1cI was a linear α-glucan composed of only (1→6)-α-D-Glc*p*, and APS-1cII had a repeating unit consisting of (1→6)-α-D-Glc*p* and (1→4)-α-D-Glc*p* with molar ratio of 1:4, [→4)-α-D-Glc*p*-(1→4)-α-D-Glc*p*-(1→6)-α-D-Glc*p*-(1→4)-α-D-Glc*p*-(1→4)-α-D-Glc*p*-(1→]$_n$ was the repeating unit of APS-1cII (Table 2).

Biological Activities

Hematopoietic activity. It has been reported that polysaccharide (ASP) was the major component responsible for the hematopoietic effect of *A. sinensis* (Liu et al., 2010b). The hematopoietic activity of ASP was through the stimulation of secretion of IL-6 and GM colony-stimulating factor. Administration of ASP could significantly accelerate the recovery of the hemoglobin levels of the blood-loss mice and markedly increased the colony-forming ability of bone marrow cells. An acidic polysaccharide isolated from the root of *A. sinensis* possessed hematopoietic-enhancing effects (Lee et al., 2012).

Chronic elevation of hepcidin, a negative regulator of body iron metabolism, could lead to systemic iron deficiency and hepcidin-induced anemia (Jin et al., 2012). ASP could significantly reduce hepcidin expression by inhibiting the expression in mothers against decapentaplegic protein 4 in liver and stimulating the secretion of erythropoietin (Liu et al., 2012). As for the mechanism, ASP could significantly reduced hepcidin expression by inhibiting the expression of phospho-SMAD1/5/8, janus-kinases 2 and extracellular signal-regulated kinase in the liver (Zhang et al., 2012; Zhang et al., 2014).

Immunomodulatory activity. The immunomodulatory activities of ASP have been widely investigated both in vitro and in vivo. It has been found that ASP increased proliferation of total spleen cells, macrophages and T cells, and also improved the gene expression and production of IL-2 and IFN-γ, through the primary activation of nonspecific immunity and secondarily activation of helper T cells (Yang et al., 2006). Meanwhile, it has been reported that ASP could induce a significant increase in cellular lysosomal enzyme activity, NO formation, reactive oxygen species (ROS) production and TNF-α secretion in macrophages (Yang et al., 2008c), which is suggested to be through the activation of toll-like receptor 4 pathway (Yang et al., 2007). In addition, ASP could up-regulate the function of dendritic cells by increase of IL-12 secretion, IFN-γ production by T cells in mixed lymphocyte reaction. Wang et al. (2011) found that ASP treatment significantly increased the respiratory burst activities and phagocytic activities, and enhance disease resistance against *Edwardsiella tarda*, which suggested dietary ASP could enhance the cellular immune function. It was also found that sulfated polysaccharide (APS-1) from *A. sinensis* could inhibit the virus replication and increase the reduced thymus/body weight index by murine leukemia virus infection (Yang et al., 2012).

Table 2 Polysaccharides isolated from *A. sinensis*

No.	Compound name	Components	M_W (Da)	Main chain composition	Bioactivites	References
1	As-IIIa	Glc	8.5×10^4	α-(1→3)-glucan	Immunomodulation	Zhang and Huang, 1999
2	As-IIIb	Glc, Man, Ara in the ratio of 10.0:10.0:4.0	4.9×10^4	Heteropolysaccharide with (1→4), (1→6) glycosidic bond	Immunomodulation	Zhang and Huang, 1999
3	XC-1	Glc	1.0×10^5	α-(1→6)-glucan	Immunomodulation	Chen et al., 2001
4	APS-1cI	Glc	1.7×10^5	Linear α-glucan composed of only (1→6)-α-D-Glc*p*	Immunomodulation	Cao et al., 2006a
5	APS-1cII	Glc	3.9×10^4	(1→4)-α-D-Glc*p* and (1→6)-α-D-Glc*p* in a molar ratio of 4:1		Cao et al., 2006a
6	APS-1d	Glc, Ara in the ratio of 13.8:1	5.1×10^3	Backbone composed of 1,4-α-D-Glc*p*, with branches attached to O-6 of some residues. Branches composed of 1,6-α-D-Glc*p* residues, terminated with β-L-Ara*f* residues	Anti-tumor	Cao et al., 2006b
7	ASDII-3-3	Rha, Ara, Xyl, Man, Gal in the ratio of 0.3:1.0:0.1:0.2:5.0	4.4×10^4	Backbone composed of (1→2)-linked-Rha and (1→4)-linked-Gal. Branches composed of (1→5)-linked-Ara terminated with Ara residues, and (1→4)-linked-Xyl terminated with Man residues		Wang et al., 2007
8	ASP3	Rha, Ara, Man, Glc, Gal in the ratio of 1.9:10.5:0.4:0.9:24.9		Backbone composed of linear homogalacturonan fragments and rhamnogalacturonan fragments. Side chains mainly composed of β-1,6- and β-1,4-galactopyranan and α-1,5-arabinofuranan	Radioprotection	Sun et al., 2010b
9	APS-1a	Ara, Glc, Gal in the ratio of 27.7:15.0:57.3	4.9×10^4	Mainly consisted of 1,4-linked galactose, 1,3,6-linked galactose, T-galactose and T-arabinose	Radioprotection	Zhao et al., 2012a
10	APS-3a	Ara, Glc, Gal in the ratio of 6.5:9.0:84.5	6.5×10^4	Mainly consisted of 1,4-linked galactose, 1,3,6-linked galactose, T-galactose and T-arabinose	Radioprotection	Zhao et al., 2012a
11	APS-3b	Glc, Gal, Ara, Rha, Man in the ratio of 2.3:5.4:6.8:1.0:1.2	2.3×10^5		Anti-tumor	Cao et al., 2010a, 2010b
12	APS-3c	Glc, Gal, Ara, Rha, Man, Xyl in the ratio of 6.3:4.7:6.7:6.5: 1.6:1.0	1.4×10^4		Anti-tumor	Cao et al., 2010a, 2010b

Note: M_W, average molecular weight; Glc, glucose; Man, mannose; Gal, galactose; Rha, rhamnose; Ara, arabinose; Xyl, xylose; Man*p*, mannopyranosyl; Gal*p*, galactopyranosyl; Glc*p*, glucopyranosyl; Xyl*p*, xylopyranosyl; Rha*p*, rhamnopyranosyl; Ara*f*, arabinopyranosyl.

Antitumor activity. The antitumor activities of ASP have been revealed that ASP could significantly inhibit the proliferation of HeLa cells, lung carcinoma cells, and inhibit the mice transplanted sarcoma-180 tumor growth (Cao et al., 2006b), which was associated with induction of tumor apoptosis through activation of the intrinsic mitochondrial pathway, such as disruption of the mitochondrial membrane, regulation of Bcl-2 family protein expression, increase of the cytosolic cytochrome c levels, improvement of the activities of caspase-9, caspase-3 (Cao et al., 2010a). Cao et al. (2010b) reported that the antitumor activities of ASP were related to stimulating host immunity which might result from activation of macrophages and splenocytes and stimulation of some cytokines secretion.

To explore new therapeutic strategies directly targeting leukemia stem cells, Liu et al. (2013a) found that ASP effectively inhibited the proliferation of human acute myelogenous leukemia $CD34^+CD38^-$ cell, normal hematopoietic stem and progenitor cells in vitro. Furthermore, ASP exerted cytotoxic effects on AML K562 cells, especially LSC-enriched $CD34^+CD38^-$ cells. Examination of the underlying mechanisms revealed that ASP induced $CD34^+CD38^-$ cell senescence, which was strongly associated with up-regulation of p53, p16, p21, and Rb genes and changes of related cell cycle regulation proteins P16, P21, cyclin E and CDK4, telomere end attrition as well as repression (Liu et al., 2013a).

Antioxidant activity. The antioxidant activities of ASP on hydrogen peroxide (H_2O_2)-mediated mouse peritoneal macrophages (Yang et al., 2007), myocardial ischemia/reperfusion

rat and alloxan-induced diabetic mice (Zhang et al., 2010), have been summarized and reviewed (Jin et al., 2012). Ai et al. (2013) investigated the antioxidant activity of ASP using the cerebral ischemia reperfusion rabbits, they found that ASP significantly decreased oxidative damage, and played an important role in protection of brain oxidative injury in animals. Yu et al. (2013) reported that ASP could significantly improve the levels of antioxidant enzymes, serum aspartate aminotransferase (AST), alanine aminotransfere (ALT) and alkaline phosphatase (ALP) of carbon tetrachloride (CCl_4) induced liver oxidative injury in rats.

Recently, Lei et al. (2014) reported that ASP could protect PC12 neuronal cells from H_2O_2-induced cytotoxicity, but also reduce apoptosis and intracellular reactive oxygen species levels, and increase the mitochondrial membrane potential induced by H_2O_2 treatment, which concluded the protective role of ASP against nerve cell injury and impairment caused by oxidative stress.

Hepatoprotective activity. The hepatoprotective activities of ASP on liver injury induced by acetaminophen in mice, acute hepatic injury induced by CCl_4 and hepatic immunological injury mice have been summarized and reviewed (Jin et al., 2012). Recently, Ji et al. (2014) and Hua et al. (2014) investigated the hepatoprotective effect mechanism of ASP using biochemical parameters coupled with metabolomics based on GC-MS and chemometrics. They found that pathological change, SOD activity, MDA content, ALT, AST, and γ-GT in plasma all had a certain degree of recovery after ASP intervention. The potential biomarkers in the liver homogenate and potential biomarkers in the plasma, such as succinic acid, glycine, palmitelaidic acid, citric acid, arachidonic acid, fumaric acid, malic acid, valine, ananine and hexadecanoic acid were found, which were associated with dysfunction of lipid peroxidation, energy metabolism, and amino acid metabolism.

Other activities. Other bioactivities such as anti-osteoarthritis activity (Wen et al., 2014), gastrointestinal protective (Cho et al., 2000), and anti-diabetic activities (Sun et al., 2005) also have been found in ASP.

Astragalus Membranaceus

Astragalus membranaceus (*A. membranaceus*) (Fig. 3C) is a popular health-promoting herbal medicine used for the treatment of common cold, diarrhea and fatigue for thousands of years (Jin et al., 2014). Polysaccharides are one of the major active ingredients in *A. membranaceus* with various bioactivities (Table 3).

Physiochemical and Structural Features

Many polysaccharides (APS) have been isolated and identified from *A. membranaceus*. The structural features of some are shown in Table 3. It has been shown that APS mainly contained 9 monosaccharides, such as Glc, Gal, Ara, Rha, Man, Xyl, Fuc, Fru and Rib, with M_w range of 8.7–4800 kDa. They might also contain GalA and GlcA. A few studies reported the detailed structural and conformational information of APS. The structural analysis of a water-soluble heteropolysaccharide (APSID3) isolated from *A. membranaceus* indicated that the minimal repeat unit was composed of one terminal Ara, one 1,5-linked Ara, one 1,3-linked Rha, one 1,3,4-linkedRha, six 1,4-linked GlcA and five 1,4-linked GalA residues, with the backbone composed of 1,4-linked GalA, 1,4-linked GlcA and a small amount of 1,3-linked Rha, and the side chain composed of 1,5-linked Ara located at C-4 of 1,3-linked Rha (Wang et al., 2006). Zhu et al. (2011) reported that the backbones of two polysaccharides isolated from *A. membranaceus* were composed of α-(1→3) Glc and a few 1→4, 1→6 Glc with the side chains composed of Ara and Xyl. Fu et al. (2013) found that the linear main chain of APS was consisted of 1,3-linked β-D-Gal residues with insertion of 1,6-linked α-Gal, β-Glc, 1,4-linked β-Gal, 1,5-linked β-Xyl,β-D-Gal, 1,2-linked α-Rha, 1,2,4-linked α-Rha residues, with C-2 and C-6 linked with H. Meanwhile, some glucans have also been identified from *A. membranaceus*, which were mainly determined as α-(1→4)-D-glucans (Jin et al., 2014). Li and Zhang (2009) reported that α-(1→4)-D-glucan from *A. membranaceus*, with a single α-D-Glc at the C-6 position every nine residue, along the backbone. The antitumor polysaccharide from *A. membranaceus* was found to be α-(1→4)-D-glucan with α-(1→6) linked branches attached to the O-6 of branch points (Li et al., 2009). Niu et al. (2011) reported that APS was a (1→4)-linked dextran with a (1→6)-linked branch every 10 residues.

Biological Activities

Immunomodulatory activities. The immunomodulatory activities of APS were widely investigated in vitro and in vivo, it was reported that APS could improve the function of T cells, B cells, macrophages cells, lymphocytes and dendritic cells (Jin et al., 2014). Recently, some new experiments have been carried out (Table 3). The immunomodulatory and growth-promoting effects of APS in *Nile tilapia* studied by Zahran et al. (2014) found that APS could significant increase in growth parameters, upregulated the phagocytic, respiratory burst, and bactericidal activities. Abuelsaad (2014) investigated immunomodulatory effect of APS treatment on *Aeromonas hydrophila*-infected mice, it was found that APS treatment reduced ROS production, downmodulated neutrophils activity, and increased $CD4^+/CD8^+$ T cells ratio in *A. hydrophila*-infected mice. Yang et al. (2014b) investigated the immunomodulatory activities of APS on an experimental colitis rat model induced by trinitrobenzene sulfonic acid; it was found that APS could significantly improve experimental TNBS-induced colitis in rats through regulation of TNF-α, IL-1β and NFATc4 expression.

Table 3 Polysaccharides from *A. membranaceus*

No.	Compound name	Components	M_W (Da)	Main chain composition	Bioactivites	References
1	AMon-S	Ara:Gal:GalA:GlcA in the ratio of 18:18:1:1	7.6×10^4	α-Arabino-β-3,6-galactan type structural units	Reticuloendothelial system-potentiating activity	Shimizu et al., 1991
2	Astragalan	Glc	1.5×10^4	(1→4)-α-Glucan	Antiviral	Liu et al., 2003
3	APSID3	Ara:Rha:Gal:Glc in the ratio of 2:2:5:6	5.8×10^5	The minimal repeat unit composed of one terminal Ara, one 1,5-linked Ara, one 1,3-linked Rha, one 1,3,4-linked Rha, six 1,4-linked GlcA and five 1,4-linked GalA residues		Wang et al., 2006
4	APS	Glc	3.6×10^4	An α-(1→4)-D-glucan, with a single α-D-Glc at the C-6 position every nine residue, on average, along the main chain	Renal protection	Li and Zhang, 2009
5	APS	Glc	3.6×10^4	An α-(1→4)-D-glucan with α-(1→6) linked branches attached to the O-6 of branch points	Antitumor and immunomodulation	Li et al., 2009
6	*Astragalus* polysaccharide	Glc		(1→4)-α-Glucan	Antioxidant and antitumor	Li et al., 2010
7	APS-II	Glc	1.2×10^4	Dextran bonded mainly with α-(1→4)-D-glycosidic linkage	Anti-atherosclerosis and anti-diabetes	Liu et al., 2010a; Wang et al., 2010d
8	APS-III	Glc	3.5×10^4	Dextran bonded mainly with α-(1→4)-D-glycosidic linkage	Anti-atherosclerosis and anti-diabetes	Liu et al., 2010a; Wang et al., 2010d
9	APS	Glc	2.1×10^4	A (1→4)-linked dextran backbone with (1→6)-linked branch every 10 residues	Antioxidant and immunomodulation	Niu et al., 2011
10	APS-I	Ara:Xyl:Glc in the ratio of 0.54:1:18.14	4.8×10^6	Backbone mainly composed of major α-(1→3) Glc and a few 1→4, 1→6 Glc, with side chain composed of Ara and Xyl	Anti-tumor	Zhu et al., 2011
11	APS-II	Ara:Xyl:Glc in the ratio of 0.23:1:29.39	8.7×10^3	Backbone mainly composed of major α-(1→3) Glc and a few 1→4, 1→6 Glc, with side chain composed of Ara and Xyl	Anti-tumor	Zhu et al., 2011
12	APS	Rha:Xyl:Glc:Gal in the ratio of 1:4:5:1.5	3.0×10^5	Backbone mainly composed of 1,3-linked β-D-Gal residues with insertion of β-Glc, 1,6-linked α-Gal, 1,5-linked β-Xyl, 1,4-linked β-Gal, β-D-Gal, 1,2-linked α-Rha, 1,2,4-linked α-Rha residues		Fu et al., 2013

Note: M_W, average molecular weight; Glc, glucose; Man, mannose; Gal, galactose; Rha, rhamnose; Ara, arabinose; Xyl, xylose; Man*p*, mannopyranosyl; Gal*p*, galactopyranosyl; Glc*p*, glucopyranosyl; Xyl*p*, xylopyranosyl; Rha*p*, rhamnopyranosyl; Ara*f*, arabinopyranosyl.

The immune adjuvant can help a vaccine to generate a strong immune response and provide long term protection against infection (Jin et al., 2014). Fan et al. (2013) found that astragalus polysaccharide liposome (APSL) could significantly promote splenocyte proliferation, enhance specific IgG, IgG1 and IgG2a antibody responses, which suggested that the adjuvanticity and drug action of APS could significantly improved by APSL. In addition, some recent studies have evaluated the immunomodulatory functions of APS on different animals immunized with various virus vaccines in order to develop a novel adjuvant (Jin et al., 2014). APS could significantly promote lymphocyte proliferation and enhance antibody titer and IFN-γ and IL-2 concentration of chickens vaccinated with Newcastle disease vaccine (Chen et al., 2013b). APS also

could efficiently enhance the immunogenicity of HBV DNA vaccines through improving DCs maturation and down-regulating the Treg frequency (Du et al., 2012). The same results reported by Sun et al. (2013b) also indicated that APS possessed reliable immunomodulatory activity and could be developed as an immunopotentiator.

Cardiovascular-protective Activity. Pathological cardiac hypertrophy is induced by increased sympathetic drive and can subsequently lead to congestive heart failure, which represents the major cause of morbidity and mortality worldwide (Dai et al., 2014). Effects of APS on cardiac hypertrophy and its possible mechanisms were investigated in vitro using the cardiac hypertrophic model induced by isoprenaline by Dai et al. (2014). It was found that APS exerted significant anti-hypertrophic activity via buffering Ca^{2+}-mediated calcineurin/NFATc3 and CaMKII signaling cascades, which provided new insights into the application of APS to the therapy of heart diseases.

It was found that APS therapy could prevent diabetic cardiomyopathy through PPARα-mediated regulatory pathways (Chen et al., 2013a). Cao et al. (2014) found that APS could suppress oxidative stress and apoptosis, ameliorate doxorubicin-mediated cardiotoxicity by regulating the PI3k/Akt and p38MAPK pathways. APS could inhibite the cohesion between HCMECs and polymorphonuclear leukocyte during IRI through the downregulation of p38MAPK signaling and the reduction of cohesive molecule expression in HCMECs (Zhu et al., 2013c). Zhu et al. (2013a) found that APS could suppress TNF-α-induced adhesion molecule expression, which suggested that APS might be used to prevent endothelial cell injury-related diseases. APS also could suppress HMGB1-induced a progressive increase in permeability in endothelial cells, which might be through the blocking of Rho/ROCK signal pathways (Zheng et al., 2013).

Antioxidant Activity. Studies on antioxidant activities of APS in vitro indicated that APS possessed considerable scavenging activities against DPPH radical, superoxide anion, and hydrogen peroxide. Further in vivo studies suggested that APS could improve the activities of antioxidant enzymes, offer good protection against age-induced and exhausting exercise-induced oxidative stress (Jin et al., 2014). Recently both in vitro and in vivo studies have been reported (Table 3). Lu et al. (2013) reported that APS could protect C2C12 myoblasts from damage by H_2O_2, promote cell proliferation and inhibit cells apoptosis, which has been proposed to involve the mitochondrial and death receptor pathways. It was found that APS could act as antioxidant by stimulating SOD production while inhibiting lipid peroxidation in the EA.hy926 cells (Huang et al., 2013). Liu et al. (2014b) found that the APS pre-treated mice showed significantly decreased alanine aminotransferase, NF-κB expression, aspartate aminotransferase and lactatedehydrogenase levels, and increased antioxidant enzymes. The results indicated APS could be explored as a prophylactic agent in the treatment of ionizing radiation-induced oxidative stress injury.

Antitumor Activity. The antitumor activity of APS has been widely studied because of its immunomodulatory and antioxidant functions, as the formation of tumor cells can be directly induced by immunosuppression and free radicals. The immunomodulatory and antitumor activities of APS studied by Yang et al. (2013) suggested that APS could effectively inhibit the solid tumor growth of H22 hepatocarcinoma transplanted in BALB/c mice, decrease the IL-10 level in serum, and promote the secretion of TNF-α, IL-2 and IL-12. The same results have reported by Tian et al. (2012), which also found that APS could downregulate MDR1 mRNA and P-GP expression levels both in H22 tumor-bearing mice and in H22 hepatoma cells in vitro. Sun et al. (2014) recently found that APS could remarkably improved the cytokine production and cytotoxicity of $\gamma\delta$T cells, increased the levels of TNF-α and IFN-γ, and decreased the levels of IL-10 and TGF-β in tumor-bearing mice. APS also inhibited the growth of stomach cancer via the stimulation of the immune response (Li et al., 2009).

Antidiabetic Activity. Insulin resistance, the basic precursor of type 2 diabetes mellitus (T2DM), is a polygenic disease accounting for about 90% of diabetic patients (Jin et al., 2014). Liu et al. (2014a) carried out some studies to investigate the function of APS in ameliorating insulin resistance in rat cells and to elucidate the associated mechanisms, and their results indicated that APS was capable of increasing adiponectin secretion. Ye et al. (2014) reported APS showed beneficial effects on the mice with insulin resistance and diabetes, such as lowering body weight, as well as blood glucose and triglyceride levels.

Some studies suggest that skeletal muscle secreted growth factor myostatin plays key role in regulating insulin signaling and insulin resistance. Liu et al. (2013c) found the elevated myostatin expression in skeletal muscle of type 2 diabetic KKAy mice and in cultured C2C12 cells exposed to palmitate. In addition, insulin resistance can lead to the impaired glucose homeostasis, which was characterized as the imbalance of glucose production and utilization. Liu et al. (2013b) found that APS could stimulate glucose uptake in L6 myotubes through the AMP-AMPK-AS160 pathway, which might contribute to its hypoglycemic effect. Zhu et al. (2014) reported that APS could inhibit the activity of α-glucosidase. The hind limb ischemia (HLI) is a common disease accompanied with a high incidence of *Diabetes mellitus*. Tu et al. (2014) found that APS could enhance angiogenesis, partially via VEGFNEGFR and Ang-1/Tie-2 signaling pathway. Those results indicated that APS could be used as a dietary supplement for health foods and therapeutics for diabetes.

Other Activities. In addition, APS has been found had anti-inflammatory and anti-HIV effects (Liu et al., 2003), to be able to mediate preventive effects on bronchopulmonary dysplasia, chronic renal failure, herpes simplex virus, H9N2 avian influenza virus, and intestinal mucosal injury (Kallon et al., 2013; Lian et al., 2014; Shi et al., 2014; Wang and Huang, 2014). The hepatoprotecitve, hematopoietic,

neuroprotecitve and growth-promoting activities have been summarized and reviewed by Jin et al. (2014).

Dimocarpus Longan Lour

Dimocarpus longan Lour. (Longan) (Fig. 3D) is a subtropical evergreen tree of the *Sapindaceae* family, has been recognized as traditional Chinese medicine. Recent research has shown that polysaccharides in Longan are the primary active ingredients exerting various bioactivities.

Physiochemical and Structural Features

The structural features of polysaccharides from longan fruit defined by monosaccharide composition, M_w, anomeric configuration and glycosidic linkage are summarized in Table 4. Different results about the features were given in various reports due to different purification methods or raw material. Four polysaccharides were isolated from "Chuliang" longan pulp, they were all composed of Ara, Glc, Man, Gal, Rha, Xyl and Rib by the main glycosidic linkages including →6)-α-D-Glcp(1→, →5)-α-L-Araf(1→, →4)-β-D-Manp(1→ and →4)-β-D-Rhap(1→. Their M_w were 14.59, 68.34, 107.4 and 5282 kDa, respectively (Yi et al., 2012a). In comparison, those from "Fenglisui" longan pulp, which were purified by anion-exchange chromatography and characterized to be β-type heteropolysaccharides with pyran group, were significant differences in monosaccharide composition and M_w. In addition, polysaccharides obtained from the different parts of "Shixia" longan fruit also exhibited structural varieties. A novel polysaccharide from the crude extract of "Shixia" longan flesh had the backbone consisting of (1→6)-α-D-Glucan with the M_w of 108 kDa (Zhu et al., 2013b). Two alkali-soluble polysaccharides of 'Shixia' longan pericarp were mainly composed of Xyl, Ara, Glc and Gal, in which Xyl constructed their backbones in combination with arabinose. The main glycosidic linkages of xylose were →3)- β-Xylp-(1→ and →3, 4)- β-Xylp-(1→(Jiang et al., 2009). A purified polysaccharide of "Shixia" longan seed was composed of →6)-Gal-(1→, →6) -Glu-(1→, →3)-Gal-(1→, Glu-(1→, →4)-Ara-(1→, →3)-Man-(1→ and →6)-Man-(1→ in the molar ratio of 24:14.6:8.4:7.8:4.7:2.4:1 (Table 5). Although many

Table 4 Polysaccharides from *Dimocarpus longan* Lour

No.	Compound name	Components	M_w (Da)	Main chain composition	Bioactivites	References
1	LP-I	Glu:Man in the ratio of 2.3:1	1.5×10^4	→6)-α-D-Glcp(1→,→4)-β-D-Manp (1→	Immunomodulation	Yi et al., 2012b
2	LP-II	Glu:Man: Ara in the ratio of 4.9:2:1	6.8×10^4	→6)-α-D-Glcp(1→,→5)-α-L-Araf (1→	Immunomodulation	Yi et al., 2012b
3	LP-III	Ara:Rha:Gal:Rib in the ratio of 4.7:3.2:2.2:1	1.1×10^5	→5)-α-L-Araf(1→, →4)-β-D-Rhap(1→	Immunomodulation	Yi et al., 2012b
4	LP-IV	Xyl:Rib:Man:Gal in the ratio of 7.8:5:2.3:1	5.3×10^6	-	Immunomodulation	Yi et al., 2012b
5	LPS-N	Xyl:Glu in the ratio of 1:1.9	1.4×10^4			Yang et al., 2008b
6	LPS-A1	Rha:Xyl:Ara:Ga in the ratio of 1:1.6:4.3:2.3	1.4×10^6			Yang et al., 2008b
7	LPS-A2	Rha	5.7×10^5			Yang et al., 2008b
8	LPS1	Glu	1.1×10^5	→6)-d-Glc-(1→(1→6)-α-D-Glucan with chemcial shift of C6	Anti-tumor	Zhu et al., 2013d
9	PLFP	Ara:Glu:Gal:GalA in the ratio of 2.1:1.1:2.1:1	4.2×10^5	→5)-α-L-Araf-(1→:→6)-β-D-Glcp-(1→:→3)-β-D-Galp-(1→:→3)-β-D-GalpA-(1→: →6)-β-D-Galp-(1→=2:1:1:1:1	Anti-glycated activity	Yang et al., 2009
10	ASPs I and ASPs II	Xyl:Ara in the ratio of (2.4–3.1):1	—	→3)- β-Xylp-(1→, and→3, 4)- β-Xylp-(1→, the substitution at C-4 position indicated that Xyl was of pyranose structure	—	Jiang et al., 2009
11	LSP	Gal:Glu:GalA:Ara:Man in the ratio of 7.7:6.7:1.9:1.4:1	—	→6)-Gal-(1→:→6)-Glu-(1→:→3)-Gal-(1→:Glu-(1→:→4)-Ara-(1→:→3)-Man-(1→:→6)-Man-(1→=24:14.6:8.4:7.8:4.7:2.4:1	Antioxidant	Jiang et al., 2013

Note: M_w, average molecular weight; Glc, glucose; Man, mannose; Gal, galactose; Rha, rhamnose; Ara, arabinose; Xyl, xylose; Man*p*, mannopyranosyl; Gal*p*, galactopyranosyl; Glc*p*, glucopyranosyl; Xyl*p*, xylopyranosyl; Rha*p*, rhamnopyranosyl; Ara*f*, arabinopyranosyl.

longan polysaccharides were obtained in different research groups, there is limited information on the sequence of glycosidic linkages in their backbones and side chains.

Chemical structures of longan polysaccharides have attracted attention, but investigations on their molecular confirmations and sizes are rare. Yi et al. (2013b) established the M_w-depended Mark-Houwink equation of longan pulp polysaccharide to obtain the relative exponent value, which was 0.61, and longan polysaccharides mainly existed as flexible chains in water at 25°C. Then, the analyses of $<S^2>z^{1/2} = kM_w^v$ equation, congo red test and atomic force microscope image confirmed the different conformations among different longan polysaccharide fractions, in which fraction LPI was a sphere-like polysaccharide with triple-helix structure, and the other fractions exhibited as chains and had low-organized confirmations without triple-helix structure. The sphere-like structure of LPI could be gradually dissociated to random coil in NaOH solution, and the degree of dissociation positively responded to the alkali concentration (Yi et al., 2012a; 2013a)

Biological Activities

Immunomodulatory activity. In traditional Chinese medicine, longan pulp was used as a tonic to prevent disease. Among all the health benefits of longan pulp which have been published, immunomodulatory effect is the most widely accepted function in practice (Zhu et al., 2013b), and polysaccharides are expected to be the critical substance contributing to the effect. Recent immunological investigations have confirmed the immunomodulatory activities of longan pulp polysaccharides in vivo and in vitro (Yi et al., 2011a; 2011b; 2012a; 2012b; Zhong et al., 2010). After peroral

Table 5 The polysaccharides isolated from *Bupleurum* and *A. senticosus*

No.	Compound name	Components	M_W (Da)	Source	Bioactivites	References
			Polysaccharides isolated from *Bupleurum*			
1	BR-2IIb	GalA, Ara, Rha, and Gal in with the molar ratios 13.0:2.1:1.4:1.0	3.6×10^4	*Bupleurum smithii*	Immunomodulation Anti-complementary	Yamada et al., 1989
2	BCPS-1	Ara, Gal, Glc in a molar ratio of 2.1:2.5:1.0	2.9×10^4	*Bupleurum chinense* DC	Antioxidant	Sun et al., 2010a
3	WBCPa	Man, Gal and Glc in molar ratios of 0.6:2.4:3.2	1.0×10^5	*Bupleurum chinense* DC	Antioxidant	Tong et al., 2013
4	WBCPb	Man, Gal, and Glc in molar ratios of 0.2:1.6:4.8	5.5×10^4	*Bupleurum chinense* DC	Antioxidant	Tong et al., 2013
5	WBCPc	Man, Glc, and GalA with molar ratio of 2.5:1:2.2	7.7×10^4	*Bupleurum chinense* DC	Antioxidant	Tong et al., 2013
6	BC-PS1	Gal, Gala, Glc, Ara and Man in the ratio of 1.6:1.1:1.8:1.7:1.0	2.0×10^6	*Bupleurum chinense* DC	Immunomodulation Anti-complementary Anti-inflammatory	Di et al., 2013
7	BPs	GalA, Ara, Rha, and Gal in with molar ratio of 13.0:2.1:1.4:1.0		*Bupleurum chinense* DC	Immunomodulation Anti-inflammatory	Wang et al., 2009; Jiang et al., 2012; Cheng et al., 2012
8	CCCP	Ara, Gal, Glc in a molar ratio of 2.1:2.5:1.0		*Bupleurum smithii*	Antioxidant Radiation protection	Li et al., 2013; Dai et al., 2011
9	BR2IIc/PG-1			*Bupleurum scorzonerifolium* Willd	Stimulates the Tyrosine Phosphorylation	Matsumot et al., 2008
			Polysaccharides isolated from *A. senticosus*			
1	PES	—	—	—	Immunomodulation	Shen et al., 1991
2	ASP	—	—	—	Immunomodulation	Han et al., 2003
3	ASP-2-1	Rha, Xyl, Glc, Man, Ara, Gla, Glc in ratio of 7.45:18.63:25.15:0. 93:8.35:2.79:5.69	1.5×10^4	—	Immunomodulation and antioxidant	Chen et al., 2011
4	CASPs	Ara, Man, Rha, Gal, Glc in the ratio of 1:1.1:3:4.7:5.	7.0×10^4, 3.8×10^4, 1.2×10^5, 1.9×10^4	—	Protective effects on cerebral Ischemia-reperfusion injury	Xie et al., 2015b
5	ANP	Ara, Man, Glc, Gal in the ratio of 1.0:2.6:2.5:1.4	1.07×10^4	An acetylated heteropol ysaccharide	Immunomodulationanti -HSV-2	Lee et al., 2015
6	AAP	Ara, Gal, 4-*O*-methyl-D-GlcA in ratio of 5:10:1	8.40×10^4	A type II arabino galactan	Immunomodulationanti -HSV-2	Lee et al., 2015

Note: M_W, average molecular weight; Glc, glucose; Man, mannose; Gal, galactose; Rha, rhamnose; Ara, arabinose; Xyl, xylose.

administration of 100 $mgkg^{-1}d^{-1}$ longan pulp polysaccharide for 15 d, the antibody production, splenocyte proliferation, macrophage phagocytosis, NK cell cytotoxicity and cytokine secretion of immunosuppressed mice were all significantly enhanced (Yi et al., 2011b). Likewise, polysaccharide UELP from longan pulp could enhance the immune functions of S180 tumor mice and inhibit tumor cell growth (Zhong et al., 2010). The enhancement of host immune system has been considered as a possible way to inhibit tumor growth. Moreover, longan pulp polysaccharides could directly stimulate immune cell response in vitro, and their effects were different from each other due to their structural differences including monosaccharide composition, M_w, glycosidic linkage and molecular conformation (Yi et al., 2012a; 2012b; 2013a). The single-helix chain of longan pulp polysaccharide LPI might be key in the activation of lymphocyte and NK cells (Yi et al., 2012a). Longan pulp polysaccharides could also directly inhibit the proliferations of A549, HeLa and HepG2 tumor cells in vitro (Yi et al., 2013a; Zhu et al., 2013b).

Antioxidant activity. The antioxidant function of longan fruit was declared to be mainly due to the high content of phenolic compounds (Yang et al., 2011). However, several studies characterized the antioxidant activities of longan polysaccharides by the direct scavenging effects on DPPH radicals, superoxide anion and hydroxyl radicals (Jiang et al., 2013; Prasad et al., 2010; Yang et al., 2008a; 2010; Zhong et al., 2010). Yang et al. (2008a) confirmed the optimal ultrasonic extraction conditions to obtain the strongest DPPH radical scavenging activity of longan pericarp polysaccharide. A high correlation coefficient between degree of methylation and scavenging superoxide anion radical activity of longan pericarp polysaccharide was found. It indicated the hydroxyl groups of monosaccharide units paly key roles in the radical scavenging activity (Yang et al., 2010).

Other activities. Longan pericarp polysaccharides also exhibited an excellent anti-glycated activity, inhibited tyrosinase activity and act as a noncompetitive inhibitor of the enzyme, and some dermatological disorders associated with melanin hyperpigmentation (Yang et al., 2008a; Prasad et al., 2010).

Bupleurum Plants

Bupleurum (Fig. 3E), as a traditional edible Chinese herb, has been used for more than thousand years for the treatment of influenza, fever, malaria in China and Japan (Di et al., 2013; Matsumoto et al., 2008; Sun et al., 2010a). Recent studies have indicated that polysaccharides are the primary active components exerting various beneficial effects (Table 5), including immunoregulation activity, resistance of radiation, anti-oxidation activities in these plants (Cheng et al., 2010; Dai et al., 2011; Tong et al., 2013).

Physiochemical and Structural Features

There have been many polysaccharides isolated from *Bupleurum* plants. The physiochemical features of some are shown in Table 5. The total carbohydrate and uronic acid and protein contents is the most basic indicators for polysaccharides, Sun et al. (2010a) found the the total carbohydrate content of water-soluble polysaccharide (BCPS-1) from *Bupleurum chinense* DC was 97.5%. An anti-complementary polysaccharide from the roots of *Bupleurum chinense* was found that contained 97.6% of total carbohydrate and 18.5 % of uronic acid (Di et al., 2013). Another polysaccharide extracted from the roots of *Bupleurum smithii* was also studied, which contained of 27.2% of uronic acid, 94.06 % of carbohydrate, and only 1.98% of protein (Yamada et al., 1989). It was also confirmed that BR-2IIb contained a large enzyme-sensitive polygalacturonan region (designated PG-1) a backbone of 4-linked GalA and 2-linked Rha to which a highly branched arabinogalactan was attached to position 4 of some 2-linked Rha units (Matsumoto et al., 1995; Yamada et al., 1989). As well as the total carbohydrate content, various results of M_w and monosaccharide composition were also found in different polysaccharides from different breed. A homogeneous polysaccharide with an average M_w about 2×10^6 Da was gained by Di et al. (2013), which was mainly comprised of Glc, Ara, Gal and Man in the ratio of 3.5:2.4:2.0:1.0, along with trace of Rha and Xyl. Meanwhile a smaller M_w polysaccharide was composed of Glc, Gal and Ara, with a molar ratio of 1.0:2.5:2.1, and its M_w was estimated as 2.9×10^4 Da (Sun et al., 2010a). As for the configuration and position of glycosidic linkages, the structure of bulpeuri polysaccharide is very complex, the structure of *Bupleurum chinense* polysaccharide (BC-PS1) is terminal, 1,3-linked and 1,4-linked Galp, terminal, 1,4,6-linked 1,4-linked and 1,6-linked, Glcp, terminal and 1,5-linked Araf, terminal, 1,4,6-linked and 1,6-linked Manp. The study also revealed BC-PS1 was a branched polysaccharide due to the identification of 1,4,6-linked Manp and 1,4,6-linked Glcp. A *Bupleurum falcatum* L. polysaccharide fraction (BL-2IIB) consisted mainly of Gal, Gra, Rha, and GalA in the molar ratios 1:2.1:1.4:13 and contained a large enzyme-sensitive polygalacturonan region (Yamada et al., 1989), which contained a backbone of 4-linked GalA and 2-linked Rha to which a highly branched arabinogalactan was attached to position 4 of some 2-linked Rha units (Matsumotoet et al., 2008). Polysaccharide (BCPS-1) isolated from the roots of *Bupleurum chinense* have a backbone composed of 1,5-linked Ara), 1,4-linked Gal and 1,3,6-linked Gal, and part of Gal and all Glc were distributed in the branches (Matsumotoet et al., 2008).

Biological Activities

Immunomodulatory Activity. Macrophages play a key role in the immune response and regulation of acquired immunity. It has been found that *Bupleurum* polysaccharides significantly

improved the immunological function, and reduced the NO production stimulated by LPS (Cheng et al., 2010). According to a study performed to the effect of B cells cultivated with polysaccharides (Guo et al., 2000; Matsumoto et al., 2003), the normal B cells from murine spleen were added with polysaccharide bupleuran 2IIc, extracted from the roots of *Bupleurum falcatum* L, the enhanced IgM secretion by bupleuran 2IIc was reduced. Besides, the results suggested that stimulation of bupleuran 2IIc enhanced the immune function of normal mice (Matsumoto et al., 2003). Furthermore, *Bupleurum* polysaccharides were found to possess beneficial effects on the systemic lupus erythematosus (Jiang et al., 2012), one of autoimmune diseases. Wang et al. (2009) also demonstrated that *Bupleurum* polysaccharide could protect kidney from glomerular injury via reduced immunoglobulin deposition and lowered proteinuria.

The Protection to Gastrointestinal Mucosa. The pectic polysaccharide, bupleuran 2IIc from *Bupleurum falcatum* L. on cytokine secretion of intestinal epithelial cells was investigated in vitro (Matsumoto et al., 2008). The ELISA and RT-PCR were used to examine the effect of 2IIc on G-CSF secretion from intestinal epithelial cells, and the promotion effect could be found that the G-CSF secretion from the cells was enhanced in dose-dependent and time-dependent manners with 2IIc, meanwhile the enhanced G-CSF gene transcription in MCE 301 cells could be observed by RT-PCR (Matsumoto et al., 2008). It is reported an antiulcer polysaccharide fraction (BR-2) from *Bupleurum falcatum* L., having a significant acceleration of the ulcer healing. In addition, some inflammation related factors, such as IL-1β, IL-6 and TNF-α were also detected by ELISA (Cheng et al., 2010). There were no significant evidence to support the effect on TNF-α secretion, but the reduction of TNF-α production was observed by the presence of BPs also suppressing IL-1β and IL-6. Recent studies demonstrated that complement represents an important role to inflammatory response, and excessive complement activation usually dedicates some tissue damage and various diseases (Di et al.,2013a; Yamada et al., 1989). The current study revealed that BC-PS1, one of *bupleurum* polysaccharides, was the exclusive active component and the inhibitory effect of BC-PS1 on activation of human complement mainly occurred through the classical pathway. Bioassays revealed that BC-PS1 coule resulted in 50 % hemolytic inhibition on classical complement pathway in 0.20 $\pm$ 0.03 mg/mL and alternative complement pathway in 0.37 $\pm$ 0.02 mg/mL, respectively (Di et al., 2013).

Anti-oxidation. BCPS-1, a polysaccharide fraction isolated from the roots of *Bupleurum chinense* DC, had a significant antioxidant activity and behaved in a concentration-dependent manner. The DPPH radical scavenging activity of BCPS-1 reached 52.9 % and 76.5 % at 8 mg/mL, respectively (Sun et al., 2010a). And the anti-oxidation of its three fractions, coded as WBCPa, WBCPb, and WBCPc, from *Bupleurum chinense* DC, were tested and the results of DPPH radical scavenging assay suggested that the scavenging rate of WBCPa, WBCPb, and WBCPc could reach 61.0 %, 65.5 %, and 93.0 % at 4 mg/mL, respectively (Tong et al., 2013). The fraction WBCPc demonstrated more effective scavenging action than two other fractions, at 0.2∼4 mg/mL (Tong et al., 2013). Meanwhile, Chinese medicine using bupleurum plays important role in hepatoprotective treatment due to antioxidant activity in vivo. A hot water soluble polysaccharide fraction (WBCP) from the roots of *Bupleurum chinense* could significant increase in the activities of SOD and GSH (Zhao et al., 2012b).

Other Activities. The protective effect of *Bupleurum* polysaccharides against UVB-induced DNA damage was also assessed by Dai et al. (2011), it was found that the DNA damage is reduced by crude *Bupleurum* polysaccharides after UVB-irradiation.

Acanthopanax Senticosus

Acanthopanax senticosus (*A. senticosus*) (Fig. 3F), belongs to the Araliaceae family, also called "*Siberian Ginseng*" or "*Eleutherococcus senticosus*", has a long history of medicinal use in China, Korea, and Japan for the treatment of hypertension, angina pectoris, rheumatism, diabetes and tumors (Huang et al., 2011). As one of the main active ingredients in *A. senticosus, A. senticosus* polysaccharides were hsve been studied with respect to various pharmacological effects (Table 5).

Physiochemical and Structural Features

There have been numerous polysaccharides isolated and identified from *A. senticosus*. Their structural features such as monosaccharide composition, M_w, primary structure information and pharmacological properties are shown in Table 5. A high yield of 10.9 mg/g was obtained under an optimum ultrasound extraction condition (Zhao et al., 2013). After further purification through ion exchange and gel filtration chromatography, a water-soluble polysaccharide ASP-2-1 from *A. senticosus* leaves was obtained with M_w of 1.5×10^4 Da (Chen et al., 2011), and two other polysaccharides abbreviated ANP and AAP were isolated from the young buds of *A. sciadophylloides* with M_ws of 1.1×10^4 Da and 8.4×10^4 Da, respectively (Lee et al., 2015). Among these polysaccharides, some are homogeneous, and the others are not. A *Acanthopanax* polysaccharide named CASPs, extracted from the root of *A. senticosus* showed two main M_w distributions (7.0×10^4 Da and 3.8×10^4 Da) and two minor M_w distributions (1.2×10^5 Da and 1.9×10^4 Da) (Xie et al., 2015b).

Biological Activities

Polysaccharides, aqueous extracts or glycoproteins obtained by different methods from different parts of *A. senticosus* possessed various bioactivities, such as the scavenging

free radicals (Chen et al., 2011; Zhao et al., 2013), cardiovascular protection, anti-inflammation, immunomodulation (Fang et al., 1985), anti-radiation (Li and Zhou, 2007), and the lowering of blood glucose (Fu et al., 2012) (Table 5).

CASPs improved nervous defect symptoms of rats with the cerebral ischemia-reperfusion injury and reduce the brain infarct volume and brain water content (Xie et al., 2015b). Fu et al. (2012) reported a homogeneous polysaccharide ASP which could fight against *diabetes mellitus* via an alloxan-induced diabetic mouse model. An aqueous extract of the stem bark of *A. senticosus* (AS) from Japan has been shown to prolong the swimming time of rats (Fujikawa et al., 2005) in a forced swimming test. An immunostimulatory polysaccharide isolated from a cell culture of *A. senticosus* was previously shown to increase lymphocyte proliferation, T-dependent antibody responses and macrophage phagocytosis by mediating TLR signaling (Han et al., 2003). Furthermore, this polysaccharide significantly inhibited the growth of sarcoma 180 and prolonged the survival time of tumor-bearing mice (Ha et al., 2004; Shen et al., 1991). A study conducted by Liao et al. (2005) proved that polysaccharides from *A. senticosus* possess good irradiation protection properties against irradiation-induced injury, which partly attributes to their strong anti-infection activity.

Due to the advantage of low toxicity and little or no side effects, *A. senticosus* polysaccharides could be explored as a novel and potential natural antioxidant and immunostimulating agent used in functional foods or medicine (Chen et al., 2011), and much attention has been paid to it. Further experiments on their structure-biological activity relationships should be conducted to get a better understanding of this plant.

Cactus *Fruits*

Cactus fruits (Fig. 3G) derived from Cactaceae family, are abundantly found in the tropics and subtropics, including the south of China, and are also grown in Mexico, the United States, Australia, Africa, Madagascar, Sri Lanka and India, are widely distributed for ornamental and medicinal use (Piga, 2004).

Moreover, soluble non-starch polysaccharide contents were quantified to be 6.18% dry matter and 10.07% in sweet fruits of *Moradaza* and *Solferino*, and in acidic Opuntia fruits the amount can be up to 35.02% DM (Peña-Valdivia et al., 2012). It has been reported that the *cactus* fruit polysaccharides have many bioactivities, such as antioxidant, antihyperglycemic, hypolipidemic, antihypertension, and anti-inflammatory activities (Feugang et al., 2006; Moßhammer et al., 2006; Liang et al., 2008, 2010; Ammar et al., 2010).

Physiochemical and Structural Features

Recently, numerous studies have been conducted about physiochemical and structural features of the polysaccharides from different part of *Cactus* fruit including the peels, pulps and seeds. Different results were given in various reports due to the different part of *Cactus* fruit or various species of cactus. The polysaccharides from *cactus* pear peel are characterized by sugar constituents typical of pectin consisting of rhamnose and galacturonic acid in the ratio of 48.2:51.8, with M_w of 2.25×10^5 g/mL, degree of methylation of 32% (Majdoub et al., 2001).

In 2003, Habibi et al. isolated a slightly water soluble (4-O-methyl-D-glucurono)-D-xylan from the skin of *Opuntia ficus-indica* (OFI) fruits by alkaline extraction (Habibi et al., 2003). This xylan consisted of a linear (1→4)-β-D-xylopyranosyl backbone decorated with 4-O-methyl-α-D- glucopyranosyluronic acid groups linked to the C-2 of the xylopyranosyl residues, in the ratio of one uronic acid for six neutral sugar units. Habibi et al. (2004a) also reported an arabinogalactan from the skin of *Opuntia ficus-indica* fruits that was consisted of galactose and arabinose residues in the ratio of 6.3:3.3, with a backbone of (1→4)-linked β-D-galactopyranosyl residues with 39.5% of these units branched at O-3, and the side-groups consisted either of single L-arabinofuranosyl units or L-arabinofuranosyl α-(1→5)-linked disaccharides. Furthermore, after removal of the mucilage, water-soluble fraction and the EDTA soluble fraction were extracted from *Opuntia ficus-indica* fruit skin, consisting of a disaccharide repeating unit →2)-β-L-Rhap-(1→4)-α-D-GalpA-(1→ backbone, with side chains attached to O-4 of the rhamnosyl residues, and the side chains contained highly branched α-(1→5)-linked arabinan and short linear β-(1→4)-linked galactan (Habibi et al., 2004b).

Another three fractions (ASP1, ASP2 and ASP3) of soluble pectic polysaccharides were isolated from the skin of *Opuntia ficus-indica* prickly pear fruits. ASP1 was consisted of a linear β-(1→4)-galactan, ASP2 consisted of a disaccharide repeating unit [→2)-α-L-Rhap-(1→4)-α-D-GalpA-(1→] backbone, with short linear β-(1→4)-linked galactan side-chains attached to O-4 of the rhamnosyl residues. ASP3 was consisted of alternating homogalacturonan blocks (1→4) α-linked and rhamnogalacturonan blocks with approximately the same amount of galactopyranosyluronic acid residues in each block (Habibi et al., 2005a). Matsuhiro et al. (2006) analyzed the crude mucilage extracted from peeled fruits of *Opuntia ficus indica*, which contained 23.4% of galacturonic acid and consisted of Ara, Rha, Xyl and Gal in the molar ratio of 1.0:1.7:2.5:4.1. After the treatment with cetrimide, they obtained an insoluble fraction (44.3% yield), which consisted of Xyl, Rha and Gal in the molar ratio of 1.0: 2.5:2.8, as well as a cetrimide soluble fraction (15.6% yield) consisted of Ara and Gal in the molar ratio of 1:2.2 (Matsuhiro et al., 2006). Recently, a novel (1→4)-α-D-Glucan has been isolated from the peeled fruits of *Opuntia ficus indica* (L.) Miller ($[\alpha]D^{161}+192^\circ$), consisting of a (1→4)-linked α-D-Glcp backbone, with (1→6)-linked (1→4)-α-D-Glcp side chains, with M_w of 3.6×10^5 Da (Ishurd et al., 2010). A novel water-soluble polysaccharide fraction was purified from the fruit of *Opuntia dillenii* Haw, which consisted of Rha, Xyl, Man and Glc in the molar ratio of 15.0:1.1:1.0:6.5, with M_w of 6.5×10^6 Da (Gao et al., 2015).

A previous study demonstrated that the pericarp of prickly pear seeds of *Opuntia ficus-indica* contained a significant amount of polysaccharides, with cellulose and xylan (Habibi et al., 2008). Six xylan fractions all have similar chemical structures of (4-*O*-methyl-D-glucurono)-D-xylans, with 4-O-α-D-Glucopyranosyluronic acid groups linked at C-2 of a (1→4)-β-D-xylan. However, they were distinguished from each other with different proportions of D-Xyl and 4-O-Me-D-GlcA, and the results indicated that the water soluble xylans have 11–14 xylose units for one non-reducing terminal residue of 4-O-methyl-D-glucuronic acid, but in the water-insoluble xylans, xylose units can varied from 18 to 65 residues (Habibi et al., 2002). Additionally, the investigation on the storage polysaccharides, extracted by boiling water (WSF) and calcium chelating agent solution (CSF) from the endosperm seed of *Opuntia ficus-indica* fruit., showed that the predominant fraction of WSF consisted of α-(1→5)-linked arabinofuranosyl residues backbone with high Ara units substituted at O-2, and the major fraction of CSF were repeating unit →2)-α-L-Rhap-(1→4)-α-D-GalpA-(1→backbone with α-(1→5)-linked arabinan side-chains attached to O-4 of the rhamnosyl residues (Habibi et al., 2005b).

Biological Activities

Anti-oxidative activity. Numerous studies have demonstrated the anti-oxidative activity of *Cactus* fruit due to its ability to neutralize reactive oxygen species such as singlet oxygen, hydrogen peroxide or H_2O_2, or suppress the xanthine/xanthineoxidase system, which may induce oxidative injury (Feugang et al., 2006). It have reported that the polysaccharides from the fresh mature prickly pear fruits of *Opuntia ficus-indica* Mill exhibited a significant antioxidant activity, which is close to ascorbic acid (Ammar et al., 2010). Recently, a study conducted by our laboratory has demonstrated that the polysaccharide from the fruit of *Opuntia dillenii* Haw has effective hypoglycemic and antioxidant properties on STZ-induced oxidative damaged rats. In particular, the cactus fruit polysaccharide significantly increased the activities of SOD, GPx and CAT in serum, liver, kidney, and pancreas of oxidative damaged rats. Moreover, histopathological examination showed that this cactus fruit polysaccharide could markedly improve the structure integrity of pancreatic islet tissue in oxidative damaged rats (Gao et al., 2015).

Antihyperglycemic activity. Cactus fruits have been extensively used in folk medicine as a remedy for diabetes due to their antihyperglycemic effects (Feugang et al., 2006; Moßhammer et al., 2006). The antihyperglycemic activity of *Cactus* fruit polysaccharide has been recently assessed. It found that polysaccharides from *O. ficus indica* fruits howed a significant antihyperglycemic effect on alloxan-induced diabetic rat. Moreover, in oral glucose tolerance test, the cactus fruit polysaccharide at a dose of 500 mg/kg caused 21% decrease in blood glucose level in diabetic group (Ammar et al., 2010). Furthermore, the extracts of *Cactus* pear fruit polysaccharide can remarkably decrease the contents of blood glucose, total cholesterol and triglyceride in diabetic rats induced by STZ. Therefore, the mechanism may be related to stimulating the secretion of insulin from β-cells. However, another study attributed the remarkable hypoglycemic effect of *Cactus* fruit polysaccharide to the increasing of the mRNA expression of insulin receptor in liver and skeletal muscle, and that of GluT4 in skeletal muscle in diabetic rats (Liang et al., 2010). Our previous study has demonstrated that the polysaccharide from the fruit of *Opuntia dillenii* Haw has significant hypoglycemic effect on STZ-induced oxidative damaged rats due to the markedly improvement of the pancreatic islet tissue (Gao et al., 2015).

Hypolipidemic and antihypertension activities. Some in vivo studies have demonstrated the hypolipidemic and antihypertension activities of the cactus fruit polysaccharides. Liu et al. (2009) investigated the effects of cactus pear polysaccharide on the experiment hyperlipemia and lipid peroxidation. It showed that the levels of the TC, TG, LDL-C, apoB and MDA decreased significantly, with the levels of the HDL-C and SOD increased remarkably, after administration of *Cactus* fruit polysaccharide for 3 weeks (Liu et al., 2009). Recently, in vivo experiments showed that cactus fruit polysaccharides exhibited effective antihypertensive effect on spontaneous hypertension rats. The level of systolic blood pressure, angiotensin I, II and endothelin were depressed obviously by cactus fruit polysaccharides (Liang et al., 2010). A more recent study suggested that antihypertensive effect of cactus fruit polysaccharides on spontaneous hypertension rats may be attributed to their effect on improving vascular endothelial function, reducing the expression of nuclear proliferation antigen and basic fibroblast growth factor in vascular smooth muscle cells (VSMC) of the aorta and renal artery, and then reducing the proliferation of VSMC (Liang et al., 2011).

Other activities. The work of Ammar et al. (2010) demonstrated the immunomodulatory and anti-inflammatory activities of polysaccharides from *O. ficus indica* fruits. *Cactus* fruit polysaccharides also possessed certain anti-tumor activity on S_{180}-bearing Mice due to their effects in inducing apoptosis, increasing antioxidation and promoting immune responses (Liang et al., 2008).

Aloe Barbadensis *Miller*

Aloe vera (*Aloe barbadensis* Miller) (Fig. 3H) is a perennial succulent cactus-like plant belonging to the *Liliaceal* family (Choi and Chung, 2003). *Aloe* has been shown to be rich in bioactive polysaccharides particularly mannans and pectins (Reynolds and Dweck, 1999).

Physiochemical and Structural Features

Acemannan (also known as carrysin) is the most widely studied polysaccharide from Aloe vera consisting of an acetylated β-1,4-linked glucomannan. It has a backbone of β-(1→4)-D-mannosyl (~80%) residues acetylated at the C-2, C-3 and C-6 positions with a Man:acetyl ratio of approximately 1:1 and it also contains a proportion of β-(1→4)-D-glucosyl (~10%) and some side chains of mainly galactose residues attached to C-6. It has an M_w of approximately 1×10^6 g/mol.

Pectins from the cell walls of *Aloe vera* demonstrate characteristics which are appealing for biomedical applications such as such as larger proportions rhamnose, the high galacturonic acid contents with variable of both methyl (DM) and acetyl (DAc) esterification (Gentilini et al., 2014; Geng et al., 2014). It is important to note that like other plant systems the physico-chemical properties of pectins are affected by extraction conditions (Denman and Morris, 2015; Geng et al., 2014). A β-(1→4)-D linkaged GGM with acetylation at C-6 of pyranosyl of $M_w \sim 2 \times 10^5$ g/mol has been extracted from the skin of *Aloe barbadensis* Miller irrigated with sea water for 3.5 years after a extensive purification using both anion-exchange column and size exclusion chromatography (Chun-hui et al., 2007). A structurally similar polysaccharide with M_w of $\sim 8 \times 10^4$ g/mol was also extracted from Aloe after partial digestion with cellulase followed by dialysis, ethanol precipitation and size exclusion chromatography (Qiu et al., 2000). The composition of these polysaccharides consisted of Man (90–95%), Glc (2–10%) and Gal (1–2%) (Chun-hui et al., 2007; Qiu et al., 2000).

Aloeride is a very high-M_w ($4–7 \times 10^6$ g/mol) polysaccharide (Pugh et al., 2001). The composition of the Aloeride polysaccharide consisted of glucose (~37%), galactose (~24%), mannose (~20%), arabinose (~10%), rhamnose (~6%) and glucuronic acid (~3%). From linkage analysis, the major derivatives included 1,6-linked glucose (~24%), 1,4-linked mannose (~19%), and 3,6- linked galactose (~11%) (Pugh et al., 2001). Due to the complex nature of this polysaccharide the anomeric configuration of the constituent sugars and detailed structure is as yet unknown.

Biological Activities

Acemannan has demonstrated immunomodulatory activity (Peng et al., 1991; Womble and Helderman, 1992) which has resulted in reduced tumour growth (Peng et al., 1991). It has been reported that it can activate macrophages (Karaca et al., 1995; Djeraba and Quere, 2000); enhance cytokine release; stimulate interactions between macrophages and enhance the generation of cytotoxic T-lymphocytes. It has been shown to increase the antibody production against the coxsackie virus and reduce radiation-induced skin reactions in C3H mice (Roberts and Travis, 1995); enhance the allo-responsiveness of human lymphocytes (Womble and Helderman, 1988); induce the phenotypic and functional maturation of immature dendritic cells (Lee et al., 2001). It could also upregulate phagocytosis and the candidicidal activity of macrophages (Stuart et al., 1997). It has also shown potential in wound healing (Kaufman et al., 1989); bone formation (Boonyagul et al., 2014); as an antibacterial agent (Tan and Vanitha, 2004) and in the treatment of diabetes (Christaki and Florou-Paneri, 2010).

Pectins are generally used as gelling agents, thickeners and stabilisers, although a number of pectins have been shown to be bioactive with properties including for example, activation of mactophages (Inngjerdingen et al., 2008), anti-oxidant activity (Košťálová et al., 2013), immunomodulatory activity (Inngjerdingen et. al., 2007) and hypoglycaemic properties (Adams et al., 2011; Simpson and Morris, 2014). Although several pectins, rich in uronic acids, with similar compositions have been found in *Aloe* extracts (Femenia et al., 1999), thus far pectins from Aloe vera have only been shown to demonstrate wound healing properties.

Although these polysaccharides exhibit antioxidant activity were relatively high concentrations (8 mg/mL) on M_w basis, and these polysaccharides have been shown to exhibit significant free radical scavenging and antioxidant activities, albeit only in vitro at this time (Chun-hui et al., 2007). A structurally similar molecule has also demonstrated immunomodulatory activities; however it was also shown to have no affect macrophage activation (Qiu et al., 2000). Galactoglucoarabinomannan from Aloeride comprises only a small fraction of the dry weight (~0.015 %), its potency in the activation of macrophages accounts fully for the activity observed in the crude Aloe juice, which leaves the authors (Pugh et al., 2001) to suggest that it is this polysaccharide which is present in trace amounts in acemannan formulations which is responsible for immunomodulatory activity.

Others

Some other polysaccharides have also been extracted and purified from other species of medicinal plants which presented bioactivities. As the space is limited, so this paper not discussed here.

CONCLUDING REMARKS AND FUTURE TRENDS

Bioactive polysaccharides deriving from the medicinal plants have been well known and widely used in far Africa, Asia, and South America as part of traditional diet and medicine. Over the last few decades, considerable efforts have been devoted to developing research on bioactive polysaccharides from the medicinal plants. The main focus of the research was on compositional analysis, structural characterization and bioactivities of polysaccharides from the medicinal plants. The structural and bioactive polysaccharides from the medicinal plants, mainly polysaccharides from *Astragalus membranaceus, Dendrobium* plants, *Bupleurum, Cactus* fruits, *Acanthopanax senticosus, Angelica sinensis* (Oliv.) Diels, *Aloe*

barbadensis Miller, and *Dimocarpus longan* Lour (Fig. 3) have been reviewed in this paper.

From this review, it it can be seen that the structural features and bioactivities have been widely explored from medicinal plants, and the structural diversity of polysaccharides depends largely on their botanical or biological sources. The unique physiochemical properties, structure diversities and biological effects can be used successfully in great numbers of medical applications, and many bioactive polysaccharides have presented promising potential as antitumor, immunostimulating or anticancer agents. This area of research has attracted a lot of interest also due to the fact that these polysaccharides are produced by medicinal plants makes them very good candidates for good medicines without any serious safety concerns as they are often eaten in the diet. Hence, this class of biopolymers forms ideal candidates for therapeutic applications. There is no doubt that bioactive polysaccharides from the medicinal plants are going to take major place in future for biomedical applications.

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