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Ginsenoside content and variation among and within American ginseng (*Panax quinquefolius* L.) populations

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Abstract

The contents of five ginsenosides (Rg1, Re, Rb1, Rc and Rd) were measured in American ginseng roots collected from 10 populations grown in Maryland. Ginsenoside contents and compositions varied significantly among populations and protopanaxatriol (Rg1 and Re) ginsenosides were inversely correlated within root samples and among populations. The most abundant ginsenoside within a root and by population was either Rg1 or Re, followed by Rb1. Ginseng populations surveyed grouped into two chemotypes based on the relative compositions of Rg1 and Re. Four populations, including the control population in which plants were grown from TN and WI seed sources, contained roots with the recognized chemotype for American ginseng of low Rg1 composition relative to Re. The remaining 6 populations possessed roots with a distinctive chemotype of high relative Rg1 to Re compositions. Chemotype did not vary by production type (wild versus cultivated) and roots within a population rarely exhibited chemotypes different from the overall population chemotype. These results provide support for recent evidence that relative Rg1 to Re ginsenoside contents in American ginseng roots vary by region and that these differences are likely influenced more by genotype than environmental factors. Because the physiological and medicinal effects of different ginsenosides differ and can even be oppositional, our findings indicate the need for fingerprinting ginseng samples for regulation and recommended usage. Also, the High Rg1/Low Re chemotype discovered in MD could potentially be used therapeutically for coronary health based on recent evidence of the positive effects of Rg1 on vascular growth.

Keywords: *Panax quinquefolius*; Araliaceae; American ginseng; Saponins; Ginsenosides; Chemical variation; Rg1; Re

1. Introduction

American ginseng (*Panax quinquefolius* L.) and Asian ginseng (*Panax ginseng*) roots are among the most widely-used traditional Chinese medicines. Recently, ginseng roots and their extracts have also become popular in the US and Europe as dietary health supplements and additives to foods and beverages. Although plants of both the Asian and American species are valued for their adaptogenic properties, these species have different uses according to traditional Chinese herbal guides. Asian ginseng is considered to be stimulating and invigorate yang, whereas American ginseng is considered to be calming and nourishing yin (Dharmananda, 2002). The pharmacological effects of ginseng roots have been attributed primarily to ginsenosides, which are triterpenoid saponin glycosides (dammarene-type saponins) (Fig. 1). More than 27 putative ginsenosides have been isolated from ginseng roots and are classified into two main groups: the glycosides of 20(*S*)-protopanaxadiol (20[*S*]-dammar-24-ene-3β, 12β, 20-triol) (Rb1, Rb2, Rc, Rd, Rg3 and Rh2, see Fig. 1) and those of 20(*S*)-protopanaxatriol (6α-hydroxy-20[*S*]-protopanaxadiol) (Re, Rf, Rg1, Rg2, Rh1 and R1, see Fig. 1) (Attele et al., 1999; Awang, 2000; Shibata, 2001). The main ginsenosides isolated from American ginseng (Rb1, Rc, Rd, Re and Rg1) typically account for greater than 70% of the total ginsenosides (Court et al., 1996b; Wills et al.,

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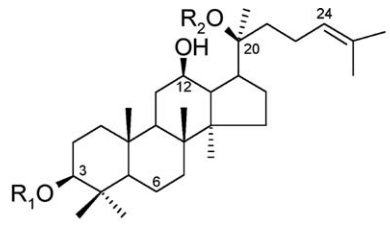
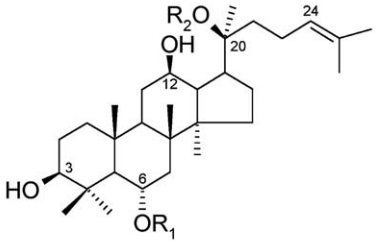
A



Ginsenoside	R_1	R_2
Rb1	-Glc^2-Glc	-Glc^6-Glc
Rb2	-Glc^2-Glc	-Glc^6-Ara(p)
Rc	-Glc^2-Glc	-Glc^6-Ara(f)
Rd	-Glc^2-Glc	-Glc
Rg3	-Glc^2-Glc	-H
Rh2	-Glc	-H

B



Ginsenoside	R_1	R_2
Re	-Glc^2-Rha	-Glc
Rf	-Glc^2-Glc	-H
Rg1	-Glc	-Glc
Rg2	-Glc^2-Rha	-H
Rh1	-H	-H

Fig. 1. Chemical structures of two major groups of ginsenosides: (A) 20(S) protopanaxadiols and (B) 20(S) protopanaxatriols. Glc, glucose; Ara(p), arabinose in pyranose form; Ara(f), arabinose in furanose form; Rha, rhamnose; H, hydrogen. Content of figure is adapted from Attele et al. (1999) and Shibata (2001).

2002; Assinewe et al., 2003). Factors found to affect ginsenoside contents of American ginseng roots include age (Court et al., 1996a; Smith et al., 1996; Wills et al., 2002; Lim et al., 2005), root dry weight (Wills et al., 2002), soil fertility (Li and Mazza, 1999), light (Fournier et al., 2003), and population/location (Li et al., 1996; Assinewe et al., 2003; Lim et al., 2005). However, the relative rankings of the main ginsenoside constituents in cultivated American ginseng root samples have been consistent across studies with the approximate profile, Rb1 > Re > Rg1 = Rc > Rd (Court et al., 1996b; Wills et al., 2002; Assinewe et al., 2003; Wang et al., 2005).

Recent clinical and laboratory studies have verified that roots of American and Asian ginseng have contradictory effects on the vascular system (Sengupta et al., 2004) and acute glycemia (Sievenpiper et al., 2004). The different bioactivities have been experimentally linked to ginsenoside fingerprint; variation attributed to differences between species, geographical origin and/or species dependent extraction methods (Sengupta et al., 2004; Sievenpiper et al., 2004). Sengupta et al. (2004) reported that Asian ginseng had a high Rg1:Rb1 ginsenoside ratio and Rg1 was shown to promote wound healing. Conversely, American ginseng had a low Rg1:Rb1 ratio and Rb1 was shown to inhibit tumor growth. The American ginseng roots in this study (Sengupta et al., 2004) produced uniform ginsenoside profiles considered characteristic of American ginseng. However, if the differences in ginsenoside profiles between species are genetically controlled, then it is likely that the profiles would also vary within the *P. quinquefolius* species because wild American ginseng populations are often geographically isolated (Cruse-Sanders and Hamrick, 2004; Grubbs and Case, 2004). Although typically American ginseng is thought to have Rg1:Rb1 ratios of less than 1.0 (~0.15), wild roots have been reported to contain much higher levels of Rg1 (Chuang et al., 1995; Assinewe et al., 2003; Lim et al., 2005). Sievenpiper et al. (2004) reported that American ginseng from two sources differed both in Rg1 content and in its effect on glycemic indices.

Over the last three centuries, the high value and a strong export market have led to overharvesting of wild American ginseng. Although American ginseng has been cultivated since the 1880s, its market export value is considerably less than the value of wild ginseng (Beyfuss, 1999; Chamberlain and Predny, 2005). The combined effects of overharvesting, deforestation, and land development threaten the number and size of wild American ginseng populations. *P. quinquefolius* L. is listed in CITES Appendix II and its harvest and commerce are regulated by the US Fish and Wildlife Service. Although ecological and biological assessments of American ginseng populations are needed to effectively develop policies for the long term sustainability of native American ginseng, there is an information gap attributed to inadequate funding (Robbins, 2000). In addition, studies of wild ginseng populations, especially those involving roots, are limited because population sizes are typically small (McGraw et al., 2003), ginseng collectors tend not to reveal collection sites, and root sampling is destructive and poses a threat to protected native populations.

Assinewe et al. (2003) provided the first comprehensive report of ginsenoside contents of roots collected from wild populations. Roots from 10 populations growing in the US and Canada, in the northern portion of the native ginseng range, were analyzed. Like cultivated samples, Rb1 contents in these Northern wild populations were greater than the contents of either Rg1 or Re (Court et al., 1996b; Wills et al., 2002; Wang et al., 2005) and variation of the content of protopanaxatriol ginsenosides (Rg1 and Re) among roots was less than found for panaxadiol ginsenosides (Rb1, Rc and Rd) (Li et al., 1996). However, Rg1 content was higher than previously reported, such that the Rg1 and Re contents were not significantly different from each other. Lim et al. (2005) analyzed roots collected from eight wild American ginseng populations found in the Catskill