

Review

Chemical constituents and biological activities of the berry of *Panax ginseng*

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Panax ginseng C. A. Meyer belongs to a member of the Araliaceae family and is a perennial plant in Korea and northern China. *P. ginseng* commonly known as Korean ginseng has a long history worldwide as an important medicinal plant. The root of ginseng is commonly used as herbal medicine. Extensive research works have been carried out chemical constituents and biological activities of the root of *P. ginseng*. However, recently some studies show that the berry of *P. ginseng* exhibits potential biological and pharmacological activities. *P. ginseng* berry has not been extensively explored and studied compared to the root of *P. ginseng*. In this review, we summarize previous and current information regarding chemical constituents and biological activities of the berry of *P. ginseng* and provide new insights for future study in this discipline.

Key words: Ginseng berry, biological activity, chemical constituent, *Panax ginseng* C. A. Meyer.

INTRODUCTION

Panax ginseng C. A. Meyer, a member of the Araliaceae family, is a slow-growing perennial plant with fleshy roots and grows in Korea and northern China. For at least 2000 years, *P. ginseng*, known as Korean ginseng, has been valued as a medicinal plant in traditional oriental medicine (Kee, 1999; Yun, 2001). The biological and pharmacological efficacy of Korean ginseng revealed by modern science includes improved brain function, adaptogenic effect, pain-relieving effects, preventive effects against tumors as well as anti-tumor activity, enhanced immune system function, anti-diabetic effects, enhanced liver function, adjusted blood pressure, anti-fatigue and anti-stress effects, improved climacteric disorder and sexual functions, as well as anti-oxidative

and anti-aging effects (Nocerino et al., 2000; Choi, 2008; Jia and Zhao, 2009; Jia et al., 2009).

Since the beginning of the 20th century, the constituents of ginseng root have been investigated and several classes of compounds have been isolated such as triterpene saponins; essential oil-containing polyacetylenes and sesquiterpenes; polysaccharides; peptidoglycans; nitrogen-containing compounds; and various ubiquitous compounds such as fatty acids, carbohydrates, and phenolic compounds (Tang et al., 1992). Ginseng contains an extraordinarily complex mixture of chemical constituents that can vary with the species used, the place of origin, and the growing conditions. Although different ginseng species may be used slightly differently in traditional medicines, all species contain ginsenosides as active components and most of the pharmacological activity of ginseng can be attributed to these compounds. Ginsenosides are specific types of triterpene saponin, a broad group of chemical

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compounds. Ginsenosides are found nearly exclusively in Panax species (ginseng) and up to now more than 150 naturally occurring ginsenosides have been isolated from different organs of ginseng (Christensen et al., 2008). Approximately 40 ginsenoside compounds have been identified in Korean ginseng (*P. ginseng*). Ginsenosides appear to be responsible for most of the activities of ginseng including anticarcinogenic, immunomodulatory, anti-inflammatory, anti-allergic, anti-atherosclerotic, anti-hypertensive, and anti-diabetic effects as well as antistress activity and effects on the central nervous system (Lu et al., 2009). Ginsenosides are classified into two groups by the skeleton of their aglycones (Figure 1): the glycosides of 20(S)-protopanaxadiol (20[S]-dammar-24-ene-3b, 12b, 20- triol) (Rb1, Rb2, Rc, Rd, Rg3 and Rh2) and those of 20(S)-protopanaxatriol (6a-hydroxy-20[S]-protopanaxadiol) (Re, Rf, Rg1, Rg2, Rh1 and R1) (Attele et al., 1999; Awang, 2000).

Ginsenosides are distributed in many parts of the ginseng plant, including the root, leaf, and berry. Different parts of the plant contain distinct ginsenoside profiles (Attele et al., 1999), and these parts may have different pharmacological activities. The root of ginseng is a commonly used herbal medicine. However, recently some studies show that the berry of *P. ginseng* exhibits significantly more potent pharmacological activities than the root. *P. ginseng* berry has not been extensively explored and studied compared to the root of *P. ginseng* (Attele et al., 2002; Wang et al., 2007). This review presents previous and current information regarding chemical constituents and biological activities of the berry of *P. ginseng* and provides new insights for future study in *P. ginseng* berry.

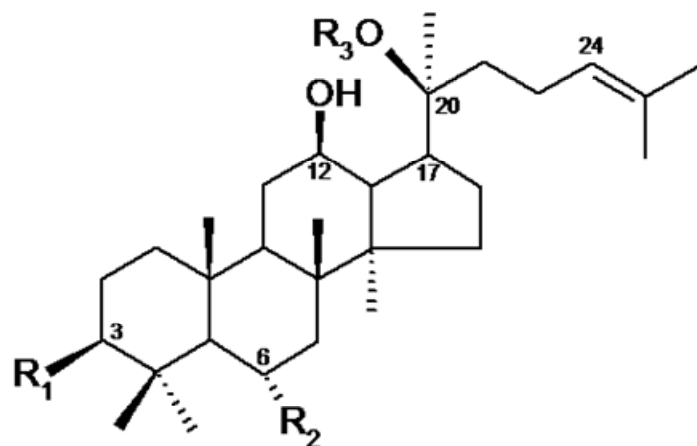
Chemical constituents of *p. ginseng* berry

The chemical constituents of *P. ginseng* berry have been investigated and several classes of primary and secondary metabolites have been isolated. Liu et al. (1988) isolated the water soluble polysaccharide from *P. ginseng* berry. Kuo et al. (2003) analyzed free amino acid contents from the seeds of *P. ginseng*. The neuro-excitatory beta-ODAP (beta-N-oxalyl-L-alpha,beta-diaminopropionic acid) was the major component in the seed extract (70% of the total free amino acids detected) and showed the highest concentration (0.43% by wt) compared to that in the different parts of young ginseng plants. Another neuro-active non-protein amino acid, GABA (gamma-aminobutyric acid), increased dramatically after germination and reached highest concentration in different parts of 3 year-old ginseng plants. Wang et al. (2006) isolated a new indole alkaloid, ginsenine, with a seven-membered lactam unit from the berry of *P. ginseng*. Its structure was established on the basis of extensive NMR (1H- and 13C-NMR, 1H-1H COSY, DEPT, HMQC, and HMBC), IR, and ESI-MS

analysis.

Some reports show that the isolation and identification of ginsenosides and triterpene saponins from berry of *P. ginseng*. Zhao et al. (1991) isolated and identified 20(R)-ginsenoside-Rh2 (an anti-cancer constituent) from the *P. ginseng* berry. Four compounds were isolated from the fruit of cultivated *P. ginseng* and identified as beta-sitosterol, 20(R)-protopanaxatriol, daucosterine and 20(R)-ginsenoside-Rg3 on the basis of physicochemical constants and spectral evidences by Zhao et al. (1993). Wang et al. (2004) isolated a new dammarane-type triterpene monoglucoside, named isoginsenoside-Rh(3) from the fruits of *P. ginseng*, together with eight known analogs, ginsenoside-Rb(1), -Rb(2), -Rc, -Rd, -Re, -Rg(1), -Rh(1), -Rh(2). On the basis of chemical and physicochemical evidence, the structure of isoginsenoside-Rh(3) has been elucidated as 3-O-beta--glucopyranosyl-dammarane-(E)-20(22),24-diene-3beta,12beta-diol. Wang et al. (2007) isolated eleven saponins from *P. ginseng* fruits and purified by use of D (101) resin and ordinary and reverse-phase silica gel column chromatography. Their chemical structures were elucidated on the basis of physicochemical constants and NMR spectra. The 11 compounds were identified as 20(R)-dammarane-3beta,12beta,20,25-tetrol (25-OH-PPD); 20(R)-dammarane-3beta,6alpha,12beta,20,25-pentol (25-OH-PPT); 20(S)-protopanaxadiol (PPD); daucosterine, 20(S)-ginsenoside-Rh(2) (Rh(2)); 20(S)-ginsenoside-Rg(3) (Rg(3)); 20(S)-ginsenoside-Rg(2) (Rg(2)); 20(S)-ginsenoside-Rg(1) (Rg(1)); 20(S)-ginsenoside-Rd (Rd); 20(S)-ginsenoside-Re (Re); and 20(S)-ginsenoside-Rb(1) (Rb(1)). Sugimoto et al. (2009) isolated a new dammarane-type triterpene ketone, panaxadione from the seeds of *P. ginseng* together with two dammarane-type and lupane-type triterpenes, an aromatic oligoglycoside, three sterol glycosides, and three dammarane-type triterpene oligoglycosides (ginsenosides Rd, Re, and Rg(2)).

Kim et al. (2009) investigated the ginsenoside content of berries and roots of three cultivars of Korean ginseng. The three typical ginseng cultivars in Korea are distinguished by berry color. The Gumpoong cultivar has yellow berries, the Chunpoong cultivar has orange berries, and the Yunpoong cultivar has red berries (Figure 2). For all cultivars, ginsenoside Re was the most abundant ginsenoside in roots and berries. However, berries produced more total ginsenosides, and berry ginsenoside profile differed from that of roots. The ginsenoside Re content of berries was 4-6 times more than that of roots. Averaged across all cultivars, the amounts of the five ginsenosides in berries was Re > Rc ≈ Rg1 ≈ Rb1 ≈ Rd. For roots, the amounts were Re > Rg1 > Rb1 > Rc > Rd. Roots of the Yunpoong cultivar had the greatest ginsenoside content, followed by roots of the Chunpoong cultivar and the Gumpoong cultivar. The total amount of ginsenosides (especially Rb1, Re, and Rg1) was greatest in the Yunpoong cultivar.



Ginsenosides	R1	R2	R3
20(s)-Protopanaxadiol			
Rb1	-O-Glc ² -Glc	-H	-Glc ⁶ -Glc
Rb2	-O-Glc ² -Glc	-H	-Glc ⁶ -Ara(p)
Rc	-O-Glc ² -Glc	-H	-Glc ⁶ -ARa(f)
Rd	-O-Glc ² -Glc	-H	-Glc
Rg3	-O-Glc ² -Glc	-H	-H
Rh2	O-Glc	-H	-H
20(s)-Protopanaxatriol			
Re	-OH	-O-Glc ² -Rha	-Glc
Rf	-OH	-O-Glc ² -Glc	-H
Rg1	-OH	-O-Glc	-Glc
Rg2	-OH	-O-Glc ² -Rha	-H
Rh1	-OH	-O-Glc	-H

Glc: Glucose. Ara (p): Arabinose in pyranose form. Ara (f): Arabinose in furanose form. Rha: Rhamnose. H: Hydrogen.

Figure 1. Chemical structure of ginsenosides.

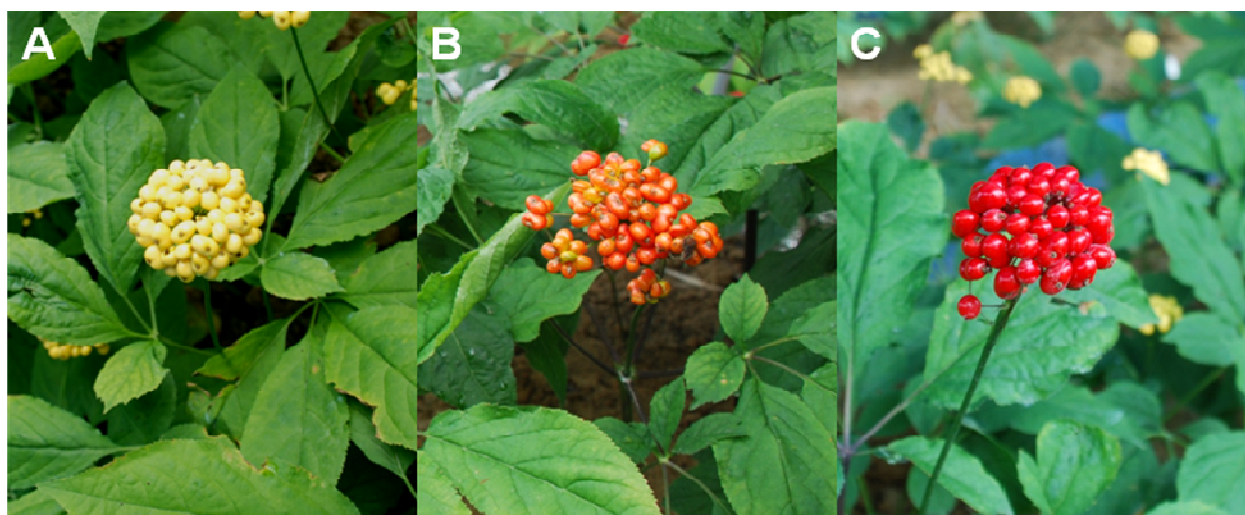


Figure 2. Three typical cultivars of *Panax ginseng* in Korea; the Gumpoong cultivar has yellow berries (A), the Chunpoong cultivar has orange berries (B), and the Yunpoong cultivar has red berries (C).

Biological activities of *P. ginseng* berry

Most studies of biological activities in Korean ginseng have used root part. Some studies show that the berry of *P. ginseng* exhibits biological and pharmacological activities more than the root. However, the biological and pharmacological activities in Korean ginseng berry have not been extensively studied. Early studies reported Antisenility action of saponin in *P. ginseng* fruit (Huo, 1984), therapeutic and preventive effects of saponin of ginseng fruit on experimental gastric ulcers (Zhang et al., 1984), treatment of systemic lupus erythematosus with saponin of ginseng fruit for an immunological study (Yang et al., 1986), and anti-stress effect of saponins extracted from *P. ginseng* fruit (Zhang et al., 1991).

In 2002, Dr. Chun-Su Yuan's research group in University of Chicago reported those anti-diabetic and anti-obese effects of *P. ginseng* berry extract and the identification of an effective component. They evaluated antihyperglycemic and anti-obese effects of *P. ginseng* berry extract and its major constituent, ginsenoside Re, in obese diabetic C57BL/6J ob/ob mice and their lean littermates. They show that the extract of *P. ginseng* berry completely normalized blood glucose levels, improved sensitivity to insulin, lowered cholesterol levels, and decreased weight by reducing appetite and increasing activity levels in obese diabetic mice. Additional studies demonstrated that ginsenoside Re plays a significant role in antihyperglycemic action. This antidiabetic effect of ginsenoside Re was not associated with body weight changes, suggesting that other constituents in the extract have distinct pharmacological mechanisms on energy metabolism (Attele et al., 2002). They also observed anti-diabetic and anti-obesity effects of *P. ginseng* berry in adult C57BL/Ks db/db mice and their lean littermates. These data suggest that *P. ginseng* berry extract may have therapeutic value in treating diabetic and obese patients (Xie et al., 2002). They made a comparison between intraperitoneal and oral administrations of ginseng berry extract for anti-diabetic and anti-obese effects (Dey et al., 2002). In 2003, they compared anti-hyperglycemic effect between *P. ginseng* root and *P. ginseng* berry in ob/ob mice. Their results suggest that, compared to ginseng root, ginseng berry exhibits more potent anti-hyperglycemic activity, and only ginseng berry shows marked anti-obesity effects in ob/ob mice (Dey et al., 2003; Xie et al., 2005). They reviewed the research on the anti-diabetic effects of ginseng and the possible mechanisms of its anti-diabetic actions (Xie et al., 2005). Another research group (Luo et al., 2005) also observed the effect of ginseng fruit saponins on insulin sensitivity index in high fat-fed rats and demonstrated that ginseng fruit saponins can improve experimental insulin resistance in rats. Yin et al. (2008) reviewed traditional Chinese medicine in treatment of metabolic syndrome. They demonstrated the traditional Chinese medicine (TCM) is an excellent representative in

alternative and complementary medicines with a complete theory system and substantial herb remedies for the management of metabolic syndrome. Ginseng extracts made from different organs (root, rootlet, berry and leaf) of *P. quinquefolium* (American ginseng) and *P. ginseng* (Asian ginseng), are proved for anti-hyperglycemia, insulin sensitization, islet protection, anti-obesity and anti-oxidation in many model systems.

Energy expenditure is enhanced by ginseng through thermogenesis. Ginseng-specific saponin (ginsenosides) are considered as the major bioactive compounds for the metabolic activities of ginseng.

Wang et al. (2007) studied *In vitro* anti-cancer activity and structure-activity relationships of natural products isolated from fruits of *P. ginseng*. They extracted and purified eleven saponins from *P. ginseng* fruits and compounds were then evaluated for the evaluation for SAR (structure-activity relationships) with their *in vitro* cytotoxicity against several human cancer cell lines. The results suggest that the type of dammarane, the number of sugar moieties, and differences in the substituent groups affect their anti-cancer activity. They demonstrated that this information may be useful for evaluating the structure/function relationship of other ginsenosides and their aglycones and for development of novel anticancer agents. Lei et al. (2008) studied the effects of extracts from *P. notoginseng* and *P. ginseng* fruit on the proliferation and migration of human umbilical vein endothelial cells *in vitro*. They found EPN and EPGF can promote vascular endothelial cells proliferation, migration, DNA synthesis and vascular endothelial growth factor mRNA expression. Their results suggest that extracts from ginseng fruit have a certain effect on the genesis and development of new vessels in the ischemic myocardium.

CONCLUSION

The chemical constituent and biological effects of Korean ginseng berry have been investigated. Korean ginseng berry can be harvested before harvesting the root as a by product as it has valuable pharmaceuticals quality. As we know the importance of several ginsenosides for its medicinal value which can easily be collected from the berry of Korean ginseng without hampering the yield of ginseng root. Most of research was based on the root of ginseng but from recent information the medicinal value of berry is going to be opened to all. The identification of compounds from Korean ginseng berry with antihyperglycemic activity may also provide an opportunity to develop a new class of antidiabetic agent. Certain ginsenosides, such as ginsenoside Re, have also been suggested to have pharmaceutical potential as a new class of drugs for diabetes treatment (Attele et al., 2002). The purpose of this review to collect all the possible information regarding the chemical constituents

and biological effects of Korean ginseng berry thus will help to the students and scientists to take action for future study in this discipline.

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