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Review

Isolation, structure and bioactivities of the polysaccharides from *Angelica sinensis* (Oliv.) Diels: A review

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ABSTRACT

The root of *Angelica sinensis* (Oliv.) Diels, a well-known Chinese herbal medicine, has been used historically as a tonic, hematopoietic and anti-inflammatory agent for thousands of years. Modern phytochemistry and pharmacological experiments have proved that polysaccharide is one of the major active ingredients in *A. sinensis*. It has been demonstrated that *A. sinensis* polysaccharides had various important biological activities, such as hematopoiesis, immunomodulation, antitumor, antioxidant, radioprotection and hypoglycemic activity. The purpose of the present review is to summarize previous and current references regarding extraction and purification techniques as well as structural characterization and biological activities of *A. sinensis* polysaccharides.

Contents

1. Introduction

The root of *Angelica sinensis* (Oliv.) Diels (Umbelliferae), a well-known Chinese herbal medicine, was first documented in Shennong Bencao Jing (Shennong's Classic of Materia Medica; 200–300 AD) (Liu, Li, et al., 2010; Monograph, 2004). It has been used historically as a tonic, hematopoietic and anti-inflammatory agent for the treatment of gynecological diseases such as menstrual disorders, amenorrhea and dysmenorrheal for thousands of years in traditional Chinese medicinal prescriptions (Cao, Li, Wang, Fan, et al., 2010; Lü et al., 2009). It has also been widely marketed as health food for women's care in Asia (Low Dog, 2005), and as a dietary supplement in Europe and America (Deng et al., 2006; Yang, Zhao, & Lv, 2008).

The bioactive constituents in the root of *A. sinensis* are complicated (Liu, Hsieh, Huang, Liao, & Chiang, 2010). With the development of analysis methods, over 70 chemical components have been identified, including carbohydrates, essential oils,

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organic acids, phenolic compounds, vitamins, amino acids and other constituents (Chao & Lin, 2011; Wong, Yu, & Cho, 2008). In the last few years, the polysaccharide as one of the major ingredients has attracted much attention (Cao, Li, Liu, Wang, et al., 2006; Cao, Li, Wang, Fan, et al., 2010). Many studies on phytochemistry and pharmacology have demonstrated that *A. sinensis* polysaccharides had various bioactivities, such as hematopoiesis (Liu, Li, et al., 2010; Liu, Hsieh, et al., 2010), immunomodulation (Wang, Chen, et al., 2011; Yang, Jia, Meng, Wu, & Mei, 2006; Yang, Zhao, Li, Wang, & Lv, 2008), anti-tumor (Cao, Li, Liu, Wang, et al., 2006; Cao, Li, Wang, Li, et al., 2010; Shang et al., 2003), antioxidant (Jiang, Guo, & Niu, 2009; Yang et al., 2007a; Zhang et al., 2010), anti-ulcer (Wong et al., 2008; Ye, So, Liu, Shin, & Cho, 2003) and radioprotection (Hong, Liu, Xiong, Zhang, & Wang, 2002; Sun, Tang, Gu, & Li, 2005; Sun, Lin, Gao, Tang, & Gu, 2009; Sun, Ma, & Tang, 2009). And this review aims at summarizing previous and current references regarding extraction and purification techniques as well as structural characterization and biological activities of *A. sinensis* polysaccharides.

2. Extraction and purification methods

Botanical polysaccharide exists as a structural constituent of cell wall, so the extraction method depends on the cell wall structure (Nie & Xie, 2011). The basic extraction rule is to break the cell wall from outer layer to the inner layer with mild-strong extraction conditions (pH and temperature) without modifying the polysaccharide materials (Zhang, Cui, Cheung, & Wang, 2007). Hot water extraction (Jiang et al., 2009; Liu et al., 2010b; Shang et al., 2003; Wang, Zeng, Liu, Guo, & Zhang, 2011; Wang, Chen, et al., 2011; Yang et al., 2006; Yang, Zhao, Zhou, et al., 2007; Yang, Zhao, Li, et al., 2008), combined with some supplementary methods such as Freeze-thaw method (Cao, Li, Liu, Yang, et al., 2006; Cao, Li, Wang, Fan, et al., 2010; Cao, Li, Wang, Li, et al., 2010), microwave (Gong, Yang, & Zeng, 2004), and ultrasonic (He, Xu, Wang, & Chen, 2010), were commonly used to extract polysaccharides from *A. sinensis*. These methods can shorten the extraction time, reduce the consumption of solvent and improve the yield of *A. sinensis* polysaccharides. Because of the dominant advantages such as simple and economical, hot water extraction has been widely used as the classical method for the preparation of polysaccharides in industrial application (Yang, Zhao, & Lv, 2008). However, hot water extraction is always associated with long time and high temperature, it could accelerate the degradation of polysaccharide, which strongly depends on polysaccharides composition, temperature and time of heat treatment. To investigate *A. sinensis* polysaccharide stability, the thermal treatment experiments were carried out by Yang, Zhao and Lv (2008), and it was found that heating temperature up to 90 °C and a further increase in the range of 90–150 °C resulted in a dramatic losses of carbohydrate and uronic acid. The prolonged heating time from 6 h to 12 h at 80 °C also caused a significant carbohydrate and uronic acid losses. Therefore, during the hot water extraction of *A. sinensis* polysaccharides, heating temperature below 90 °C for a short time was recommended and the concentrating process before drying should be carried out under a decompression condition in order to maintain the functions and bioactivities of *A. sinensis* polysaccharides as possible (Yang, Zhao, & Lv, 2008).

Extracted *A. sinensis* polysaccharides can be further purified using a combination of techniques, such as ethanol precipitation, factional precipitation, ion-exchange chromatography, gel filtration, and affinity chromatography (Wasser, 2002). Basically, gel filtration could separate polysaccharides with different molecular weight, and ion-exchange chromatography could separate neutral polysaccharides from acidic ones with different eluent. Cao, Li, Liu, Wang, et al. (2006) separated two fractions from *A. sinensis* polysaccharides by gel filtration chromatography on a column of Sephadex G-100. Their molecular weights were determined to be 1.7×10^5 and 3.9×10^4 Da. Sun et al. (2005) fractionated *A. sinensis* polysaccharides by ion exchange chromatography on a column of DEAE-Sepharose CL-6B eluted with water and NaCl gradient. It was found that neutral polysaccharide fraction eluted with water was rich in glucose (Glc), galactose (Gal) and arabinose (Ara), and acidic polysaccharide fraction eluted with NaCl solution ranging from 0.2 to 0.6 M consisted mainly of galacturonic acid (GalA) along with rhamnose (Rha), Ara, and Gal indicating the pectic polysaccharide.

The procedures for separating and purifying polysaccharide from *A. sinensis* are summarized as follows: the dried roots were grind to fine powder and pre-extracted with 80% ethanol to remove the fat, pigment and some small molecules. By extracting the residue with hot water, the solution of polysaccharides was collected after filtration and concentration. After deproteinized by Freeze-thaw method or the Sevag method (Staub, 1965), dialysed, evaporated, precipitated with ethanol, filtered and lyophilized, the crude polysaccharides were obtained. Be redissolving the crude extracts, the resultant solution was applied to different column chromatography mentioned above, eluting with appropriate running buffer, collecting, dialyzing, concentrating and lyophilizing, the pure polysaccharides could be obtained (Cao, Li, Liu, Wang, et al., 2006; Cao, Li, Wang, Fan, et al., 2010; Cao, Li, Wang, Li, et al., 2010; Jiang et al., 2009; Liu, Hsieh, et al., 2010; Shang et al., 2003; Sun et al., 2005; Wang, Zeng, et al., 2011; Yang et al., 2006). The content of polysaccharide could be determined by the phenol-sulphuric method (Dubois, Gilles, Harmilton, Rebers, & Smith, 1956), and protein in the polysaccharides could be quantified according to the Bradford' method (Bradford, 1976).

3. Physiochemical and structural features

The physiochemical and structural features of a polysaccharide are defined by molecular weight, monosaccharide composition, sequence of monosaccharide, configuration and position of glycosidic linkages, type and polymerization degree of branch, spatial configuration, particle size, solubility, rheological properties, *etc.* (Jin, Lu, Huang, Wang, & Wang, 2011; Nie & Xie, 2011). There were total 36 polysaccharides identified from the root of *A. sinensis* up to date. Their primary structural features such as monosaccharide composition and molecular weight are shown in Table 1. Besides, their names and corresponding references are also included.

Most of the polysaccharides isolated from *A. sinensis* reported in literatures are heteropolysaccharides. Due to different purification process or raw material, different results about molecular weight and monosaccharide composition of *A. sinensis* polysaccharides were given in various reports. Chen, Liu, Wang, Xu, and Xu (2001), Chen, Wang, Xu, Xu, and Chang (2001), and Chen, Xu, Wang, Xu, and Liu (2001) isolated four polysaccharides XC-1, X-C-3II, X-C-3III, X-C-3IV, from *A. sinensis* by hot water extraction, ethanol precipitation, and DEAE-Sephadex A-25 column chromatography. The molecular weights of XC-1, X-C-3II, X-C-3III and X-C-3IV were determined to be 1.0×10^5, 1.0×10^5, 8.5×10^4 and 6.6×10^4 Da, respectively. Their monosaccharide compositions were analyzed by the capillary gas chromatography, as shown in Table 1. Sun et al. (2005) analyzed the monosaccharide composition of three radioprotective neutral (ASP1) and acidic polysaccharides (ASP2, ASP3) isolated from *A. sinensis* by hot water extraction and DEAE-Sepharose CL-6B column chromatography and found that ASP1 consisted of GalA, Ara, Glc and Gal in the molar ratio of 5.35:9.15:65.00:3.66, whereas ASP2 consisted of GalA, Rha, Ara, mannose (Man), Glc and Gal in the molar ratio of 35.38:1.11:16.31:0.89:26.96:15.75, and ASP3, with the molecular weight of 3.4×10^4 Da, was composed of the above monosaccharides in the proportions of

Table 1
The polysaccharides isolated from the root of *A. sinensis*.

No.	Compound name	Monosaccharide composition	Molecular weight (Da)	Structures	Pharmacological properties	Reference
1	As-IIIa	Glc	8.5×10^4	α-(1 → 3)-glucan		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		
3	X-C-3-II	Glc, Gal, Ara, Rha, GalA in the ratio of 56.0:22.1:18.9:1.9:1.1	1.0×10^5		Immunomodulating	Chen, Liu, et al. (2001)
4	X-C-3-III	Gal, Ara, Rha, GlcA, GalA in the ratio of 24.3:15.8:4.2:3.1:52.6	8.5×10^4		Immunomodulating	Chen, Wang, et al. (2001)
5	X-C-3-IV	Gal, Ara, Rha, GlcA, GalA in the ratio of 12.6:10.7:7.2:8.3:61.2	6.6×10^4		Immunomodulating	
6	XC-1	Glc	1.0×10^5	α-(1 → 6)-glucan	Immunomodulating	Chen, Xu, et al. (2001)
7	*A. sinensis* polysaccharide	Fuc, Gal, Glc, Ara, Rha, Xyl in the ratio of 1.0:13.6:15.0:8.7:21.3:3.7				Wang et al. (2003)
8	ASP1	GalA, Ara, Glc, Gal in the ratio of 5.35:9.15:65.00:3.66				Sun et al. (2005)
9	ASP2	GalA, Rha, Ara, Man, Glc, Gal in the ratio of 35.38:1.11:16.31:0.89:26.96:15.75				Sun et al. (2005)
10	ASP3	GalA, Rha, Ara, Man, Glc, Gal in the ratio of 58.27:1.87:10.50:0.37:0.94:24.93	3.4×10^4		Radioprotective	Sun et al. (2005)
11	APF1	Rha, GalA, Glc, Gal, Ara in the ratio of 1.00:2.65:2.02:3.45:10.64				Yang et al. (2005)
12	APF2	Man, Rha, GalA, Glc, Gal, Ara in the ratio of 0.44:1.00:10.52:7.52:8.19:14.43				Yang et al. (2005)
13	APF3	Man, Rha, GlcA, GalA, Glc, Gal, Ara in the ratio of 0.74:1.00:0.25:9.06:8.62:5.94:9.28				Yang et al. (2005)
14	W-ASP11	Ara, Glc, Gal in the ratio of 0.5:26.0:0.6	3.8×10^5			Sun et al. (2006)
15	W-ASP12	Ara, Man, Glc, Gal in the ratio of 21.1:1.6:16.3:1.3	1.9×10^4			Sun et al. (2006)
16	W-ASP-2	Rha, Ara, Man, Glc, Gal in the ratio of 1.0:14.7:0.8:24.3:14.2				Sun et al. (2006)
17	W-ASP-3	Rha, Ara, Man, Glc, Gal in the ratio of 1.0:5.6:0.2:0.5:13.3	6.2×10^4			Sun et al. (2006)
18	APS-1cI	Glc	1.7×10^5	Linear α-glucan composed of only (1 → 6)-α-D-Glc*p*		Cao, Li, Liu, Wang, et al. (2006)
19	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, Li, Liu, Wang, et al. (2006)
20	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, Li, Liu, Yang, et al. (2006)
21	AP	Rha, Ara, Man, Glc, Gal in the ratio of 1.00:4.54:2.98:11.09:7.45	5.0×10^4		Immunomodulating	Yang et al. (2006)
22	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)
23	APF1	Ara, Glc, Rha, Gal, GalA in the ratio of 11.0:2.6:1.0:3.5:2.5			Antioxidant	Yang, Zhao, Zhou, et al. (2007)
24	APF2	Ara, Glc, Rha, Gal, Man, GalA in the ratio of 18.2:7.4:1.0:8.4:0.5:12.3			Antioxidant	Yang, Zhao, Zhou, et al. (2007)
25	APF3	Ara, Glc, Rha, Gal, GlcA, GalA in the ratio of 9.4:8.7:1.0:6.0:0.3:12.1			Antioxidant	Yang, Zhao, Zhou, et al. (2007)
26	APF1	Rha, Ara, Glc, Gal in the ratio of 1.00:2.27:7.80:2.69	1.2×10^5		Immunostimulating	Yang, Zhao, Lv (2008) and Yang, Zhao, Li, et al. (2008)

Table 1 (*Continued*)

No.	Compound name	Monosaccharide composition	Molecular weight (Da)	Structures	Pharmacological properties	Reference
27	APF2	Rha, Ara, Man, Glc, Gal in the ratio of 1.00:5.29:3.66:9.11:5.17	5.2×10^4		Immunostimulating	Yang, Zhao, Lv (2008) and Yang, Zhao, Li, et al. (2008)
28	APF3	Rha, Ara, Man, Glc, Gal in the ratio of 1.00:4.54:2.98:11.09:7.45	1.6×10^4		Immunostimulating	Yang, Zhao, Lv (2008) and Yang, Zhao, Li, et al. (2008)
29	APS-2a	Glc, Gal, Ara, Rha, GalA in the ratio of 1.0:7.5:38.2:2.6:4.9	7.4×10^5		Antitumor	Cao et al. (2008)
30	ASP	Man, Rha, GlcA, GalA, Glc, Gal, Ara, Fuc in the ratio of 1.2:4.5:1.0:10.5:17.8:37.5:8.7:4.9			Antioxidant	Jiang et al. (2009)
31	Angelica polysaccharide	Rha, GalA, Glc, Gal, Ara in the ratio of 0.05:0.26:14.47:1.00:1.17	5.0×10^4		Colon-specific drug carrier	Zhou et al. (2009)
32	APS-bII	Glc, Gal, Xyl, Ara in the ratio of 8.4:2.7:1.8:1.0	1.3×10^4		Antitumor	Chen et al. (2010)
33	APS-3a	Glc, Gal, Ara, Rha, Man in the ratio of 3.2:1.7:2.5:1.3:1.0	5.9×10^5		Antitumor	Cao, Li, Wang, Li, et al. (2010)
34	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		Antitumor	Cao, Li, Wang, Li, et al. (2010)
35	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		Antitumor	Cao, Li, Wang, Li, et al. (2010)
36	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	Radioprotective	Sun et al. (2010)

58.27:1.87:10.50:0.37:0.94:24.93. The monosaccharide compositions of three *A. sinensis* polysaccharide fractions (APF1, APF2 and APF3), isolated by hot water extraction, Freeze-thaw method and Sephacryl S-400 gel chromatography were analyzed by 1-phenyl-3-methyl-5-pyrazolone (PMP) precolumn high performance liquid chromatography method (Yang, Zhao, Wang, Wang, & Mei, 2005). The results showed that APF1 consisted of Rha, GalA, Glc, Gal and Ara with the molar ratio of 1.00:2.65:2.02:3.45:10.64, APF2 consisted of Man, Rha, GalA, Glc, Gal and Ara with the molar ratio of 0.44:1.00:10.52:7.52:8.19:14.43, and APF3 consisted of Man, Rha, glucuronic acid (GlcA), GalA, Glc, Gal and Ara with the molar ratio of 0.74:1.00:0.25:9.06:8.62:5.94:9.28. Yang, Zhao, Zhou, et al. (2007) identified the monosaccharide component of the same antioxidant polysaccharide fractions by an analytical method of high performance capillary electrophoresis (HPCE). It was found that APF1 consisted of Rha, GalA, Glc, Gal, and Ara with the molar ratio of 1.0:2.5:2.6:3.5:11.0, APF2 consisted of Man, Rha, GalA, Glc, Gal and Ara with the molar ratio of 0.5:1.0:12.3:7.4:8.4:18.2, and APF3 consisted of Rha, GlcA, GalA, Glc, Gal and Ara with the molar ratio of 1.0:0.3:12.1:8.7:6.0:9.4. An antitumor polysaccharide (APS-1d) isolated from *A. sinensis* and further purified by DEAE-Sephadex A-25 and Sephadex G-100 chromatography was found to be a heteropolysaccharide consisted of Glc and Ara in the molar ratio of 13.8:1 with a molecular weight of 5.1×10^3 Da determined by high-performance gel-permeation chromatography (Cao, Li, Liu, Yang, et al., 2006). Yang, Zhao, and Lv (2008) and Yang, Zhao, Li, et al. (2008) isolated three immunomodulatory *A. sinensis* polysaccharide fractions, named APF1, APF2 and APF3. The monosaccharide compositions of these fractions were analyzed by trifluoroacetic acid (TFA) hydrolysis and gas chromatography (GC) analysis. It was found that APF1 consisted of Rha, Ara, Glc and Gal in the ratio of 1.00:2.27:7.80:2.69, with the molecular weight of 1.2×10^5 Da; APF2 and APF3 consisted of Rha, Ara, Man, Glc and Gal in the ratio of 1.00:5.29:3.66:9.11:5.17 and 1.00:4.54:2.98:11.09:7.45, with the molecular weight of 5.2×10^4 and 1.6×10^4 Da, respectively. Jiang et al. (2009) characterized the antioxidant polysaccharide isolated from *A. sinensis* (ASP) by high performance liquid chromatography (HPLC) and found that it was composed of eight kinds of monosaccharides, namely Man, Rha, GlcA, GalA, Glc, Gal, Ara and fucose (Fuc), in the molar ratio of 1.2:4.5:1.0:10.5:17.8:37.5:8.7:4.9. Quantitative analyses of Angelica polysaccharide, a new promising colon-specific drug carrier, indicated that it was composed of Rha, GalA, Glc, Gal, and Ara in the molar ratio of 0.05:0.26:14.47:1.00:1.17 with a molecular weight of 5.0×10^4 Da (Zhou et al., 2009). Two antitumor polysaccharides, APS-2a and APS-bII, were isolated and purified from *A. sinensis* by Cao et al. (2008) and Chen, Cao, Sun, and Mei (2010), respectively. APS-2a, with a molecular weight of 7.4×10^5 Da, consisted of Glc, Gal, Ara, Rha and GalA in the molar ratio of 1.0:7.5:38.2:2.6:4.9, whereas APS-bII, with a molecular weight of 1.3×10^4 Da, consisted of Glc, Gal, xylose (Xyl), Ara in the molar ratio of 8.4:2.7:1.8:1.0. Three acidic polysaccharides with anti-tumor effects, APS-3a, APS-3b and APS-3c, were successfully isolated from *A. sinensis* by Cao, Li, Wang, Li, et al. (2010). Neutral monosaccharide compositions determined by GC analysis showed that APS-3a and APS-3b, with the molecular weight of 5.9×10^5, 2.3×10^5 Da, were composed of Glc, Gal, Ara, Rha, and Man in the molar ratio of 3.2:1.7:2.5:1.3:1.0 and 2.3:5.4:6.8:1.0:1.2, respectively, whereas APS-3c, with the molecular weight of 1.4×10^4 Da, was composed of Glc, Gal, Ara, Rha, Man and Xyl in the molar ratio of 6.3:4.7:6.7:6.5:1.6:1.0.

Although the repeated deproteination such as Sevag method, Freeze-thaw method and different column chromatography has been used during the isolation and purification procedures, many *A. sinensis* polysaccharides still combined with certain proteins. The protein might be bound to the polysaccharide chains *via* electrostatic force interaction (Yang, Zhao, & Lv, 2008). For instance,

Sun et al. (2005) found that three radioprotective polysaccharides isolated from *A. sinensis* using anion-exchange chromatography contained certain amount of protein (0.69%, 3.62% and 2.53%). Three anti-tumor polysaccharides isolated from *A. sinensis* and further purified by DEAE-Sephadex A-25, Sephacryl S-400 and Sephadex G-100 chromatography were found to combine with 2.7%, 1.4%, and 7.8% protein (Cao, Li, Wang, Li, et al., 2010).

Except for molecular weights and monosaccharide components, little structural and conformational information about *A. sinensis* polysaccharide were published. The structural analysis of an anti-tumor polysaccharide (APS-1d) isolated from *A. sinensis* indicated that APS-1d had a backbone composed of 1,4-α-D-glucopyranosyl residues, with branches attached to O-6 of some residues. The branches were composed of 1,6-α-D-Glc*p* residues, and terminated with β-L-arabinofuranose residues (Cao, Li, Liu, Yang, et al., 2006).

The structural features of a pectic polysaccharide (ASP3) isolated from the root of *A. sinensis* were studied using partial acid hydrolysis and enzymic digestion, combined with methylation analysis, and ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectral data (Sun, Shen, Tang, & Gu, 2008; Sun, Shen, Tang, Gu, & Li, 2008; Sun, Shan, Cui, Tang, & Gu, 2009; Sun, Cui, Tang, & Gu, 2010). The results indicated that a backbone of linear homogalacturonan fragments occupied the main part of ASP3 as smooth regions, and rhamnogalacturonan blocks with repeating unit of [→4)-α-D-Gal*p*A-(1 → 2)-α-L-Rha*p*-(1→] formed ramified parts as hairy regions, with a total of 58.8% rhamnopyranose residues in the backbone substituted at O-4 position by the side chains. The side chains contained mainly β-1,6- and β-1,4-galactopyranan bearing 3,6- and 4,6-substituted β-D-galactopyranose residues as branched points and short α-1,5-arabinofuranan possessing 3,5-substituted α-L-arabinofuranose residues as branching points. In addition, β-1,6-galactopyranan side chains were highly branched with α-1,5-arabinofuranan carrying 3-O-substituents (1,3,6-Gal) and terminated by the α-arabinofuranose residues which form arabinogalactan.

Apart from heteropolysaccharides mentioned above, some glucans have been isolated and purified from *A. sinensis*. Zhang and Huang (1999) extracted one glucan (As-IIIa) with the molecular weight of 8.5×10^4 Da from *A. sinensis*. It had typical absorption of polysaccharide in Fourier transform infrared (FTIR) spectra, which indicated α-glycosidic bond in As-IIIa. Periodate oxidation and Smith degradation analysis suggested that As-IIIa was composed of α-(1 → 3)-glucan. Chen, Xu, et al. (2001) reported that the polysaccharide extracted from *A. sinensis* was composed of α-(1 → 6)-glucan, with the molecular weight of 1.0×10^5 Da.

The primary structures of two water-soluble glucans (APS-1cI and APS-1cII) were investigated using a combination of chemical and instrumental analysis, such as methylation analysis, periodate oxidation, gas chromatography–mass spectrometry (GC–MS), as well as FTIR and NMR spectroscopy (Cao, Li, Liu, Wang, et al., 2006). 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 → 4)-α-D-Glc*p* and (1 → 6)-α-D-Glc*p* in a molar ratio of 4:1. The following repeating unit for APS-1cII was established: [→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→]$_n$.

4. Biological activities

4.1. Hematopoietic activity

A. sinensis polysaccharide is an important bioactive component of *A. sinensis* that has been used in traditional Chinese medicine for treating anemia and gynecological disorders (Wang, Chen, et al., 2011). It has been found that *A. sinensis* polysaccharide was effective in enhancing hematopoiesis by increasing the secretion of some hematopoietic growth factors such as erythropoietin *via* stimulating hematopoietic cells and muscle tissues (Sarker & Nahar, 2004).

Liu, Hsieh, et al. (2010) compared the hematopoietic activity of the crude extract of *A. sinensis* and its two fractions, polysaccharides (ASPS) and small molecular weight compounds, by granulocyte macrophage (GM) colony-forming assay *in vitro*. They found that ASPS was the major component responsible for the hematopoietic effect of *A. sinensis*. The hematopoietic activity was improved mainly through the stimulation of interleukin-6 (IL-6) and GM colony-stimulating factor secretion. Furthermore, the mice bled approximately 0.5 mL by retro-orbital bleeding were used as the anemia model to investigate the possible mechanism related to its hematopoietic activity. It was found that administration of ASPS (2.3 mg/kg body weight per day) significantly accelerated the recovery of hemoglobin level of the blood-loss mice to its original value ($P < 0.05$). Moreover, the colony forming ability of bone marrow cells removed from the mice that received ASPS was also markedly increased ($P < 0.05$).

Hepcidin, the central regulator of body iron metabolism, can bind to ferroportin, thus diminish duodenal transfer of iron into the circulation and promote iron retention within macrophages (Kemna, Tjalsma, Willems, & Swinkels, 2008; Theurl et al., 2008). Chronic elevation of hepcidin levels could lead to systemic iron deficiency and hepcidin-induced anemia (Wang, Zeng, et al., 2011). Wang, Zeng, et al. (2011) reported that intragastrically administration of *A. sinensis* polysaccharides (ASP, 1 g/kg) everyday for 14 days promoted erythropoietin secretion and reduced hepcidin levels in rat. Western blot was further used to investigate the expression of 6 pertinent signal proteins in liver in order to clarify the involved mechanisms. The results showed that ASP significantly inhibited the expression of signal transducer and activator of transcription 3/5 (STAT3/5) and mothers against decapentaplegic protein 4 (SMAD4) in liver and stimulated the secretion of erythropoietin, which further down-regulated hepcidin by repressing CCAAT/enhancer-binding protein α (C/EBPα), SMAD4, and the phosphorylation process of STAT3/5. It indicated that ASP could participate in the regulation of iron homeostasis, and it could be applied in the treatment of anemia caused by hepcidin overexpression.

Liu, Li, et al. (2010) tested the hematopoietic and particularly, thrombopoietic effects of polysaccharide-enriched fractions from the root of *A. sinensis* polysaccharides (APS). They found that in myelosuppression mouse model, APS significantly enhanced not only the recovery of platelets, other blood cells and their progenitor cells, but also the formation of colony forming unit (CFU). *In vitro* studies, it was found that APS inhibited the apoptosis of megakaryocytic cells. Treatment by Ly294002, a Phosphatidylinositol 3-Kinase (PI3K) inhibitor, increased the percentage of cells undergoing apoptosis. And APS significantly reduced the percentage of cells undergoing apoptosis in Ly294002-treated cells. The activation of the PI3K/AKT pathway that protects cells from undergoing apoptosis was likely to be involved in hematopoiesis and thrombopoiesis of APS.

4.2. Immunomodulatory activity

The immunomodulatory activities of an *A. sinensis* polysaccharide (AP) were previously investigated *in vitro* in relation to the specificity to immune cells by Yang et al. (2006). It was found that the proliferation of total spleen cells, macrophages and T cells were promoted by the action of AP. The treatment of AP increased the gene expression and production of IL-2 and interferon-γ (IFN-γ), while that of IL-4 were decreased. The differences in cytokines secretion pattern showed that the expression of IFN-γ was rapidly augmented while that of IL-2 responded later. The treatment of AP

also remarkably increased the percentage of CD4+ T cell in total spleen cells, while slightly decreased the percentage of CD8+ T cell. The above results suggested the immunomodulatory activity of AP was mainly conducted by regulating expression of Th1 and Th2 related cytokines. The time-effect relation of cytokines response also indicated macrophages and natural killer cells involved in non-specific immunity were primary activated, and helper T cells were secondarily affected after the treatment of AP.

Yang, Zhao, Li, et al. (2008) reported that various *A. sinensis* polysaccharide fractions (APFs, namely APF1, APF2, and APF3) could induce a significant increase in cellular lysosomal enzyme activity, nitric oxide (NO) formation, reactive oxygen species (ROS) production and tumor necrosis factor-α (TNF-α) secretion in macrophages *in vitro*. Furthermore, APFs dose-dependently stimulated macrophages to produce NO through the up-regulation of inducible NO synthase (iNOS) activity and the maximal effect occurred at a concentration of 500 μg/ml by APF2. Further bioactive investigations *in vivo* also showed that intraperitoneal administration of APFs significantly induced peritoneal macrophage to release NO, ROS and enhanced cellular lysosomal enzyme activity ($P < 0.05$) (Yang, Zhao, & Lv, 2008).

Yang, Zhao, Wang, and Mei (2007) studied the mechanism of macrophage activation of AAP, an acidic polysaccharide fraction isolated from *A. sinensis*. They found that AAP could significantly improve the mRNA expression of toll-like receptor 4 (TLR4), and the pretreatment of macrophages with anti-TLR4 antibody significantly blocked AAP-induced NO release, TNF-α secretion, and the increase of iNOS activity.

The effects of *A. sinensis* polysaccharide (ASP) supplemented in diet on the innate cellular immune response and disease resistance in grouper, *Epinephelus malabaricus*, were investigated by Wang, Chen, et al. (2011). Fish were fed with diets containing different doses of ASP (0, 500 and 3000 mg/kg diet) for 12 weeks. It was found that ASP treatment significantly increased the respiratory burst activities and phagocytic activities, and stimulated the head kidney leukocytes proliferation. The cumulative mortalities of fish fed with ASP at the dose of 3000 mg/kg diet were significantly lower compared with control after 96 h of challenge with live *Edwardsiella tarda*. Those results suggested dietary ASP could enhance some cellular immune parameters and disease resistance against *E. tarda* in grouper.

As is well-known, dendritic cells (DCs) are the most powerful antigen presenting cells of the immune system, which are closely related to the occurrence and development of tumor (Sun, 2011). Shen, Hou, Hu, Zhang, and Zhou (2007) found that *A. sinensis* polysaccharide (ASP) could significantly increase the secretion of IL-12 in DCs, enhance IFN-γ level produced by T cells in mixed lymphocyte reaction, thus up-regulate the function of DCs in hepatitis B virus (HBV) transgenic mice. Up-regulation of DCs might be one of the mechanisms involved in immunoregulatory activity of ASP.

4.3. Antitumor activity

Shang et al. (2003) previously reported that the total polysaccharide (AP-0) isolated from *A. sinensis* could significantly increase the survival time of mice bearing Ehrlich ascites carcinoma (EAC) and leukemia L1210. AP-0 and its sub-constituent AP-2 had significant inhibitory effects on the invasion of human hepatocelluar carcinoma cells (HHCC) to the Matrigel reconstituted basement membrane with the inhibitory rates of 56.4% and 68.3%, respectively. The sub-constituent AP-3 had significant blocking effect on the adhesion of HHCC to fibronectin with an inhibitory rate of 30.3%. Meanwhile, AP-0 and its sub-constituents AP-1 and AP-3 could partially inhibit the chemotactic migration abilities of HHCC. Those results suggested that the polysaccharides from *A. sinensis* possessed antitumor effects on experimental tumor models *in vivo* and inhibitory effects on invasion and metastasis of tumor cells *in vitro*.

An arabinoglucan, named as APS-1d with a molecular weight of 5.1 kDa, was extracted from *A. sinensis* and further purified by DEAE-Sephadex A-25 and Sephadex G-100 columns (Cao, Li, Liu, Yang, et al., 2006). 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay revealed that APS-1d significantly inhibited the proliferation of two kinds of human solid cancer cell lines, human cervix carcinoma HeLa cells and lung carcinoma A549 cells *in vitro*. Furthermore, APS-1d inhibited the growth of tumors on the mice transplanted Sarcoma-180 (S180) in a dose-dependent manner. In addition, APS-1d significantly increased the weights of immune organs such as spleens, which suggested that activating immune responses in the host might be one of the mechanisms of antitumor activity of APS-1d as many other polysaccharides found in the world (Ooi & Liu, 2000).

Tumor growth and development are considered as a result of the high proliferative capacity of tumor cells (Cao, Li, Wang, Fan, et al., 2010). Apoptosis and its related signaling pathways have a profound effect on the progression of cancer (Lowe & Lin, 2000). To elucidate the precise antitumor mechanism of *A. sinensis* polysaccharides, the pro-apoptotic effects of APS-1d in HeLa cells were investigated by Cao, Li, Wang, Fan, et al. (2010). APS-1d decreased HeLa cell proliferation *in vitro*, and significantly inhibited tumor growth in athymic nude mice. Characteristic manifestations of apoptosis including apoptotic morphological features and the sub-G0/G1 peaks were observed when the cells were treated with APS-1d. Further analysis showed that APS-1d-induced apoptosis was associated with the regulation of Bcl-2 family protein expression, disruption of the mitochondrial membrane potential, and increase of the cytosolic cytochrome *c* levels. Sequentially, APS-1d increased the activities of caspase-9, caspase-3, and poly (ADP-ribose) polymerase in a concentration-dependent manner, however, no obvious activation of Bid and caspase-8 was observed. The results indicated that APS-1d was capable of inhibiting HeLa cell proliferation and inducing apoptosis through activation of the intrinsic mitochondrial pathway. In addition, Zeng et al. (2007) reported that *A. sinensis* polysaccharides could significantly induce K562 leukemic cell apoptosis and inhibit its DNA synthesis through preventing the tumor cells to S phase and down-regulating the expression of Bcl-2.

Cao, Li, Wang, Li, et al. (2010) isolated and purified three acidic homogeneous polysaccharides (APS-3a, APS-3b and APS-3c) from *A. sinensis*. The antitumor studies showed that APS-3b and APS-3c could cause a concentration-dependent proliferation of splenocytes, up-regulate IFN-γ, IL-2 and IL-6 mRNA expression in splenocytes and stimulate the production of NO and TNF-α in peritoneal macrophages. The antitumor effects of APS-3b and APS-3c were related to stimulating host immunity which might result from activating splenocytes and macrophages and stimulating secretion of some cytokines.

4.4. Antioxidant activity

Three fractions of polysaccharides, named as APF1, APF2 and APF3, were isolated and purified from *A. sinensis* using an analytical method of HPCE, and the antioxidant activities of APFs against hydrogen peroxide (H_2O_2)-mediated oxidative stress were evaluated in isolated mouse peritoneal macrophages (Yang, Zhao, Zhou, et al., 2007). The results indicated that APF3 was the most active fraction to effectively inhibit H_2O_2-induced decrease of cell viability, lactose dehydrogenase (LDH) leakage and malondialdehyde (MDA) formation, and also reduce H_2O_2-caused decline of superoxide dismutase (SOD) activity and glutathione (GSH) depletion. Furthermore, it was found that APFs could protect macrophage

by inhibiting the release of excess NO and ROS induced by high concentration of H_2O_2.

The effects of *A. sinensis* polysaccharides and Tai Chi exercise on free radical generation and lipid peroxidation in middle-aged women subjects were studied by Jiang et al. (2009). It was found that antioxidant activities such as SOD, catalase (CAT), glutathione peroxidase (GSH-Px) in *A. sinensis* polysaccharides group were significantly enhanced, whereas lipid peroxidantion level was reduced compared to the control group. It indicated that ASP could reduce oxidative stress and improve blood lipid metabolism in middle-aged women.

The antioxidant activities of *A. sinensis* polysaccharides were evaluated by using myocardial ischemia/reperfusion (I/R) rat (Zhang et al., 2010). The results showed that myocardial I/R injury was accompanied by the decrease of antioxidant levels/activities in blood and heart, which are indirect indices of mitochondrial function and antioxidant status. Administration of *A. sinensis* polysaccharides at the dose of 100 mg/kg, 200 mg/kg and 300 mg/kg body weight could decrease the release of free radicals, and enhance blood and heart antioxidant components (SOD, CAT, GSH-Px, GSH) during I/R injury.

Diabetes is associated with significant oxidative stress, and increasing evidences in both experimental and clinical studies suggested that oxidative stress caused by hyperglycemia plays a major role in pathogenesis of diabetes mellitus (Celikler et al., 2009). The influence of *A. sinensis* polysaccharides on antioxygenic property of alloxan-induced diabetic mice was studied by Xu and Ding (2004). It was found that after 30 days' administration of *A. sinensis* polysaccharides to diabetic mice, the activity of SOD in the brain, heart, kidney and pancreas significantly improved, while the MDA content greatly decreased, which in turn released the oxidative injury in diabetic mice.

4.5. Gastrointestinal protective effects

Cho et al. (2000) previously reported that the crude polysaccharides isolate from *A. sinensis* (ASCE) could prevent ethanol- and indomethacin-induced gastric mucosal damage of rat, perhaps through the inhibitory action on neutrophil infiltration in the gastrointestinal mucosa. *In vitro* studies showed that ASCE significantly promoted the migration of gastric epithelial cells (RGM-1) over an artificial wound. And this extract also stimulated the incorporation of [^{3}H]-thymidine in RGM-1 cells in a dose-dependent manner and concomitantly increased the mRNA expression of epidermal growth factor (EGF). These results strongly suggested that ASCE had a direct wound healing effect on gastric mucosa partially through an EGF-mediated pathway (Ye, Koo, et al., 2001). In another study, Ye, Liu, Shin, et al. (2001) found that ASCE significantly stimulated ornithine decarboxylase (ODC) activity and c-Myc protein expression in RGM-1 cells. Pretreatment with c-Myc antisense oligodeoxynucleotides blocked the stimulatory action of ASCE on [^{3}H]-thymidine incorporation and ODC protein expression, which indicated that ODC and c-Myc were closely associated with the mucosal healing effect of ASCE. To investigate the possible mechanisms underlined, the effects of ASCE on gastric ulcer healing in rat model were analyzed (Ye et al., 2003). It was found that ASCE could promote ulcer healing, accompanied with a significant increase in mucus synthesis. Meanwhile, angiogenesis was inhibited by the treatment of ASCE, however, cell proliferation, ODC and epidermal growth factor receptor (EGFR) protein expression was not affected in this process.

Liu, Dong, Wu, Luo, and Yu (2003) studied the protective effect of *A. sinensis* polysaccharide (ASP) on experimental immunological colon injury in rats. They found that enhanced colonic mucosal injury, inflammatory response and oxidative stress were observed in colitis rats induced by intracolon enema with 2,4,6-trinitrobenzene sulfonic acid (TNBS) and ethanol. The significant increases of colon mucosa damage index, histopathological score, myeloperoxidase (MPO) activity, MDA and NO contents, as well as the levels of TNF-α and IL-2, and decreases of colonic transforming growth factor-β (TGF-β) protein expression, SOD activity and IL-10 content in colonic tissues were found to be significantly ameliorated when the colitis rats were treated with ASP at the dose of 400 and 800 mg/kg ($P < 0.05$). Meanwhile, colonic EGF protein expression in colitis rats was significantly up-regulated. It concluded that ASP had a protective effect on immunological colon injury induced by TNBS and ethanol, which was probably due to the mechanism of immunomodulation, antioxidant and promotion of wound repair.

The effects of *A. sinensis* polysaccharides on rats with acute ulcerative colitis induced by 2,4-dinitrobenzene sulphonic acid (DNBS) were investigated by Wong et al. (2008). It was found that *A. sinensis* polysaccharides pretreatment significantly attenuated the reduction of GSH content, the increase of MDA concentration and the raise of apoptotic cells amount in colon tissues induced by intrarectal injection of DNBS. These findings suggested that the protective effects of *A. sinensis* polysaccharides were closely related to the prevention of oxidative stress, which might occur during neutrophil infiltration in the pathological process of ulcerative colitis.

4.6. Hepatoprotective activity

Ye, Liu, Li, et al. (2001) reported that intra-gastric administration of *A. sinensis* polysaccharides (AP) at the dose of 50 and 75 mg/kg body weight dose-dependently prevented liver toxicity induced by acetaminophen in mice. It also normalized the rises of serum alanine transferase (ALT) and hepatic nitric oxide synthase (NOS) activates and decrease of the GSH level in the liver, and reduced the hepatic MDA concentration. It suggested that the protective effect of AP on hepatic injury induced by acetaminophen was associated with the GSH depletion and NOS activation in the liver. Furthermore, it was found that the protective effect was less evident in carbon tetrachloride (CCl_4)-treated animals including mice and rats. However, Nie (2008) demonstrated that *A. sinensis* polysaccharides (ASP) could significantly improve the acute hepatic injury induced by CCl_4. Compared with tetrachloride control, ASP (200 mg/kg) could depress the increasing levels of glutamate pyruvate transaminase (GPT) and glutamic oxaloacetic transaminase (GOT) in serum, alleviate the degressive extents of blood glucose and hepatin contents, and significantly recover the histopathological changes induced by CCl_4.

The modulating effects of *A. sinensis* polysaccharides (ASP) on differentially expressed genes in liver of hepatic immunological injury mice were studied by cDNA microarray assay (Ding, Shi, Yu, Yu, & Huang, 2003). Hepatic immunological injury was induced by LPS in Bacillus Calmette-Guerin primed mice. It was found that pretreatment of ASP at the dose of 30 mg/kg body weight for 7 days significantly up-regulated the expression of Humnlk gene, and down-regulated the expression of Humscp2a, Humoat, Hsngmrna, humpafaa, humhbgfb and Hsu83843 genes in liver tissue of hepatic immunological injury mice.

4.7. Radioprotective activity

Many studies have demonstrated the exposure to radiation could induce apoptosis in various mammalian cells (Fuks et al., 1994; Okunieff et al., 1998; Sun et al., 2005). Some of the radioprotectors could protect cells against DNA damage and radiation-induced apoptosis (Vijayalaxmi Meltz, Reiter, & Herman, 1999; Warters, Roberts, Wilmore, & Kelley, 1997). Sun et al. (2005) investigated the radioprotective effect of the pectic polysaccharide ASP3 isolated from *A. sinensis* in murine model. After orally

administration of ASP3 at the dose of 50 and 200 mg/kg body weight for 7 days, the mice were exposed to a ^{60}Co source at the irradiation dose of 3.0 Gy at a uniform dose rate of 80.0 cGy/min. The result showed 200 mg/kg ASP3 pretreatment significantly decreased the apoptosis of peripheral lymphocytes ($P < 0.05$) compared with the irradiated control, which suggested that ASP3 could protect leucocytes and lymphocytes against radiation induced damage.

The radioprotective effects of ASP3 on subchronic radiation-injured mice were further studied by Sun, Ma, et al. (2009). After orally administration of ASP3 at the dose of 50 and 200 mg/kg body weight for 5 days, the mice were irradiated by ^{60}Co at the irradiation dose of 0.125 Gy for 20 days. It was found that ASP3 could protect leucocytes against radiation, prohibit formation of micronucleus of polychromatic erythrocytes in bone-marrow and sperm aberration, speed transformation rates of spleen lymphocyte, and enhance the radiation endurance of the body.

4.8. Antidiabetic activity

Diabetes mellitus is a serious chronic metabolic disease which now afflicts approximately 4% of population worldwide and is expected to increase by 5.4% in 2025 (Dahech et al., 2011). There are many oral hypoglycemic agents for the treatment of diabetes, such as biguanides and sulfonylureas, however, these synthetic agents are associated with certain adverse side effects (Grover, Yadav, & Vats, 2002). To explore and discover novel safer and more effective substitutes, Li and Chen (2007) evaluated the effects of *A. sinensis* polysaccharides (APS) on streptozotocin (STZ)-induced diabetic rats. The results showed that AP could significantly reduce blood glucose level compared with diabetic control group with time and dosage depended relationship. The research also found that AP could improve the clinical symptoms of diabetes mellitus, however, the level of serum insulin did not statistically change during the test. Li, Zhang, and Meng (2007) found that oral administration of *A. sinensis* polysaccharides (200 mg/kg body weight) for 42 days significantly reduced the serum glycosylated hemoglobin, total cholesterol (TC), triglycerides (TG) and low density lipoprotein (LDL) levels, and improved the serum high density lipoprotein (HDL) level in STZ-induced diabetic rats. Chen (2010) reported that oral administration of *A. sinensis* polysaccharides (20 mg/kg and 100 mg/kg body weight) for 21 days resulted in a significant reduction in blood glucose levels coupled with improvement of plasma insulin level in alloxan-induced diabetic rats, which might be associated with the repair and regeneration of the damaged islet B cells. All these findings suggested that *A. sinensis* polysaccharides had the possibility to be used as an adjuvant drug of oral hypoglycemic agents.

5. Correlation of structure and biological activities

Polysaccharides with different biological activities differ greatly in their chemical composition and configuration, as well as their physical properties (Wasser, 2002). The biological activities of the polysaccharide are strongly related to its structure. As little structure-function relationship of *A. sinensis* polysaccharides has been reported, it is difficult to correlate the structure and biological activities of such complex macromolecules. However, some relationships can be inferred as follows.

Unlike α-(1 → 3)-glucuronoxylomannans with medical properties that are not strongly dependent on molecular weight (Gao, Seljelid, Chen, & Jiang, 1996), the biological activities of *A. sinensis* polysaccharides have great relationship with their molecular weight. Sun, Ma, et al. (2009) prepared the low molecular weight polysaccharides (ASP3-PH) with similar composition by partial hydrolysis of *A. sinensis* polysaccharides (ASP3). It was found that ASP3 exhibited higher radioprotective activities compared with ASP3-PH as the high molecular weight played a crucial role in the maintenance of the spatial conformation of *A. sinensis* polysaccharides. In addition, the polysaccharides with medical properties may contain biological information since the polysaccharide contains types of essential sugars (*e.g.* Glc, Man and Xyl) that predominate in human glycoproteins and glycoprotein receptors (Jin, Lu, Huang, Wang, & Wang, 2012).

It is well known that uronic acid residues can alter physicochemical property and modify the solubility of the polysaccharide (Yang, Zhao, & Lv, 2008). The uronic acids in *A. sinensis* polysaccharides have been found to be important for their biological activities, and the fraction rich in uronic acids exhibited higher activities. Shang et al. (2003) reported that AP-0 and AP-3 with the highest amounts of uronic acid among the four polysaccharides from *A. sinensis* had the strongest inhibitory effects on invasion and metastasis of hepatocellular carcinoma cells *in vitro*. It has also been found that high content of galacturonic acid in the acidic *A. sinensis* polysaccharide fraction contributed to the protective and antioxidant actions on H_2O_2-injuried macrophages (Yang, Zhao, Zhou, et al., 2007). Yang, Zhao, and Lv (2008) reported that the *A. sinensis* polysaccharide fraction rich in uronic acid possessed higher immunomodulatory activity, and it has been proved to be most potent as an activator of murine macrophages.

Previous research indicated that structural features such as β-(1 → 3) linkages in the main chain of the glucan and additional β-(1 → 6) branches were important for the antitumor activity by increasing immune-competent cell activity (Wasser, 2002). However, the antitumor polysaccharide from *A. sinensis* with different chemical structures was reported, such as the arabinoglucan with a backbone composed of (1,4)-α-D-Glc*p* (Cao, Li, Liu, Yang, et al., 2006; Cao, Li, Wang, Fan, et al., 2010). Those researches facilitated the understanding of the structural basis of the polysaccharides with antitumor effects and their antitumor mechanisms.

It has been reported that some kinds of polysaccharides with a backbone mainly composed of Glc*p* residues, such as Maitake mushroom polysaccharide, could induce apoptosis in cancer cells (Cao, Li, Wang, Fan, et al., 2010; Fullerton et al., 2000). A novel polysaccharide (ASP-1d) isolated from *A. sinensis* with a backbone composed of (1,4)-α-D-Glc*p* residues, and branches composed of (1,6)-α-D-Glc*p* residues was found to be capable of inhibiting HeLa cell proliferation and inducing apoptosis in these cells (Cao, Li, Wang, Fan, et al., 2010).

Furthermore, contemporary investigations confirmed that polysaccharide structure had more influence than that of sugar composition on biological activity (Deters, Lengsfeld, & Hensel, 2005; Yang et al., 2006; Zhao, Kan, Li, & Chen, 2005). Sun, Lin, et al. (2009) investigated the effects of neutral sugars in the branched chain, degree of esterification and GalA residues on the radioprotective function of *A. sinensis* polysaccharide (ASP3). The results showed that the radioprotective function of ASP3 was mainly expressed by the neutral sugars-branched chain of hairy regions, and modulated by the hemigalacturonan main chain of smooth regions. Meanwhile, different formation of space configuration caused by various degree of esterification influenced the radioprotective function of ASP3.

6. Summary

The root of *A. sinensis* has been used historically as a tonic, hematopoietic and anti-inflammatory agent for thousands of years. Polysaccharides have been proved to be one of the components responsible for those biological activities. It has been demonstrated that *A. sinensis* polysaccharides had various important bioactivities, such as hematopoiesis, immunomodulation, antitumor, antioxidant, radioprotection and hypoglycemic activity. The chemical

structures and chain conformations of polysaccharides are very important to their biological activities. However, the high order structure of this active component as well as the relationship between the bioactivity and the chemical structure are still not well established. Further research on the exact order structure and the structure-bioactivity relationship of *A. sinensis* polysaccharide are required, which would allow a better understanding of the functional effects about this macromolecule.

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