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Review

Structure and biological activities of the polysaccharides from the leaves, roots and fruits of *Panax ginseng* C.A. Meyer: An overview

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ABSTRACT

Panax ginseng C.A. Meyer, with thousands of years of history, has been known as a valuable traditional Chinese medicine. The plant has been valued for its important biological and chemical perspectives and its use in the treatment of a variety of pathological conditions and illnesses have been documented in ethnobotanical reports. Modern pharmacological experiments have proved that ginsenosides is the most active ingredients. Most recent interest has been focused on the ginsenosides to explore the pharmacological mechanisms of *P. ginseng*. Whereas it is difficult to make significant progress to elucidate the underlying mechanism by which *P. ginseng* take effect only by ginsenoside. As we know, ginseng contains multiple constituents, such as ginsenosides, essential oil, polysaccharides and peptides, and especially more and more attentions have been cast on ginseng polysaccharides by medical scientists and nutritionists due to their various important biological activities. Therefore the aim of present review is to give a comprehensive summary of information regarding the chemical constituents and biological effects of polysaccharides form the leaves, roots and fruits of *P. ginseng* to help us to take action for future study in this discipline.

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1. Introduction

Panax ginseng C.A. Meyer (*P. ginseng*), a well-known traditional Chinese medicine, has been used for several thousand years with mysterious powers in the Orient as a tonic, prophylactic and restorative agent, etc. People believed it to be the king of the herbs. Particularly in China, Korea and Japan, it has been known as the most valuable medicine of all medicinal herbs. *P. ginseng* contains many classes of compounds, including ginsenosides, essential oil, peptidoglycans, polysaccharides, nitrogen-containing compounds, fatty acids and phenolic compounds (Choi, 2008; Lee et al., 2010; Xiang, Shang, Gao, & Zhang, 2008). The aboveground and underground parts of *P. ginseng* are showed in Figs. 1 and 2, respectively.

Originally, the efficacy of *P. ginseng* was attributed to the theory of traditional Chinese medicine. Since the 1970s, modern scientific theory and technology had enabled scientists to explore the pharmacological mechanisms of *P. ginseng*. However, scientific research and study on the pharmacological efficacy of *P. ginseng* had not made significant progress. In addition, most scientists concentrated on the small molecular weight of components of *P. ginseng*. Nevertheless these studies could not satisfactorily explain the mystery of ginseng that gave rise to its efficacy.

Nowadays polysaccharides as biological response modifiers (BRMs) were attached on more and more importance by biochemical and nutritional researchers due to their various biological activities used in health-care food or medicine. Since the mid of the 20th century, many studies had been conducted on the purification, structural analysis and bioactivities of polysaccharides from *P. ginseng*. Many biological active polysaccharides have been isolated from the leaves, roots or fruits of *P. ginseng*. Modern pharmacological studies had showed that *P. ginseng* polysaccharides had immunomodulation, anti-tumor, anti-adhesive, antioxidant, hypoglycemic activities, and so on (Choi, 2008; Gao, Kiyohara, Cyong, & Yamada, 1989; Lee et al., 2010; Xiang et al., 2008; Zhang, Yin, & Wei, 2010). Meanwhile, Shin, Kiyohara, Matsumoto, and Yamada (1997) proved that the leaves and fruits of *P. ginseng* might have similar pharmacological activity as the roots. Accordingly they will be available for clinical uses like the roots.

Therefore this review aims at summarizing previous and current references regarding chemical properties and biological activities of polysaccharides form the leaves, roots and fruits of *P. ginseng* that have been scientifically identified by modern science to date and provide new insights for future study to unveil the mystery of ginseng.

2. Chemical structural characterization of polysaccharides

Since the first research on *P. ginseng* polysaccharide reported by Ovodov and Solov'eva (1966), there were total 35 polysaccharides identified from the leaves, roots and fruits of *P. ginseng* up to date. Out of these polysaccharides, 16 ones came from the leaves, 18 ones from the roots and one from the fruits of *P. ginseng*. Their monosaccharide composition and molecular weight were shown in the Table 1. Besides, their name, the corresponding plant sources and references were also included.

2.1. Polysaccharides from the leaves of P. ginseng

2.1.1. GL-BIII

The structural features of an anti-ulcer polysaccharide (GL-BIII), isolated from leaves of *P. ginseng*, were investigated by Kiyohara et al. (1994). GL-BIII was a pectic polysaccharide with a rhamnogalacturonan core as determined by Base-catalysed β-elimination and partial acid hydrolysis, and composed of rhamnose (Rha), arabinose (Ara), mannose (Man), galactose (Gal), glucose (Glc), galacturonic acid (GalA) and glucuronic acid (GlcA) in molar ratios of 3:4:2:10:1:7:4. Structural analysis indicated that some 2,4-

Fig. 1. Aboveground parts of *P. ginseng*.

Fig. 2. Underground parts of *P. ginseng*.

Table 1
The polysaccharide from the leaves, roots and fruits of *P. ginseng*.

No.	Compound name	Monosaccharide composition	Molecular weight	Source	Ref.
1	GL-BIII	Rha, Ara, Man, Gal, Glc, GalA, GlcA in the ratio of 3:4:2:10:1:7:4		The leaves of *P. ginseng*	Kiyohara et al. (1994)
2	GL-3	Rha, Ara, Gal, Glc, GalA, GlcA in the ratio of 27.0:11.8:24.1:12.5:12.8:11.5	4.2×10^4		Gao et al. (1989)
3	GL-4	Rha, Ara, Xyl, Man, Gal, Glc, GalA, GlcA in the ratio of 10.9:22.6:3.0:4.8:33.5:6.0:9.8:9.1	8.6×10^4		Gao et al. (1989)
4	GL-5	Rha, Ara, Gal, Glc, GalA, GlcA in the ratio of 11.6:27.5:25.9:25.0:5.6:4.3	7.8×10^3		Gao et al. (1989)
5	GLA-3	Ara, Man, Gal, Glc, GalA, in the ratio of 19.3:4.6:3.4:5.7:66.9	5.0×10^3		Gao et al. (1989)
6	GLA-4	Ara, Man, Gal, Glc, GalA, in the ratio of 29.3:8.5:5.6:8.5:47.8	3.2×10^3		Gao et al. (1989)
7	GLA-5	Ara, Glc, GalA, in the ratio of 18.5:27.8:53.7	8.0×10^3		Gao et al. (1989)
8	GL-NIa	Ara, Ga, Glc in the ratio of 1.2:1.0:0.5			Gao et al. (1991)
9	GL-NIb	Ara, Gal, Glc in the ratio of 0.8:1.0:1.6			Gao et al. (1991)
10	GL-AIa	Rha, Ara, Gal, GalA, GlcA in the ratio of 0.3:1.0:1.0:0.2:0.1			Gao et al. (1991)
11	GL-AIb	Rha, Ara, Gal, GalA, GlcA in the ratio of 1.2:0.8:1.0:1.1:0.5			Gao et al. (1991)
12	GL-PI	Rha, Gal, Glc, GalA, GlcA in the ratio of 38.8:18.8:5.6:34.3:2.4	5.0×10^4		Gao et al. (1988)
13	GL-PII	Rha, Gal, Glc, GalA, GlcA in the ratio of 30.9:27.0:2.5:32.7:5.8			Gao et al. (1988)
14	GL-PIII	Rha, Ara, Fuc, Gal, Glc, GalA, GlcA in the ratio of 19.0:4.0:17.4:25.0:3.3:28.0:2.5			Gao et al. (1988)
15	GL-PIV	Rha, Ara, Fuc, Xyl, Gal, Glc, GalA, GlcA in the ratio of 7.2:4.2:4.0:1.6:27.8:11.1:36.8:7.0			Gao et al. (1988)
16	GL-4IIb2	2-MeFuc, Rha, Fuc, 2-MeXyl, Ara, Xyl, Api, Man, AceA, Gal, Glc, Dha, Kdo, GalA, GlcA in the ratio of 5.2:16.5:3.9:3.8:8.8:0.5:4.3:1.4:1.6:10.2:1.6:4.1:5.4:25.1:7.8	1.1×10^4		Shin et al. (1997)
17	PA	Ara, Gal, Rha, GalA, GlcA in the ratio of 11:22:1:6:1	1.6×10^5	The roots of *P. ginseng*	Tomoda, Takeda, et al. (1993)
18	PB	Ara, Gal, Rha, GalA, GlcA in the ratio of 3:7:2:8:1	5.5×10^4		Tomoda, Takeda, et al. (1993)
19	S-IA	Ara, Gal, GalA in the ratio of 8:8:1	5.6×10^4		Tomoda, Hirabayashi, et al. (1993)
20	S-IIA	Ara, Gal, Glc, GalA in the ratio of 15:10:2:5	1.0×10^5		Tomoda, Hirabayashi, et al. (1993)
21	GR-3	Rha, Ara, Gal, Glc, GalA, GlcA in the ratio of 15:8.2:10:4.5:49.3:12.5	8.6×10^4		Gao et al. (1989)
22	GR-4	Rha, Ara, Gal, GalA, GlcA in the ratio of 12.3:20.5:25.6:33.3:8.3	9.0×10^4		Gao et al. (1989)
23	GR-5	Ara, Glc, GalA, GlcA in the ratio of 16.6:67.3:8.0:8.0	7.5×10^4		Gao et al. (1989)
24	GRA-3	Rha, Ara, Gal, Glc, GalA, GlcA in the ratio of 18.4:8.6:9.6:4.3:46.9:12.2	3.6×10^4		Gao et al. (1989)
25	GRA-4	Rha, Ara, Gal, GalA, GlcA in the ratio of 11.8:16.2:21.6:40.3:10.0	8.6×10^4		Gao et al. (1989)
26	GRA-5	Ara, Gal, Glc, GalA, GlcA in the ratio of 9.6:5.6:70.9:7.2:6.5	8.6×10^4		Gao et al. (1989)
27	WGPN	Gal, Glc, Ara in the ratio of 3.3:95.3:1.3			Zhang et al. (2009)
28	WGPA-N	Gal, Glc, Ara in the ratio of 18.0:66.3:15.7			Zhang et al. (2009)
29	WGPA-1RG	Gal, Glc, Ara, Rha, Man, GalA, GlcA in the ratio of 56.2:3.5:34.0:0.2:2.5:1.8:1.9	1.0×10^5		Zhang et al. (2009)
30	WGPA-2RG	Gal, Glc, Ara, Rha, Man, GalA, GlcA in the ratio of 44.4:2.9:40.9:4.1:0.4:5.3:2.0	1.1×10^5		Zhang et al. (2009)
31	WGPA-1HG	Gal, Glc, Ara, Rha, Man, GalA, GlcA in the ratio of 15.2:7.6:7.1:1.6:3.6:62.4:2.6	3.5×10^3		Zhang et al. (2009)
32	WGPA-2HG	Gal, Glc, Ara, Rha, Man, GalA, GlcA in the ratio of 5.1:1.9:4.6:3.0:0.2:83.6:1.6	6.5×10^3		Zhang et al. (2009)
33	WGPA-3HG	Gal, Glc, Ara, Rha, GalA, GlcA in the ratio of 3.5:1.3:2.2:1.5:90.9:0.5	1.6×10^4		Zhang et al. (2009)
34	WGPA-4HG	Gal, Glc, GalA, in the ratio of 5.9:2.0:92.1	4.5×10^4		Zhang et al. (2009)
35	Heteropolysaccharide F	Ara, Rha, Xyl, Glc, Gal, GalA in the ratio of 5.9:4.3:0.3:1.0:17.4:0.7	1.9×10^6	The fruits of *P. ginseng*	Liu et al. (1988)

disubstituted Rha of the rhamnogalacturonan cores possessed GalA side chains at the O-4 position of the Rha. The terminal glycosyl residues were attached to rhamnogalacturonan core through GalA. However, the present results could not clarify whether the branched GalA was located in the rhamnogalacturonan core or in the side chains. The acidic oligosaccharides liberated by partial acid hydrolysis was analyzed by methylation analysis and GC–MS, and the results indicated that GL-BIII contained a GalA-(1 → 4)-Rha unit and longer acidic units consisting of 2-substituted Rha and 4-substituted GalA. When GL-BIII was degradated by borohydride reduction mediated by lithium, GL-BIII yield few fractions containing long and intermediate neutral oligosaccharide-alditols, as well as large numbers of fractions containing short oligosaccharide-alditols. The long neutral oligosaccharide-alditol fraction mainly comprised 4- or 5-substituted Ara, terminal Gal*f*, 6-substituted Glc and 2-substituted Man, whereas the intermediate oligosaccharide-alditol fraction consisted mainly of terminal and 6-substituted Gal*p*, 6-substituted Glc and 2-substituted Man. Methylation analysis and GC-MS analysis of the short oligosaccharide-alditol fraction suggested that it contained at least 14 kinds of di- to tetra-

saccharide-alditols, such as Gal-(1 → 2)-Rha-ol, Gal-(1 → 4)-Rha-ol, Ara → Ara-ol, and Ara → Ara → Ara-ol.

2.1.2. GL-3, GL-4, GL-5, GLA-3, GLA-4 and GLA-5

In 1989, the water-soluble (GL-3, GL-4 and GL-5) and alkaline-soluble polysaccharide fractions (GLA-3, GLA-4 and GLA-5) were identified from the leaves of *P. ginseng* by Gao et al. (1989) for the first time. These polysaccharides were fractionated into strongly acidic, weakly acidic, and neutral polysaccharide fractions by cetyltrimethyammonium bromide, respectively. The polysaccharide moieties of GLA-3, GLA-4, and GLA-5 contain large amounts of GalA, and contained no or negligible amount of Rha. The presence of homogalacturonan moiety in these polysaccharides confirmed that they may had the pectic nature. The polysaccharide fractions from the leaves showed different chemical properties in comparison with their corresponding fractions from the roots. The chemical properties of these polysaccharides are summarized in Table 1. The leaves mainly contained pectins and heteroglycans.

2.1.3. GL-NIa, GL-NIb, GL-AIa and GL-AIb

Four anti-complementary neutral (GL-NIa and GL-NIb) and acidic (GL-AIa and GL-AIb) polysaccharides from the leaves of *P. ginseng* were reported by Gao, Kiyohara, Cyong, and Yamada (1991). By means of glycosyl linkage analysis they speculated that GL-NIa mainly contained an arabinogalactan moiety, whereas GL-NIb consisted of more (1 → 4)-linked glucosyl residues than GL-NIa. GL-NIa was mainly composed of terminal Ara*p*, (1 → 4)- or (1 → 5)-linked Ara, and (1 → 3, 6)-linked Gal. GL-NIb consisted of (1 → 4)-linked Glc and (1 → 3, 6)-di-substituted Gal for the most part. β-Elimination indicated that GL-AIa and GL-AIb were pectic polysaccharides consisting of a rhamnogalacturonan core with neutral side chains. GL-Ala contained a large amount of (1 → 4)-linked GalA, besides small amounts of terminal and (1 → 4)-linked GlcA. GL-AIb contained large amounts of (1 → 4)-linked GalA, as well as small amounts of (1 → 3, 4)-di-substituted GalA and terminal (1v→ 4)-linked/(1 → 2, 4)-di-substituted GlcA. The neutral groups of GL-AIa and GL-AIb were composed of Ara and Gal with various linkages, and gel diffusion studies indicated that GL-AIa had large amounts of arabino-3, 6-galactan moiety as neutral side chains, whereas GL-AIb contained no.

2.1.4. GL-PI, GL-PII, GL-PIII and GL-PIVV

Four anti-complementary polysaccharides, GL-PI, GL-PII, GL-PIII and GL-PIV, were successfully isolated from the leaves of *P. ginseng* by Gao, Kiyohara, Cyong, and Yamada (1988). The properties of these pectic polysaccharides were summarised in Table 1. They commonly contained about 40% of uranic acid and a small amount of protein (0.5–1%). A trace of methyl ester was also detected in GL-PIII and GL-PIV. GL-PI and GL-PII consisted mainly of Rha, Gal and GalA in the molar ratios of 2.0:1.0:1.8 and 1.1:1.0:1.2, respectively. GL-PIII consisted mainly of Rha, Fuc, Gal and GalA (1.1:1.0:1.4:1.6), whereas GL-PIV consisted mainly of Rha, Gal, Glc, GalA and GlcA (1.0:3.9:1.5:5.1:1.0). The results of base-catalysed β-elimination indicated that these four polysaccharides have a rhamnogalacturonan backbone consisting of 4-linked GalA and 2-linked Rha*p*. Some 6-linked Gal*p* was attached to GalA or GlcA. Due to the different structures, GL-PI, GL-PII, and GL-PIV exhibited more potent anti-complementary activity than GL-PIII. GL-PI, GL-PII, and GL-PIV, which each had a rhamnogalacturonan backbone, were substituted by neutral sugar side-chains consisting of β-D-galactan (in GL-PI and GL-PII) or arabinogalactans (in GL-PIV) attached at O-4 of Rha*p*. However GL-PIII contained a rhamnogalacturonan backbone substituted with arabinogalactan, highly branched Fuc chains, and GalA mostly at O-3 or O-2 of GalA. These results proved that the branched GalA in the GL-PIII may suppress the anti-complementary activity. The rhamnogalacturonan moieties of GL-PI and GL-PII contained an alternating sequence of 2- or 2,4-di-O-substituted α-L-Rha*p* and 4-O-linked α-D-GalA, but the branching frequencies of 2,4-di-O-substituted α-L-Rha*p* was different. GL-PIII and GL-IV contained a galacturonan moiety consisting of 4-O-linked α-D-GalA in addition to the rhamnogalacturonan moiety. GL-PII also contained a small proportion of 2-linked Rha in the backbone, and GL-PIII was rich in highly branched GalA. The β-D-galactan side-chains in GL-PI and GL-PII consisted mainly of 4-O-linked and 6-O-linked Gal*p*.

2.1.5. GL-4IIb2

Shin et al. (1997) reported a complex pectic polysaccharide (GL-4IIb2) from the leaves of *P. ginseng* C.A. Meyer, which was believed to be a macrophage Fc receptor expression-enhancing polysaccharide. GL-4IIb2, with a molecular weight of 1.1×10^4, contained about 65% total carbohydrate, 33.7% uronic acid, 0.82% acetyl-group and 2.2% protein. The primary structure of GL-4IIb2 was investigated by a combination of chemical and instrumental analysis. Monosaccharide analysis indicated GL-4IIb2 comprised 15 different monosaccharides which included rarely observed sugars, such as 2-O-methylfucose, 2-O-methylxylose, apiose, 3-C-carboxy-5-deoxy-L-xylose (acetic acid, AceA), 3-deoxy-D-*manno*-2-octulosonic acid (Kdo), and 3-deoxy-D-*lyxo*-2-heptulosatic acid (Dha). The above sugars were characteristic monosaccharide constituents of rhamnogalacturonan II (RGII) of plant cell-wall polysaccharides, in addition to Fuc, Ara, Xyl, Rha, Man, Gal, Glc, GlcA, and GalA. Methylation analysis indicated that GL-4IIb2 consisted of 34 different glycosyl linkages, such as 3, 4-linked Fuc, 3- and 2, 3, 4-linked Rha, and 2-linked GlcA, which are characteristic of RG-II. Sequential degradation using partial acid hydrolysis indicated that GL-4IIb2 contained α-Rha*p*-(1 → 5)-Kdo and Ara*f*-(1 → 5)-Dha structural units, an AceA-containing oligosaccharide, uronic acid-rich oligosaccharide chains as well as an α-(1 → 4)-galacturono-oligosaccharide chain. Fast-atom-bombardment mass spectrometry (FABMS) and methylation analyses proved that the AceA-containing oligosaccharide was a nonasaccharide in which terminal Rha was additionally attached to position 3 of 2-linked Ara*p* of the octasaccharide chain observed in sycamore RG-II. Sugar composition and methylation analyses assumed that the uronic acid-rich oligosaccharides possessed a similar structural feature as those in sycamore RG-II.

2.2. Polysaccharides from the roots of P. ginseng

2.2.1. PA and PB

Two acidic polysaccharides, named PA and PB, were isolated form the roots of *P. ginseng* by Tomoda, Takeda, et al. (1993). They were homogeneous on electrophoresis and gel chromatography, and their molecular weights were evaluated to be 1.6×10^5 and 5.5×10^4, respectively. Quantitative analyses indicated that PA consist of L-Ara, D-Gal, L-Rha, D-GalA and D-GlcA in the molar ratios of 11:22:1:6:1, and PB were composed of the above monosaccharide composition in the proportions of 3:7:2:8:1, in addition to small amounts of O-acetyl groups. Reduction of carboxyl groups, methylation analysis, NMR and periodate oxidation studies suggested that their structural features included mainly both α-arabino-β-3, 6-galactan type and rhamnogalacturonan type structural units.

2.2.2. S-IA and S-IIA

Almost at the same time Tomoda, Hirabayashi, et al. (1993) characterized the structural features of PA and PB, they also purified another two acidic polysaccharides from the roots of *P. ginseng*, namely S-IA and S-IIA. Each polysaccharide gave a single spot on glass-fiber paper electrophoresis and a single peak on gel chromatography with Toyopearl HW-55F. Gel chromatography gave values of 5.6×10^4 and 1.0×10^5 for the molecular masses of S-IA and S-IIA, respectively. S-IA consisted of L-Ara, D-Gal and D-GalA

in the ratios of 8:8:1. S-IIA was composed of L-Ara, D-Gal, D-Glc and D-GalA in the ratios of 15:10:2:5. Reduction of carboxyl groups, methylation analysis, NMR and periodate oxidation studies indicated that their structural features included mainly (1 → 5)-linked-α-L-Ara*f* and (1 → 3)-linked-β-D-Gal*p* type structural units, occasionally branched at O-3 of Ara*f* or O-4 and O-6 of Gal*p*. These substances were the first examples having a relatively high content of both α-3, 5-branched L-Ara and β-1, 4-linked D-Gal units among the acidic arabinogalactans with activities on phagocytosis and anti-complement.

2.2.3. GR-3, GR-4, GR-5, GRA-3, GRA-4 and GRA-5

In addition to finding six polysaccharides from the leaves of *P. ginseng*, Gao et al. (1989) also purified the corresponding polysaccharides from its roots, namely GR-3, GR-4, GR-5, GRA-3, GRA-4 and GRA-5. The results showed that the polysaccharides from the roots had higher uronic acid content than the corresponding fractions from the leaves, except GLA-5. On the opposite side, the polysaccharides from the leaves had higher protein content than those from the roots. The water-soluble polysaccharide fractions and the corresponding alkaline-soluble polysaccharide fractions from the roots consisted of the same sugar composition with similar molar ratios, as shown in Table 1. GR-3, GR-4, GRA-3, and GRA-4 were believed to be acidic pectic polysaccharides because of much GalA predominantly existing in them. However, GR-5 and GRA-5 seemed mainly to contain glucans because their high Glc content.

2.2.4. WGPN, WGPA-N, WGPA-1RG, WGPA-2RG, WGPA-1HG, WGPA-2HG, WGPA-3HG and WGPA-4HG

Zhang et al. (2009) adopted a combination method of ethanol precipitation, ion-exchange and gel permeation chromatography to fraction water-soluble polysaccharides from the roots of *P. ginseng* into two groups, namely neutral (WGPN and WGPA-N) and acidic polysaccharides (WGPA-1-RG, WGPA-2-RG, WGPA-1-HG, WGPA-2-HG, WGPA-3-HG and WGPA-4-HG).

By hydrolyzed with α-amylase and tested with iodine, the results demonstrated WGPN was mainly composed of starch-like glucans and WGPA-N was a mixture of starch-like glucan and arabinogalactan.

WGPA-1-RG and WGPA-2-RG mainly consisted of Gal and Ara in the ratios of 1.7:1.0 and 1.1:1.0, respectively. In addition they were also both composed of Glc, Rha, Man, GalA and GlcA as minor components. The total amount of Gal and Ara accounted for 90.2% in WGPA-1-RG and 84.9% in WGPA-2-RG, whereas the amounts of uronic acid in WGPA-1-RG and WGPA-2-RG were 3.7% and 7.3%, respectively. Based on the pectolytic hydrolysis and NMR analysis, they concluded that WGPA-1-RG and WGPA-2-RG were composed of major neutral sugars and minor acidic sugars that belong to the type-I rhamnogalacturonan (RG-I)-rich pectins.

WGPA-1-HG, WGPA-2-HG, WGPA-3-HG and WGPA-4-HG were mainly composed of GalA from 62.4 to 92.1%, which was in agreement with the elution sequence from the DEAE-Cellulose column. Combining the pectolytic hydrolysis and NMR analysis they have been identified to be homogalacturonan (HG)-rich pectins with different degrees of methyl-esterification, ranging from 0% to 30%. The six acidic fractions all showed single and symmetrical narrow peaks, with molecular weights approximately ranging from 3.5×10^3 to 1.1×10^5.

2.3. Polysaccharides from the fruits of P. ginseng

2.3.1. Heteropolysaccharide F

Up to now, there was only one polysaccharide from the fruit of *P. ginseng* identified by Liu, Zhang, and Li (1988). By ethanol precipitation and chromatography on the Sepharose 4B, they obtained one homogeneous heteroglycan (Mw = 1.9×10^6 Da) composed of Ara, Rha, Xyl, Glc, Gal and GalA in the ratio of 5.9:4.3:0.3:1.0:17.4:0.7. By means of partial hydrolysis with acid or pectinase, periodate oxidation, Smith degradation, methylation analysis, GC and GC-MS, the structure of Heteropolysaccharide F had been proved to be a highly branched polysaccharide with β-1, 3-Gal linkages as its main chain and the side chains on the main chain at C-4 and C-6 positions.

3. Biological activities

3.1. Antitumor activity

Kim et al. (1998) and Lee et al. (1997) previously reported that an acidic polysaccharide (ginsan) from *P. ginseng* inhibited the incidence of benzo[α]pyrene-induced autochthonous lung tumors in mice through activating multiple effector arms of the immune system. To elucidate the mechanism of antineoplastic activity, ginsan was tested for its ability to generate LAK cells and to produce cytokines. The results demonstrated that ginsan induced the production of Thl-cell and macrophage cytokines but not Th2-cell cytokines, and activated tumor killing cytotoxic cells through these endogenously produced cytokines. Furthermore, ginsan synergized with rlL-2 to generate LAK cells *in vitro* and to inhibit development of pulmonary metastasis of B16-F10 melanoma. This property may contribute to its effectiveness in the immunoprevention and immunotherapy of cancer.

A neutral polysaccharide fraction (WGPN), from the roots of *P. ginseng*, was tested its anticancer activity alone and in combination with 5-fluorouracil (5-FU) in Sarcoma-180 (S180) tumor-bearing mice by intragastric administration by Ni et al. (2010). WGPN alone inhibited S180 tumor growth in a bell-shaped dose–response curve, and the combination with 5-FU showed a synergistic effect. Studies of various immunological activities in S180-bearing mice revealed that WGPN stimulated the proliferation of lymphocytes; increased natural killer cell cytotoxicity; enhanced the phagocytosis and nitric oxide production by macrophages and increased the level of tumor necrosis factor-α in serum. In combination with 5-FU, WGPN reduced side-effect of 5-FU to the immune system in S180-bearing mice. These results suggested that WGPN might be a potential adjuvant for chemotherapeutic drugs.

In order to develop the novel anti-cancer immunotherapy for the treatment of human prostate cancer, a newly developed acidic polysaccharide (MB40), isolated from the leaves of *P. ginseng*, were studied *in vivo* cancer animal models by Park et al. (2004). The results of this novel studies indicated that combination therapy using paclitaxel or cisplatin with MB40 could significantly increase therapeutic effect and decrease haematopoietic complications induced by systemic chemotherapy or radiation therapy. MB40 can be developed as a novel and potent adjuvant of anticancer drug for the treatment of clinical cancer patients in urology including prostate cancer, bladder cancer, and renal cell carcinoma.

Shin et al. (2004) reported that an acidic polysaccharide (RGAP), isolated from *P. ginseng*, shows immunomodulatory and antitumor activities, which was mainly mediated by the nitric oxide (NO) production of macrophages. Thereafter they continued to evaluate a synergistic antitumor effect of RGAP and paclitaxel in mice transplanted with S 180 and B16 melanoma. Combined treatment with paclitaxel (5 or 15 mg/kg) and RGAP (25 mg/kg) resulted in a 28.6 or 42.8 increase in the life span of ICR mice bearing S 180 tumor cells, while no obvious effect was seen on single paclitaxel treatment. When a combination of paciltaxel (10 mg/kg) and RGAP (100 mg/kg) was administrated to C58BL/6 mice implanted with B16 melanoma, the tumor weight per mouse also decreased by 76.3%, suggesting that RGAP may be used as an adjuvant in medicinal applications of paclitaxel. The augmented antitumor effect of paclitaxel was supposed to be the result of the immunomodulat-

ing antitumor effect of RGAP. RGAP had the tendency to stimulate B cell specific mitogenic activity and induced the secretion of interleukin-6 (IL-6) in spleen cells in a concentration-dependent manner (5–500 μg/μL). RGAP also restored the proliferation of splenocytes and NK cell activity suppressed by paclitaxel. Flow cytometric analysis of splenocytes in mice treated with paclitaxel showed a significant increase of $CD11b^+$ cells. Additionally, a synergistic effect of RGAP and paclitaxel was found to give rise to an increased tumoricidal activity of macrophages. The above results suggested that clinical trials of RGAP as an adjuvant in cancer chemotherapy, combined with paclitaxel, are highly feasible. In another research, Du, Jiang, Wu, Won, & Choung (2008a) investigated the synergistic effect of combined treatment with RGAP and pidotimod on cell-mediated immunity in cyclophosphamide-treated mice. The combination of pidotimod and RGAP significantly restored concanavalin A or LPS-stimulated lymphocytes proliferation. The production of NO from peritoneal macrophages, the level of serum IL-12 and interferongamm, as well as NK cell activity were increased by the combinations of two samples. Meanwhile they made a further investigation about synergistic immunostimulatory effect of pidotimod and RGAP on humoral immunity of immunosuppressed mice (Du, Jiang, Wu, Won, & Choung, 2008b). Combined treatment with pidotimod and RGAP significantly increased the number of plaque-forming cells in the spleen in response to both LPS and SRBC, whereas treatment with either pidotimod or RGAP individually had no such effect. IgG levels in serum were augmented for secondary responses to SRBC in co-treated mice, but not in mice treated with either drug alone. Two drugs combination showed more efficiencies in almost all cases than the respective monotherapies. These results indicated that combinations of pidotimod and RGAP could improve both cell and humoral immune activities, and may give greater effectiveness over the use of either, which also provided reference for the combined use of western and oriental medicines to offer alternative therapies for immunosuppression in the course of cancer chemotherapy.

Kim, Kang, and Kim (1990) made a comparison of the antitumor and immunomodulating activities between neutral and acidic polysaccharide fraction from *P. ginseng*. The chemical compositions were 85.0% carbohydrate and 15.0% protein for the neutral fraction, and 28.4% carbohydrate, 10.0% protein and 29.0% uronic acid for the acidic fraction. The acidic fraction was more effective in increasing of the ratio of spleen to body weight, the number of antibody secreting ceils to sensitization red blood cell and phagocytic activity of reticuloendothelial system, as well as antitumor activity against the solid form of S 180 in ICR mice than the neutral fraction. At the same time the acidic fraction may stimulate B and T cells as well as macrophages, whereas the neutral fraction may stimulate only B cells and macropages.

3.2. Immunoregulatory activity

Wang, Cui, and Liu (1982) tested one polysaccharide (PSG) on immue function. The results indicated PSG was found to be able to markedly stimulate phagocytosis of the reticuloendothelial system and the production of antibody. In addition, PSG caused an increase of serum complement content in quinea pigs, and raised serum IgG level in mice. Besides, an increased B-lymphatic to T-lymphatic cell ratio was observed after PSG administration.

Na, Lim, Yun, Kweon, and Lee (2010) identified that ginsan effectively enhanced the humoral immune response to orally delivered antigen, mediated by CCL3 via cyclooxygenase (COX). Therefore ginsan might serve as a potent vaccine supplement for oral immunization.

Gamma radiation causes suppression of the immune function, and decrease the production of cytokine. In one study (Han, Song, Yun, & Yi, 2005), the polysaccharide, ginsan, was studied to assess its recovery competency on the immunosuppressive activities of gamma radiation. The results showed that ginsan could restore the T lymphocytes function that had been suppressed by gamma irradiation in allogenic MLR (mixed lymphocyte reactions), by inducing the mRNA expressions of Thl and Th2 type cytokines, and restoring the mRNA expression of IFN-γ and Thl cytokine. The above results indicated that ginsan might be a promising agent for fighting against the immunosuppression induced by gamma radiation.

A water-soluble ginseng marc polysaccharide (GMP) was examined for immunomodulatory effects in murine peritoneal macrophages by Lim, Na, Choi, Chung, and Hwang (2004). GMP significantly increased the lysosomal phosphatase activity and the phagocytic index of peritoneal macrophages ($P < .05$). The peritoneal macrophages treated with GMP also produced significantly more H_2O_2 and nitrite than the control without GMP treatment ($P < .05$). In addition, GMP (100 mg/mL) significantly increased the cell viability of peritoneal macrophages ($P < .05$). These results suggested that GMP was an effective nonspecific immunomodulatory agent, and its immunostimulating effects may be due to its ability to stimulate the production of reactive oxygen intermediates.

As is well known, dendritic cells (DCs) was closely related to the occurrence and development of tumor, which are the most powerful antigen presenting cells of the immune system. Kim et al. (2009) found ginsan significantly enhanced the expression of CD86 on DCs surfaces, whereas it weakly increased that of MHC class II. In 3H-thymidine incorporation assays, ginsan-treated DCs stimulated profoundly higher proliferation of allogeneic CD4+T lymphocytes than did medium-treated DCs. Taken together, the above evidences identified that ginsan stimulated DCs by inducing maturation.

Because DCs acted as critical antigen-presenting cells in immune responses, this study provided valuable information on the activities of ginsan.

Calcineurin (CN), a unique Ca^{2+}/calmodulin (CaM)-dependent serine/threonine protein phosphatase, played a pivotal role in the activation and proliferation of T lymphocytes. Zhang et al. (2010) found a polysaccharide from the stem and leaves of *P. ginseng*, termed PGP-SL, could exhibit immunopotentiation effects on murine spleen lymphocytes by the Ca^{2+}–CN–NFAT–IL-2 signaling pathway (via upregulating calcineurin activity).

Ginsan could enhance cytotoxic and phagocytic activity of murine peritoneal macrophages, in addition to the levels of cytokines, including tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), IL-6 and interferon-γ (IFN-γ) these results suggested that ginsan had an immunopotentiating effects on macrophages and these abilities could be used clinically for the treatment of diseases such as cancer (Shin et al., 2002).

As NO plays an important role in immune function. Park et al. (2001) reported an acidic polysaccharide from the roots of *P. ginseng* stimulated the immune activity by the production of NO.

As IL-8 is a potent inflammatory cytokine involved in neutrophil chemotaxis and activation, Sonoda et al. (1998) found that one acidic polysaccharide (ginsenan S-IIA) from the root of *P. ginseng* was a potent inducer of IL-8 production by human monocytes and THP-1 cells, and this induction was accompanied by increased IL-8 mRNA expression.

Using Cell Counting Kit-8® solution and trypan blue solution, Ko and Joo (2010) found that ginsan significantly enhanced viability and proliferation of spleen cells.

3.3. Anti-adhesive activity

Recently, many scientists had made a series of research on bacteria-host interactions. An increasing body of evidence suggested that bacterial adhesion to human cells was a key step in initiating the infection that may lead to the development of diseases. It is now well established that in many cases adhesion is

mediated by specific interactions between microbial adhesions and carbohydrates on the surface of host cells through single or multiple interactions. Previously, acidic polysaccharides purified from the roots of *P. ginseng* were reported to exhibit a marked inhibitory effect against the adhesion of *Helicobacter pylori* to gastric epithelial cells and erythrocytes (Belogortseva, Yoon, & Kim, 2000; Lee, Lee, Chung, & Kim, 2004). In addition, a polysaccharide obtained from *P. ginseng* had been shown to exert a comparable inhibitory effect on the binding of *Porphyromonas gingivalis* to erythrocytes (Lee, Lee, et al., 2004; Lee, Park, et al., 2004). Besides, an acidic polysaccharide (PG-F2) was further investigated to test its antiadhesive effects against various pathogenic bacteria by using hemagglutination assays (Lee et al., 2006). The minimum inhibitory concentrations (MIC) of PG-F2 against *Actinobacillus actinomycetemcomitans*, *Propionibacterium acnes*, and *Staphylococcus aureus* were found to be in a range of 0.25–0.5 mg/mL, whereas it did not work against *Lactobacillus acidophilus*, *Escherichia coli*, or *Staphylococcus epidermidis*. In 2009, they examined the antiadhesive role of acidic polysaccharides (PG-F2 and PG-HMW) of *P. ginseng* against oral and skin bacterial adhesion to human and mouse cell lines (Lee, Shim, Chung, Lim, & Kim, 2009). Both the adhesion of *P. gingivalis* and *A. actinomycetemcomitans* to human oral epithelial cells and the adhesion of *P. acnes* and *S. aureus* to mammalian fibroblast cells were inhibited greatly by two polysaccharides in a dose-dependent manner form 0.1 to 2.0 mg/ml. Moreover it had been found that PG-F2 and PG-HMW significantly inhibited the attachment of *H. pylori* to AGS human gastric cells. Total results suggested that these polysaccharides may exert a selective antiadhesive effect against pathogenic bacteria, and multivalent polysaccharides might act as a selective carbohydrate mimetic to affect the blockage of a variety of host–pathogen interactions without adverse effects on commensal bacteria.

3.4. Antioxidant activity

Superoxide dismutases (SODs), catalyzing the dismutation of superoxide radicals to hydrogen peroxide, was believed to be one of the most important anti-oxidant metallo-enzymes protecting cells against oxidative stress arising from reactive oxygen species (ROS) produced during aerobic respiration. Manganese superoxide dismutase (MnSOD) was one of these enzymes and located in mitochondria. Akashi, Watanabe, and Park (2005) examined the effect of ginsan on the MnSOD activity in neutrophils from human peripheral blood *in vitro*. The findings suggested that ginsan activated MnSOD through the autocrine mechanism, involving the production of TNF-α in neutrophils. On the other hand, the extracellular signal-related protein kinase (ERK) pathway was also involved in the activation of MnSOD by ginsan in neutrophils. Therefore activation of MnSOD might be one of the important mechanisms responsible for biological activities of ginsan in neutrophils.

Many studies indicated that irradiation resulted in emergency of reactive oxygen species (ROS), which induced radiation damage of the cell as an important factor. Han, Song, et al. (2005) and Han, Son, et al. (2005) evaluated the effects of ginsan on the γ-radiation induced alterations of some antioxidant systems in the spleen of Balb/c mice. The combination of irradiation with ginsan effectively increased the SODs and glutathione peroxidase (GPx) transcription, as well as their protein expressions and enzyme activities. In addition, the expression of heme oxygenase-1 and non-protein thiol induced by irradiation was restored in combination with ginsan. Evidence indicated that transforming growth factor-β and other important cytokines such as IL-1, TNF and IFN-γ might be associated with evoking the antioxidant enzymes. In conclusion, the radioprotective action of ginsan in irradiated mice was partly contributed to rapid regeneration of hematopoietic cells and also due to the modulation of antioxidant enzymes. Therefore it was expected to be applied as a therapeutic remedy for various ROS-related diseases.

3.5. Anti-ulcer activity

Sun, Matsumoto, and Yamada (1992a) compared the anti-ulcer activity of water-soluble and alkaline-soluble crude polysaccharides from the roots or leaves of *P. ginseng*. The water-soluble polysaccharide fractions (GL-2, GL-4 and GL-4IIb$_1$IIII) from the leaves had a more potent activity to prevent HCl/ethanol-induced ulcerogenesis in mice than GRA-2 from the roots, and showed the most potent inhibition of gastric lesion formation. However in their early work (Sun, Matsumoto, Kiyohara, Hirano, & Yamada, 1991), they reported an acidic polysaccharide fraction (GRA-4), purified from GRA-2, inhibited gastric lesions induced by HCl/ethanol or absolute ethanol in a dose-dependent manner when administered from 50 to 200 mg l kg orally. The activity of these polysaccharides from the leaves and GRA-4 decreased after treatment with periodate or digestion with endo-polygalacturonase, indicating that the carbohydrate moiety may contribute to the expression of the activity. In their subsequent work, the effects of GL-4 on various experimental gastric ulcer models in mice and rats had been investigated (Sun, Matsumoto, & Yamada, 1992b). Both oral administration of GL-4 at doses of 50–200 mg/kg and subcutaneous administration of GL-4 (50–100 mg/kg) inhibited the formation of the gastric lesions induced by necrotizing agents such as HCl/ethanol and ethanol in a dose-dependent manner. GL-4 also inhibited the formation of gastric ulcers which were induced by water immersion stress, indomethacin or pylorus-ligation. The contents of prostaglandin E2 in the gastric juice from rats were not affected by oral administration of GL-4. In addition, the protective action of GL-4 against HCl/ethanol-induced gastric lesions was immune to indomethacin. When GL-4 was administered into pylorusligated rats, both gastric acidity and pepsin activity in the gastric juice decreased significantly.

3.6. Anti-radiation activity

Ginsan was found to significantly increase the number of bone marrow cells, spleen cells, granulocyte-macrophage colony-forming cells (GM-CFC), circulating neutrophils, lymphocytes and platelets in irradiated mice. Moreover, ginsan induced the endogenous production of cytokines such as IL-1, IL-6, IL-12 and TNF-α, which are required for hematopoietic recovery (Song et al., 2003). Kim et al. (2007) also identified ginsan alter the phenotype of bone marrow cells, and increased the viability and alloreactivity of bone marrow cells after gamma radiation both *in vitro* and *in vivo*. In addition, ginsan modulates the radiation-induced disturbance of antioxidant enzymes such as superoxide dismutase (SOD), catalase and glutathione peroxidase (GPx) (Han, Song, et al., 2005; Han, Son, et al., 2005). Recently, Park, Hwang, Song, and Jee (2011) draw a conclusion that ginsan protected mice from radiation-induced damage of the small intestine via the lengthening of villi and a numerical increase of crypt cells in the small intestine at 3.5 days after 7 Gy irradiation compared to irradiated, non-treated controls. Additionally ginsan significantly decreased the amount of pro-apoptotic p53 and Bax to inhibit irradiation-induced apoptosis; on the other hand, it increased that of anti-apoptotic Bcl-2 at 24 h after irradiation. Therefore, these results indicated that ginsan might be a useful candidate radioprotective adjunct for cancer patients.

The frequency of micronucleated polychromatic erythrocytes (MNPCE) in the bone marrow of C57BL/6 male mice was assessed to evaluate the radioprotective effect of ginsan by Ivanova, Han, Son, Yun, and Song (2006). When the mice was treated with ginsan [100, 200 or 300 mg/kg body weight (b.w.)] or amifostine (200 mg/kg b.w.) 30 min before as well as 15 min after 1.5 Gy of

c-irradiation, ginsan and amifostine did not alter the frequency of MNPCE of control mice ($P > 0.05$) by themselves, showing that they are not mutagenic source; c-irradiation induced a statistically significant ($P < 0.001$) increase of MNPCE and decrease of Polychromatic erythrocytes/normochromatic erythrocytes (PCE/NCE) ratio ($P < 0.001$) compared to control group. In contrast, ginsan dose-dependently reduced MNPCE. Amifostine (200 mg/kg b.w.) did not reduce the level of MNPCE induced by radiation, but stimulated erythropoiesis. Based on the above results, radioprotective effect of ginsan can be partially attributed to reduction of radiation-induced genotoxicity.

3.7. Anti-septicaemic activity

In early years, through determination of NO production, phagocytic activity and cytokines production *in vitro*, as well as *in vivo* using C57BL/6J mice infected by *S. aureus*, an anti-septicaemic activity of a polysaccharide (PS) isolated from *P. ginseng* was evaluated by Lim et al. (2002). The production of NO and cytokines, such as TNF-α, IL-1 and IL-6, as well as the phagocytic activity increased greatly in PS-treated groups in certain concentrations compared with the untreated groups. Furthermore combination therapy with PS and vancomycin resulted in hundred percent survivals; however only 67% or 50% of the animals survived was achieved when treated with either PS or vancomycin. These results suggested that PS possessed a potent anti-septicaemic activity by stimulating macrophage to product much NO against sepsis induced by *S. aureus*.

In 2006, Ahn, Choi, et al. (2006) and Ahn, Song, Yun, Jeong, and Choi (2006) reported another potent polysaccharide (ginsan) could protect mice from lethality infected by *S. aureus* in a dose of 25 μg/kg, and elucidated the possible antiseptic mechanism. This survival benefit was associated with enhanced bacterial clearance from circulation, spleen and kidney. The phagocytic activity of ginsan-treated macrophage was considerably enhanced against *S. aureus*. However, the production of proinflammatory cytokines, such as tumor necrosis factor-α interleukin (IL)-1β, IL-6, IFN-γ, IL-12, IL-18 and interferon γ, was markedly down-regulated at the early phase of sepsis in mice that were treated with ginsan before the bacterial challenge. In addition, the expression of Toll-like receptors (TLRs) and the adaptor molecule MyD88, which was greatly increased in septic macrophages, was considerably reduced by ginsan treatment *in vitro* before a subsequent contact with S. aureus. Similarly, the expression of phospho-JNK1/2, phospho-p38 MAPK, and NF-κB was decreased in the same culture system. These data illustrated that the antiseptic activity of ginsan against *S. aureus* can be attributed to the suppression of acute inflammatory responses at an early phase, and enhanced bacterial clearance at subsequent phases of infection.

3.8. Hepatoprotective activity

Song et al. (2004) analyzed the effects of polysaccharide ginsan from *P. ginseng* on liver function. The data showed that ginsan treatment did not seem to cause hepatic injury, since serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) activities as well as levels of total bilirubin and albumin were not changed.

In order to make a good recognition for ginsan as a hepatoprotective formulations as well as combined application with other drugs, ginsan on carbon tetrachloride (CCl_4)-induced liver injury was examined in their next research (Shim et al., 2010). BALB/c mice were injected intraperitoneal (i.p.) with ginsan 24 h prior to CCl_4 administration. Serum liver enzyme levels, histology, expression of antioxidant enzymes, and several cytokines/chemokines were subsequently estimated. The results suggested that ginsan effectively prevented liver injury, mainly through downregulation of oxidative stress and inflammatory response.

3.9. Antiasthmatic activity, antidepressant activity, qi-invigorating and anti-fatigue activity and antiviral activity

Asthma is recognized as a major medical problem worldwide, and one of four stubborn diseases by the World Health Organization. Asthma treatment by corticosteroid frequently induced many side effects. For the purpose of finding a safe and high efficacy substitute, Lim et al. (2009) evaluated the effect of ginsan against allergic reaction in an ovalbumin (OVA)-induced murine asthmatic model in comparison with dexamethasone, and investigated its underlying mechanism. To elucidate the mechanism of ginsan, expression of inflammation-related genes were screened. Interestingly, ginsan treatment upregulated cyclooxygenase (COX)-1 and COX-2 mRNA, and expression of their proteins in the lung were also increased. To sum up, ginsan had antiasthmatic effects, which seem to be partially mediated by enhancing the synthesis of COX gene products.

Unlike other previous studies, Wang, Flaisher-Grinberg, et al. (2010) and Wang, Li, et al. (2010) demonstrated that one acidic polysaccharide (WGPA) from *P. ginseng*, which containing arabinogalactan, RG-I and HG-rich pectins, has antidepressant activity. The utilization of different ginseng preparations in different studies might be one of many reasons resulting in this contrasting result. Mice were tested for spontaneous activity, social interactions, anxiety-like behavior in the elevated plus-maze (EPM) and despair-like behavior in the forced swim test (FST). WGPA did not work on spontaneous activity or behavior in the EPM. However, WGPA significantly reduced immobility time in the FST at dose of 100 mg/kg (but not the 200 mg/kg) and both doses significantly increased social interactions and decreased aggressive behaviors in mice. These results suggested that long-term WGPA use might have antidepressant-like effects that was unrelated to generalized behavioral changes.

The roots of *P. ginseng* had long been used as a drug for reinforcing vital energy of the weak, which could be attributed to its invigorating qi, enriching the blood and anti-fatigue activity. Li, Chen, Jin, and Chen (2009) investigated the effects of *P. ginseng* polysaccharide (PGP) on energy metabolism and mitochondrial protection. The result showed that PGP could inhibit mitochondrial injury and swelling induced by Fe^{2+}–L-Cys in a concentration-dependent manner. PGP could inhibit the formation of lipid peroxidation product malondialdehyde (MDA) in mice brain, and increased levels of adenosine triphosphate (ATP), adenosine diphosphate (ADP), total adenylate pool (TAP) and adenylate energy charge (AEC), as well as ratio of ATP/ADP and ATP/AMP in liver cells and increased creatine kinase (CK) activities in mice skeletal muscle under chronic hypoxia condition. In view of this we can concluded that PGP protect mitochondria by inhibiting mitochondrial swelling, and improving energy metabolism. In a word, PGP had the pharmaceutical activities of antihypoxia, antioxidation and improving energy status. Wang, Flaisher-Grinberg, et al. (2010) and Wang, Li, et al. (2010) firstly evaluated the anti-fatigue activity of the crude ginseng polysaccharides (WGP) in an animal test for fatigue, and compared the activities between neutral (WGPN) and acidic (WGPA) portions. Anti-fatigue activity was assessed using the forced swim test (FST) and serum biochemical parameters were determined by autoanalyzer and commercially available kits. The results indicated all three compounds have anti-fatigue activity, which was also identified by the FST-induced reduction in glucose (GLU) and glutathione peroxidase (GPx) and increase in creatine phosphokinase (CK), lactic dehydrogenase (LDH) and malondialdehyde (MDA) levels, all indicators of fatigue. Particularly the acidic polysaccharide was more potent than the neutral polysaccharide.

Rotavirus infection can cause severe diarrhea. Two pectic polysaccharides, named as GP50-dHR (56.0 kDa) and GP50-eHR (77.0 kDa), were evaluated the antivirus effect *in vitro* model of rotavirus infection. Both polysaccharides rescued cell viability from rotavirus infection in a dose-dependent manner, with IC_{50} of 15 μg/mL (GP50-dHR) and 10 μg/mL (GP50-eHR). The homogalacturonan backbone of two polysaccharides itself did not show an antirotavirus effect, whereas the hairy regions of RG-1 as functional sites might block rotavirus attachment to cells. Therefore arabinose-rich side chains with more abundant branch points existing in GP50-eHR than GP50-dHR would lead a greater antirotavirus effect. Generally polysaccharide showed little side effect in many situations in human or animals. All these findings suggested that ginseng polysaccharides were ideal therapeutic options for rotavirus diarrhea.

4. Concluding remarks

To the best of our knowledge, the chemical constituent research of ginseng has being done for a hundred years of history. The ginsenoside had been recognized as one of the active ingredients. But ginsenoside could not fully represent all the active components of ginseng, and fully elucidated the pharmacological effects of ginseng and clinical efficacy. It is worth noting that ginseng is used in its entirety rather than only by ginsenosides, which conformed to the concept of wholism of traditional Chinese medicine. With modern science and technology, the chemical composition and pharmacological activities of ginsenosides had been elucidated generally. In recent years, with the aim at fully elucidating the medicinal mechanism of ginseng, many scholars had focused on studies of the essential oil, polysaccharides, peptides and other chemical constituents of ginseng in addition to the in-depth pharmacological and chemical research of ginseng saponin monomer. Moreover the chemical and pharmacological aspects of ginseng stem, leave, reed head, bud and fruit were studied and compared. Although most of research was based on ginsenosides, from recent information we can see the medicinal value of polysaccharides was going to be opened to all. The identification of polysaccharide from the leaves, roots and fruits of *P. ginseng* with biological activity might also provide an opportunity to develop a new way to expand the utilization of ginseng. On the basis of detailed information as presented in this review on the phytochemistry and biological properties of ginseng polysaccharides, we assured that this might help us to carry out deeper research on this plant for the use in medicine.

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