Ginseng, American

Panax quinquefolius L.

[Fam. *Araliaceae*]

Overview

Ginseng is one of the most widely used medicinal herbs with at least six species used in traditional systems of medicine. Most world production and trade of ginseng involves two species: Asian ginseng (*Panax ginseng*) and American ginseng (*P. quinquefolius*). The U.S. exports up to two million pounds of cultivated ginseng roots annually and approximately 132,000 pounds of wild ginseng, primarily to China. Wisconsin produces 97% of all U.S.-grown ginseng. American ginseng consumption in the U.S. trails far behind that of Asian ginseng and eleuthero (also called Siberian ginseng, *Eleutherococcus senticosus*). Besides being sold as a dietary supplement, American ginseng's primary use is as an ingredient in beverages. Compared to the scores of clinical trials on Asian ginseng, few clinical studies have been conducted on American ginseng. Each species of ginseng has similar but distinct chemical profiles, and therefore exhibits different pharmacological and clinical activity.

Photo © 2003 stevenfoster.com

Primary Uses

- Reduces postprandial glycemia in non diabetics and in patients with type 2 diabetes

Other Potential Uses

- Possible reduction of ventilation and increased oxygen consumption ability during submaximal exercise (based on small trial)
- Possible benefit in mental performance (proofreading) based on small trial
- In Traditional Chinese Medicine (TCM), American ginseng is used for various tonic purposes

Pharmacological Actions

ROOT POWDER: Reduced postprandial glycemia in type 2 diabetes mellitus and in nondiabetic subjects.

ROOT EXTRACT: Acted on the Fourier components of the radial artery pulse, increased respiratory endurance in exercise.

Dosage and Administration

For therapeutic effectiveness, American ginseng is probably optimally used continuously over an extended period of time, although published clinical trials over 90 days are lacking.

DECOCTION: 3–6 g dried root simmered in 720–960 ml water for approximately 45 minutes; alternatively, 2–9 g simmered.

INFUSION: 150–240 ml boiling water poured over 1–2 g dried root and steeped for 20 minutes.

DRY ROOT POWDER: 3 g daily for postprandial glycemia in type 2 diabetes mellitus.

DRY EXTRACT: 330 mg, 3 times daily for improving physical endurance during work.

Contraindications

None known.

PREGNANCY AND LACTATION: None known.

Adverse Effects

None known.

Drug Interactions

None known. Diabetics may need to monitor insulin levels due to hypoglycemic action.

Clinical Review

In 6 clinical studies on American ginseng that included a total of 126 participants, all but one (ergonomic response to intense excercise) demonstrated positive effects on athletic performance, diabetes, and circulation. One double-blind, placebo-controlled (DB, PC) study and one PC, crossover (CO) study reported beneficial effects of an American ginseng root powder on postprandial glycemia in type 2 diabetes mellitus subjects. A subsequent randomized, PC, crossover study revealed that powdered American ginseng reduced postprandial glycemia in healthy individuals. Improved athletic performance was the focus of two small PC studies; one study showed no positive effect, and the other resulted in reduced ventilation requirements and increased ability to consume oxygen in submaximal exercise. One small comparative, PC study examined the effects of ginseng on psychomotor skills and found Asian and American ginseng to have equal effects on improving proofreading, error-detection, and mood-fatigue.

Ginseng, American

Panax quinquefolius L.
[Fam. *Araliaceae*]

Overview

Medicinal use of Asian ginseng (*Panax ginseng*) dates back at least 5,000 years in Asia. American ginseng is produced in North America from a plant that has similar but different chemistry and slightly different biological activity. In the U.S., it is used in a wide range of tonic, energy, and immune-stimulating dietary supplements.

Uses

Promotes blood sugar metabolism in healthy people and persons with type 2 (non-insulin dependent) diabetes.

Dosage

In general, short-term use may not be beneficial, so continued use over an extended period of time is usually recommended. However, American ginseng was shown in clinical trials to be effective in lowering blood sugar levels directly after meals in both healthy and diabetic (type 2) persons when taken during or just after the meal.

Decoction (tea): Simmer 3–6 g dried root in 720–960 ml water for approximately 45 minutes; alternatively, simmer 2 to 9 g.

Infusion (tea): Pour 150–240 ml boiling water over 1–2 g dried root and steep for 20 minutes.

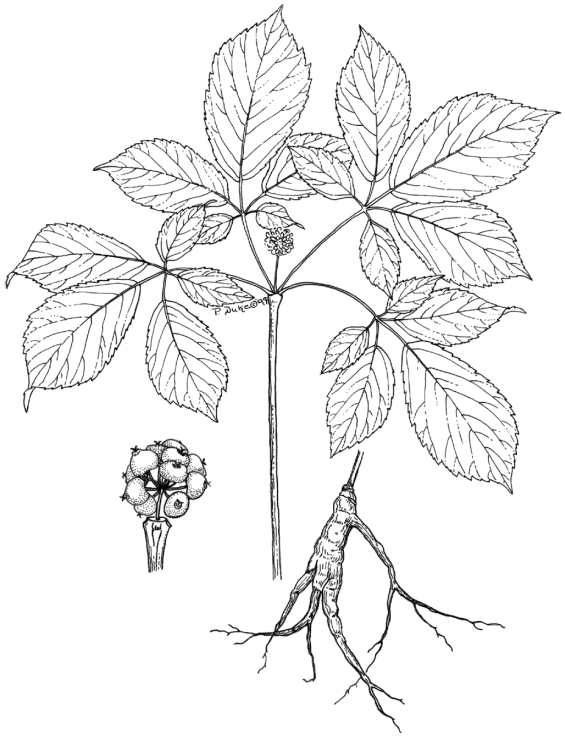
Dry root powder: 3 g daily for regulation of postprandial (after meal) glycemia (blood sugar level) in type 2 diabetes mellitus (non-insulin dependent diabetes).

Dry Extract: 330 mg, 3 times daily, for improvement of oxygen uptake during moderate exercise.

Contraindications

None known.

Pregnancy and Lactation: None known.



Adverse Effects

None known.

Drug Interactions

None known. Diabetics may need to monitor insulin levels because of the blood sugar-lowering effect.

Comments

When using a dietary supplement, purchase it from a reliable source. For best results, use the same brand of product throughout the period of use. As with all medications and dietary supplements, please inform your healthcare provider of all herbs and medications you are taking. Interactions may occur between medications and herbs or even among different herbs when taken at the same time. Treat your herbal supplement with care by taking it as directed, storing it as advised on the label, and keeping it out of the reach of children and pets. Consult your healthcare provider with any questions.

Ginseng, American

Panax quinquefolius L.
[Fam. *Araliaceae*]

Overview

Ginseng is one of the most widely used medicinal herbs with at least six species used in traditional systems of medicine. Most world production and trade of ginseng involves two species: Asian ginseng (*Panax ginseng*) and American ginseng (*P. quinquefolius*) (AAFC, 2000). According to TRAFFIC USA (the division of the World Wildlife Fund that monitors the status of threatened and endangered species), no other plant better represents the cultural and economic value of medicine harvested from the wild in North America than American ginseng (Robbins, 1997). The U.S. Department of Commerce (USDOC) measures ginseng production separately from other herbs due to its significant economic value. The U.S. exports up to two million pounds of cultivated ginseng roots annually (USDOC, 1995; USFWS, 1999a) and approximately 132,000 pounds of wild ginseng, primarily to China (Robbins, 1997; USDOC, 2000). Wisconsin produces 97% of all U.S.-grown ginseng. In 1998, Canada produced over 60% of the world supply of American ginseng (approximately four million pounds annually), the U.S. produced approximately 30%, and China produced the balance (approximately 7%). China remains the largest consumer of American ginseng (Xiao, 2000).

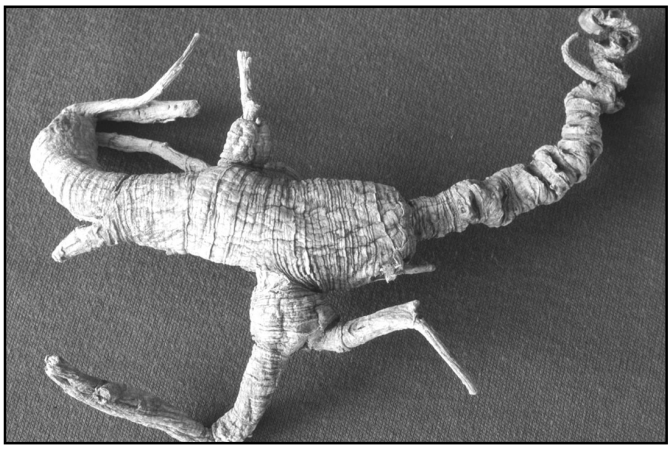


Photo © 2003 stevenfoster.com

Native to North America, American ginseng is used in traditional indigenous medicine, particularly by the Cherokee, Creek, Iroquois, Menominee, Ojibwa, Pawnee, and Seneca tribes (Foster, 1999; Heffern, 1976; Moerman, 1998). In 1718, Canadian Jesuits began organizing the collection of American ginseng from the wild for export to China (Rafinesque, 1830), where in 1765, during the Qing dynasty, it was added to the *Supplement to the Grand Materia Medica* (a.k.a., *Omissions from Ben Cao Gang Mu*), by Zhao Xuemin (Bensky *et al.,* 1986; Foster and Chongxi, 1992). American ginseng (*xi yang shen*) has since become integrated into Traditional Chinese Medicine (TCM) with indications for use distinctly different from those of Asian ginseng (*ren shen*) (Awang, 1998; Xiao, 2000). American ginseng became official in the *United States Pharmacopeia* (USP) in 1842. It was removed from the USP in 1882, but its popular use by American Eclectic medical doctors and homeopaths continued (Felter and Lloyd, 1898; Foster, 1999; HPUS, 1992; Millspaugh, 1892; Scudder, 1891). Its primary use was as a stomach tonic, though it was also used for nervous exhaustion from overwork (Felter and Lloyd, 1898; Scudder, 1891). By the late 19th century, American ginseng was already a threatened species due to overcollecting, and extensive cultivation efforts began (Millspaugh, 1892; USFWS, 1977; Wood *et al.*, 1926). In 1947, the cultivation of American ginseng also began in China, but did not become large-scale until 1980 (AAFC, 1998; Xiao, 2000). American ginseng consumption in the U.S. trails far behind that of Asian ginseng and eleuthero (previously called Siberian ginseng, *Eleutherococcus senticosus*). Besides being sold as a dietary supplement, American ginseng's primary use is as an ingredient in beverages. Compared to the scores of clinical trials on Asian ginseng, few clinical studies have been conducted on American ginseng (see table below). Each species of ginseng has similar but distinct chemical profiles, and therefore exhibits different pharmacological and clinical activity.

Description

American ginseng root consists of the mature, dried, (usually) cultivated root of *Panax quinquefolius* L. [Fam. *Araliaceae*], harvested in the fall, separated from rhizomes, dried at low temperature, and containing no less than 1.0% of ginsenoside Rb1 as determined by HPLC (PPRC, 2000). American ginseng is harvested usually after a minimum of five years growth, although many roots cultivated in North America are harvested after four years. The highest-quality dried roots break with a somewhat soft and waxy fracture, while immature or undersized roots dry hard and glassy (USDA, 1978). Plant maturity can be determined before harvesting using two methods: counting the number of leaves (a.k.a., prongs) and/or removing soil where the stem joins the root to count the number of bud scale scars on the root. A single scar is produced every autumn after the plant's stem falls (USFWS, 1999b). In December 1998, China issued quality control standards for American ginseng and its products entitled *Grade and Quality Standards of Products of Processed American Ginseng* (State Standard of People's Republic of China, 1998).

Primary Uses

Endocrinology

- Reduces postprandial glycemia in non-diabetics and type 2 diabetes patients (Vuksan *et al.,* 2001, 2000a, 2000b)

Other Potential Uses

Sports Medicine

- May improve cardio-respiratory endurance during submaximal work (reduced ventilation and increased oxygen consumption ability) (Goode *et al.*, 1993)

Cognition

- May improve mood-fatigue, may improve proofreading error detection (Johnson *et al.,* 1980)

Traditional Chinese Medicine (TCM)

- Deficiency of *qi* (diminished function of the internal organs and lowered body resistance); deficiency of *yin* (lack of body fluid, vital essence and blood, often resulting in endogenous heat); *internal-heat* (heat syndrome typically manifested by fever, night sweating, thirst, and constipation); cough and asthma; phlegm mixed with the blood; dysphoria and tiredness; diabetes; dry mouth and throat (PPRC, 2000). (These are terms and concepts used in TCM and may not always be correlated easily to Western biomedical terminology.)

Dosage

Internal

Crude Preparations

DECOCTION: 3–6 g dried root simmered in 720–960 ml water for approximately 45 minutes (PPRC, 2000; Yen, 1992). Other sources recommend simmering 2–9 g (Bensky *et al.*, 1986; Foster and Chongxi, 1992).

INFUSION: 150–240 ml boiling water poured over 1–2 g cut, dried root and steeped for 20 minutes (Xiao-fan and Liscum, 1996).

ROOT POWDER (DRY): 1–3 g in capsules 40 minutes prior to meal for normalization of blood sugar in postprandial glycemia with or after meal (Vuksan *et al.,* 2001).

WHOLE ROOT POWDER: 3 g daily for postprandial glycemia in type 2 diabetes mellitus (Vuksan *et al.*, 2000a).

DRY EXTRACT: 330 mg, 3 times daily for improving physical endurance during work (Goode *et al.*, 1993).

Duration of Administration

According to previous Eclectic medical use, American ginseng does not have an immediate effect and short-term use provides little benefit. Thus, continued use over an extended period of time is usually recommended (Felter and Lloyd, 1898). However, recent clinical trials have demonstrated an almost immediate effect in blood sugar metabolism when taken before meals (Vuksan *et al.,* 2001, 2000a).

Chemistry

American ginseng has a chemical profile distinct from that of Asian ginseng. Its concentration of ginsenosides varies considerably depending on root age, month of harvest, method of drying, and method of analysis (Court *et al.*, 1996; Reynolds, 1998). Studies identified 3.0–7.3% dammarane-type triterpene glycosides (saponins) including 1.22–1.6% ginsenoside Rb1, 0.02–0.27% ginsenoside Rb2, 0.18–0.29% ginsenoside Rc, 0.09–0.8% ginsenoside Rd, 0.9–1.1% ginsenoside Re, 0.12–0.2% ginsenoside Rg1; oleanolic acid derived ginsenoside: 0.1–0.25% ginsenoside Ro (Chuang *et al.*, 1995; Li *et al.*, 1996; Yen, 1992); 0.78% malonyl (m) ginsenosdes: 0.78% m-Rb1, 0.20% m-Rb2, 0.24% m-Rc, 0.14% m-Rd (Ren and Chen, 1999); dammarane-type triterpene oligoglycosides: quinquenosides I, II, III, IV, V (Yoshikawa *et al.*, 1998); acetylenic alcohols: panaxynol, falcarindiol, panaxydol, and panaxytriol (Wang *et al.*, 2000); a homodimeric protein quinqueginsin (Wang and Ng, 2000); and 0.04–0.97% volatile oil (Zheng *et al.*, 1989).

Due to the potential adulteration of American ginseng with Asian ginseng in the marketplace, methods have been developed to differentiate the two species. For example, 24(R)-pseudo-ginsenoside-F11 is a characteristic constituent of American ginseng but occurs only in minute quantities in Asian ginseng, whereas ginsenoside-Rf is the characteristic constituent of Asian ginseng that is lacking in American ginseng (Chan *et al.*, 2000; Dou *et al.*, 1998; Shaw and But, 1995; Wenkui *et al.*, 2000). Malonyl ginsenosides are found at much lower levels in Asian ginseng, at 10% total ginsenoside content compared to 40% total ginsenoside content in American ginseng (Awang, 2000). Thorough reviews of ginseng chemistry have been or will soon be published (Court, 2000; Chen *et al.,* 2003).

Pharmacological Actions

Human

American ginseng whole root powder reduced postprandial glycemia in type 2 diabetes mellitus and in nondiabetic subjects (Vuksan *et al.*, 2000a; 2000b). American ginseng root powder reduced glycemia in healthy individuals (Vuksan *et al.,* 2001). American ginseng total extract demonstrated specific effect on the Fourier components of the radial artery pulse, confirming TCM descriptions (Wang *et al.*, 1994), and increased respiratory endurance in exercise (Goode *et al.*, 1993).

Traditional Chinese Medicine (TCM) Actions

Dispel *wind* (exogenous pathogenic factor with symptoms such as upper respiratory catarrh with headache and urticaria) and remove *heat* (symptoms such as fever, flushed face, thirst); relieve cough and resolve *phlegm* (secretions of the respiratory system) (PPRC, 2000).

Animal

American ginseng root stimulated copulatory behavior in male rats (Murphy *et al.*, 1998); aqueous extract possessed significant gastricmodulating effect on brain neuronal activity in rats (Yuan *et al.*, 1998a, 1998b); methanolic American ginseng extract exhibited liver-protective effect against D-galactosamine- and lipopolysaccharide-induced injury in mice (Yoshikawa *et al.*, 1998); aqueous American ginseng extract significantly exhibited hypoglycemic activity in mice (Oshima *et al.*, 1987); inhibitory effect on the cerebral cortex and moderately stimulates subcortical centers (Bensky *et al.*, 1986); saponin extract decreased plasma glucose levels in resting rats (Martinez and Staba, 1984). Research on fractions and isolated constituents have been conducted, yielding results which may or may not be consistent with studies on whole American ginseng extracts: isolated saponins significantly elevated total and maximum heat production and improved cold tolerance in rats (Wang and Lee, 2000); pseudo-ginsenoside-F11 antagonized scopolamine-induced memory impairment in mice and rats (Li *et al.*, 1999); ginsenoside Rb1 prevented scopolamine-induced amnesia in rats (Benishin *et al.*, 1991).

In vitro

American ginseng root extract showed effective antioxidant activity in both lipid and aqueous mediums by chelation of metal ions and free radical scavenging (Kitts *et al.*, 2000); ethanolic extract showed nicotinic activity by displacement of 3H-(-)nicotine from human brain cerebral cortex membranes (Lewis *et al.*, 1999); inhibited thrombin-induced endothelin release in cultured human umbilical vein endothelial cells (Yuan *et al.*, 1999); ethyl acetate American ginseng extract inhibited nitrite production by inducible nitric oxide synthase (iNOS) (Wang *et al.*, 2000);

isolated quinqueginsin inhibited human immunodeficiency virus-1 reverse transcriptase (Wang and Ng, 2000); standardized extract and breast chemotherapeutic drugs synergistically inhibited MCF-7 breast cancer cell growth (Duda *et al.*, 1999); extract exhibited estrogenic activity in MCF-7 breast cancer cells (Duda *et al.*, 1997).

Mechanism of Action

The mechanisms of action of American ginseng are not fully understood. Some suggested mechanisms include:

Animal

- Reduced plasma prolactin levels and significantly stimulated copulatory behavior due to ginseng-induced alterations in dopaminergic neurotransmission (Murphy *et al.*, 1998). Research also suggests that American ginseng's apparent increase of the male sexual arousal response is the result of relaxing and vasodilating the corpus cavernosum, allowing greater erectile performance, which appears to occur by means of an interaction with nitric oxide synthase (Nocerino *et al.*, 2000).
- Regulated GABAergic neurotransmission (Yuan *et al.*, 1998a; Yuan *et al.,* 1998b).

In vitro

- Facilitated the release of acetylcholine (ACh) from hippocampal slices (ginsenoside Rb1, isolated from American ginseng roots and fibers), which is associated with an increased uptake of choline into nerve endings. The ability of Rb1 to prevent memory deficit in animal experiments may be related to ACh metabolism in the central nervous system (Benishin *et al.*, 1991).

Contraindications

None known.

Traditional Chinese Medicine (TCM) Contraindications

Cold-Damp Stomach (condition marked by intolerance of cold and abdominal distention) (Bensky *et al.*, 1986).

Pregnancy and Lactation: No known restrictions (McGuffin *et al.*, 1997).

Adverse Effects

None known.

Drug Interactions

None known. Insulin levels in diabetic patients may need monitoring due to American ginseng's blood sugar modulating effect.

American Herbal Products Association (AHPA) Safety Rating

Class 1: Herbs that can be safely consumed when used appropriately (McGuffin *et al.*, 1997).

Regulatory Status

Canada: Food, if no therapeutic claims are made, and New Drug if drug claims are made (HPB, 1993) except as per the Traditional Herbal Medicine (THM) Policy. Permitted as a THM, if the claim(s) are supported by traditional references, requiring premarket authorization and assignment of a Drug Identification Number (DIN) (Health Canada, 1999). Also, permitted as a homeopathic over-the-counter (OTC) drug with premarket authorization and assignment of a DIN (Health Canada, 2001).

China: Regulated as a drug, which must meet the State Standard of People's Republic of China 1998: Grade and Quality Standards of American Ginseng. American ginseng dried roots and teas are Class 3 materials (herbal pharmaceuticals). American ginseng capsules are also Class 3 drugs, but require additional premarket licenses and inspection from the Ministry of Health (AAFC, 1998; Xiao, 2000).

France: No official monograph for this species of *Panax*.

Germany: No official monograph for this species of *Panax.*

Italy: No official monograph for this species of *Panax.*

Japan: Used in traditional Kampo medicine (Rister, 1999). Before May 23, 2000, American ginseng was considered a drug; now deregulated by Japan's Ministry of Health and Welfare, and may be sold as a food product without medical efficacy claims (USDS, 2000).

Sweden: Possible Natural Remedy for self-medication requiring advance application for marketing authorization. As of January 2001, no American ginseng products have been listed in the Medical Products Agency (MPA) "Authorised Natural Remedies" (MPA, 2001). Food, if no therapeutic claims are made.

Switzerland: No official monograph for this species of *Panax.*

U.K.: Entered in *General Sales List*, Table A (internal or external use) of Schedule 1 (subject to a full product license) (GSL, 1994).

U.S.: Dietary supplement (USC, 1994). The homeopathic tincture (1X) of the fresh or dried root is an OTC Class C drug of the *Homeopathic Pharmacopoeia of the United States* (HPUS, 1992).

Clinical Review

Six studies are outlined in the following table, "Clinical Studies on American Ginseng," including a total of 126 participants. All but one of the studies (Morris *et al.*, 1996), demonstrated positive effects on diabetes, circulation, or oxygen utilization during athletic performance. One double-blind placebo-controlled (DB, PC) study and one PC crossover (CO) study reported beneficial effects of American ginseng root powder on postprandial glycemia in type 2 diabetes mellitus subjects (Vuksan *et al.*, 2000a; 2000b). A subsequent randomized, PC, CO study evaluated the effects of powdered American ginseng on postprandial glycemia in healthy individuals (Vuksan *et al.*, 2001). These subjects experienced a reduction in postprandial glycemia. Improved athletic performance was the focus of two PC studies (Goode *et al.*, 1993; Morris, 1996). One small comparison, PC study examined the effects of ginseng on psychomotor skills and found Asian and American ginseng to have equal effects on improving proofreading error-detection and mood-fatigue (Johnson *et al.*, 1980). All these studies are small and need confirmation in larger trials. The evidence on American ginseng's ability to lower postprandial blood sugar levels in both healthy individuals and type 2 diabetics in one dose is mounting but needs validation in larger, longer-term studies.

Branded Products

Chai-Na-Ta® CNT2000™ capsules: Chai-Na-Ta Corp., 5965 205A Street / Langley, BC / V3A 8C4 / Canada / Tel.: (800) 406-7668 / Fax (604) 533-8891 / www.chainata.com. One capsule, standardized to 6% genenosides, contains 500 mg of 3-year-old Ontario-grown, dried and ground American ginseng root, standardized to 6% ginsenosides.

References

AAFC. See: Agriculture and Agri-Food Canada.

Agriculture and Agri-Food Canada (AAFC). Ginseng and Nutraceuticals in China. Ottawa, ON: Agriculture and Agri-Food Canada; 1998, Sept.

Agriculture and Agri-Food Canada (AAFC). Special Crops: Canadian Ginseng Profile. Ottawa, ON: Agriculture and Agri-Food Canada; 2000; Available at: http://www.agr.ca/misb/spcrops/gin_e.html.

Awang D. The neglected ginsenosides of North American ginseng (*Panax quinquefolius* L.). *J Herbs Spices & Med Plants* 2000;7(2):103–9.

Awang D. The anti-stress potential of North American ginseng (*Panax quinquefolius* L.). *J Herbs, Spices & Med Plants* 1998;6(2):87–91.

Benishin C, Lee R, Wang L, Liu H. Effects of ginsenoside Rb1 on central cholinergic metabolism. *Pharmacology* 1991;42(4):223–9.

Bensky D, Gamble A, Kaptchuck T. *Chinese Herbal Medicine Materia Medica.* Seattle, WA: Eastland Press; 1986;518.

Chan T, But P, Cheng S, *et al*. Differentiation and authentication of *Panax ginseng*, *Panax quinquefolius*, and ginseng products by using HPLC/MS. *Annl Chem* 2000;72(6):1281–7.

Chen YJ, Wu CF, Awang DVC, *et al*. *Ginsenosides: The Chemistry, Pharmacology, and Clinical Perspectives.* 2003 [in press].

Chuang W, Wu H, Sheu S, *et al*. A comparative study on commercial samples of Ginseng Radix. *Planta Med* 1995;61:459–65.

Court W. *Ginseng: The Genus Panax*. Amsterdam: Harwood Academic Publishers; 2000.

Court W, Reynolds L, Hendel J. Influence of root age on the concentration of ginsenosides of American ginseng (*Panax quinquefolium*). *Can J Plant Sci* 1996;76:853–5.

Dou D, Hou W, Chen Y. Studies on the characteristic constituents of Chinese ginseng and American ginseng. *Planta Med* 1998;64:585–6.

Duda R, Zhong Y, Navas V, *et al*. American ginseng and breast cancer therapeutic agents synergistically inhibit MCF-7 breast cancer cell growth. *J Surg Oncol* 1999;72(4):230–9.

Duda R, Taback B, Navas V, Zhong Y, Slomovic B, Alvarez J. Comparison of estrogenicity of *Panax quinquefolium* and *Panax ginseng* in MCF-7 breast cancer cells (meeting abstract). *Proc Annu Meet Am Assoc Cancer Res* 1997;38:A756.

Felter H, Lloyd J. *King's American Dispensatory*, 18th edition, 3rd revision. Cincinnati, OH: The Ohio Valley Co.; 1898;1429–30.

Foster S. *American Ginseng Panax quinquefolius*. Austin, TX: American Botanical Council; Botanical Series No. 308;1999.

Foster S, Chongxi Y. *Herbal Emissaries: Bringing Chinese Herbs to the West*. Rochester, VT: Healing Arts Press; 1992;102–12.

General Sale List (GSL). Statutory Instrument 1994 No. 2410 – The Medicines (Products Other Than Veterinary Drugs). Amendment Order 1994. London, U.K.: Her Majesty's Stationery Office (HMSO). 1994.

Goode R, Chatha D, Baker J, *et al*. The Effects of Ginseng on Physical Performance in Human Subjects. Toronto, ON: University of Toronto Dept. of Physiology, Faculty of Medicine and School of Physical and Health Education; 1993.

GSL. See: General Sale List.

Health Canada. *Listing of Drugs Currently Regulated as New Drugs*—Revised April 1999. Ottawa, ON: Health Canada; 1999, April;11, 21–2.

Health Canada. Product Information: *Aralia quinquefolia*. In: *Drug Product Database (DPD).* Ottawa, ON: Health Canada Therapeutic Products Programme; 2001.

Health Protection Branch (HPB). Ginseng. In: *HPB Status Manual*. Ottawa, ON: Health Protection Branch; 1993, Feb. 19;89.

Heffern R. The Use of North American Ginseng. In: *The Complete Book of Ginseng*. Millbrae, CA: Celestial Arts; 1976;81–9.

Homeopathic Pharmacopoeia of the United States (HPUS) Revision Service Official Compendium from July 1, 1992. Washington, DC: Homeopathic Pharmacopoeia Convention of the United States; 1992;0201—ARQU.

Hou J. The chemical constituents of ginseng plants. *Comparative Med East and West* 1977;5(2):123–45.

HPB. See: Health Protection Branch.

HPUS. See: *Homeopathic Pharmacopoeia of the United States*.

Johnson A, Jiang N, Stuba E. Whole ginseng effects on human response to demands for performance. *Proceedings of the 3rd International Ginseng Symposium*, Sept. 8–10;1980. Seoul Korea: Korea Ginseng Research Institute.

Kitts D, Wijewickreme A, Hu C. Antioxidant properties of a North American ginseng extract. *Mol Cell Biochem* 2000;203(1–2):1–10.

Lewis R, Wake G, Court G, *et al.* Non-ginsenoside nicotinic activity in ginseng species. *Phytother Res* 1999;13(1):59–64.

Li T, Mazza G, Cottrell A, Gao L. Ginsenosides in roots and leaves of American ginseng. *J Agric Food Chem* 1996;44:717–20.

Li Z, Guo Y, Wu C, Li X, Wang J. Protective effects of pseudoginsenoside-F11 on scopolamine-induced memory impairment in mice and rats. *J Pharm Pharmacol* 1999;51(4):435–40.

Martinez B, Staba E. The physiological effects of *Aralia*, *Panax* and *Eleutherococcus* on exercised rats. *Jpn J Pharmacol* 1984;35(2):79-85.

McGuffin M, Hobbs C, Upton R, Goldberg A (eds.). *American Herbal Products Association's Botanical Safety Handbook*. Boca Raton, FL: CRC Press; 1997;82.

Medical Products Agency (MPA). *Naturläkemedel: Authorised Natural Remedies* (as of January 24, 2001). Uppsala, Sweden: Medical Products Agency. 2001.

Millspaugh C. *Medicinal Plants*. Philadelphia, PA: John C. Yorston & Co.; 1892;276–9.

Moerman D. *Native American Ethnobotany*. Portland, OR: Timber Press; 1998;376–7.

Morris A, Jacobs I, McLellan T, *et al*. No ergogenic effect of ginseng ingestion. *Int J Sport Nutr* 1996;(6):263–71.

MPA. See: Medical Products Agency.

Murphy L, Cadena R, Chavez D, Ferraro J. Effect of American ginseng (*Panax quinquefolium*) on male copulatory behavior in the rat. *Physiol Behav* 1998;64(4):445–50.

Nocerino E, Amato M, Izzo A. The aphrodisiac and adaptogenic properties of ginseng. *Fitoterapia* 2000, Aug;71(0):S1–S5.

Oshima Y, Sato K, Hikino H. Isolation and hypoglycemic activity of quinquefolans A, B, and C, glycans of *Panax quinquefolium* roots. *J Nat Prod* 1987;50(2):188–90.

Pharmacopoeia of the People's Republic of China (PPRC 2000 English Edition). Beijing, China; Chemical Industry Press. 2000;183–84.

PPRC. See: *Pharmacopoeia of the People's Republic of China*.

Rafinesque C. *Medical Flora: Manual of the Medical Botany of the United States of America,* Volume II. Philadelphia, PA: Samuel C. Atkinson; 1830;53.

Ren G, Chen F. Simultaneous quantification of ginsenosides in American ginseng (*Panax quinquefolium*) root powder by visible/near-infrared reflectance spectroscopy. *J Agric Food Chem* 1999;47(7):2771–5.

Reynolds L. Effects of drying on chemical and physical characteristics of American ginseng (*Panax quinquefolius* L.). *J Herbs, Spices & Med Plants* 1998;6(2):9–21.

Rister RS. American Ginseng. In: *Japanese Herbal Medicine: The Healing Art of Kampo*. Garden City Park, NY: Avery Publishing Group; 1999;23–4.

Robbins C. *Panax quinquefolius* popularity prompts probe. *Medicinal Plant Conservation* 1997, Nov.1;4:13–5.

Scudder J. *The American Eclectic Materia Medica and Therapeutics*. Cincinnati, OH: John M. Scudder; 1891;454.

Shaw P, But P. Authentication of *Panax* species and their adulterants by random-primed polymerase chain reaction. *Planta Med* 1995;61:466–9.

Sontaniemi E, Haapakoski E, Rautio A. Ginseng therapy in non-insulin-dependent diabetic patients. *Diabetes Care* 1995;18:1373–5.

State Standard of People's Republic of China. *Grade and Quality Standards of Products of Processed American Ginseng*. Beijing, China: Standards Press of China; 1998;GB/T 17356.1~17356.5.

United States Congress (USC). Public Law 103–417: Dietary Supplement Health and Education Act of 1994. Washington, DC: 103rd Congress of the United States; 1994.

United States Department of Agriculture (USDA). Farmers Bulletin Number 2201: Growing Ginseng. Washington, DC: United States Department of Agriculture; 1978, June.

United States Department of Commerce (USDOC). Ginseng: United States Exports by Type and Unit Value. Washington, DC: U.S. Department of Commerce. 1995, April;83–85.

United States Department of Commerce (USDOC). Ginseng Roots, Fresh or Dried, Whether or not Cut, Crushed or Powdered. U.S. Domestic Exports: November 2000 and 2000 YTD, not Seasonally Adjusted; December 1999 and 1999 YTD, not Seasonally Adjusted. Washington, DC: U.S. Department of Commerce; 2000.

United States Department of State (USDS). Deregulation of Herbs Used as Dietary Supplements. Country: Japan. Washington, DC: U.S. & Foreign Commercial Service and U.S. Department of State; June 12, 2000; Available at: http://www.csjapan.doc.gov/imi0006/herb.html.

United States Fish and Wildlife Service (USFWS). News Release: Status Review of American Ginseng Plant. Washington, DC: Department of the Interior: U.S. Fish and Wildlife Service; 1977, Aug. 11;INT:4735–77.

United States Fish and Wildlife Service (USFWS). U.S. Fish and Wildlife Service Announces First-Ever Export Restrictions for Ginseng Roots. Washington DC: U.S. Fish and Wildlife Service International Affairs; 1999a. Available at: http://international.fws.gov/global/ginsenpr.html.

United States Fish and Wildlife Service (USFWS). How to Determine the Age of Ginseng Plants. Washington DC: U.S. Fish and Wildlife Service International Affairs; 1999b. Available at: http://international.fws.gov/global/ginseng.html.

United States Fish and Wildlife Service (USFWS). Convention Permit Applications for Ginseng. Washington DC: U.S. Fish and Wildlife Service International Affairs; 1999c. Available at: http://international.fws.gov/animals/gingfind.html.

USC. See: United States Congress.

USDA. See: United States Department of Agriculture.

USDOC. See: United States Department of Commerce.
USDS. See: United States Department of State.
USFWS. See: United States Fish and Wildlife Service.
Vuksan V, Sievenpiper J, Wong J, *et al*. American ginseng (*Panax quinquefolius* L.) attenuates postprandial glycemia in a time-dependent but not dose-dependent manner in healthy individuals. *Am J Clin Nutr* 2001;73:753–8.
Vuksan V, Sievenpiper, J, Koo, V, *et al.* American ginseng (*Panax quinquefolius* L.) reduces postprandial glycemia in nondiabetic subjects and subjects with type 2 diabetes mellitus. *Arch Intern Med* 2000a;160:1009–13.
Vuksan V, Stavro MP, Sievenpiper JL, *et al.* Similar postprandial glycemic reductions with escalation of dose and administration time of American ginseng in type 2 diabetes. *Diabetes Care* 2000b;23(9):1221–6.
Wang C, Lee T. Effect of ginseng saponins on cold tolerance in young and elderly rats. *Planta Med* 2000;66:144–7.
Wang C, Shiao Y, Kuo Y, *et al*. Inducible nitric oxide synthase inhibitors from *Saposhnikovia divaricata* and *Panax quinquefolium*. *Planta Med* 2000;66:644–7.
Wang H, Ng T. Quinqueginsin, a novel protein with anti-human immunodeficiency virus, antifungal, ribonuclease and cell-free translation-inhibitory activities from American ginseng roots. *Biochem Biophys Res Commun* 2000;269(1):203–8.
Wang W, Chen H, Hsu T, Wang Y. Alteration of pulse in human subjects by three Chinese herbs. *Am J Chin Med* 1994;22(2):197–203.
Wenkui L., Chungang G., Hongjie Z. *et al.* Use of High-Performance Liquid Chromatography—Tandem Mass Spectrometry to Distinguish *Panax ginseng* C.A. Meyer (Asian Ginseng) and *Panax quinquefolius* L. (North American Ginseng). *Anal Chem* 2000;72:5417—5422.
Wood G, Bache F. *Panax*, U.S. In: *The Dispensatory of the United States of America*, 11th edition. Philadelphia, PA: J.B. Lippincott and Co; 1858;575–6.
Wood H, LaWall C, Youngken H, *et al*. *The Dispensatory of the United States of America*, 21st edition. Philadelphia, PA: J.B. Lippincott Co.; 1926;1316.
Xiao M. *The Canadian Ginseng Industry: Preparing for the 21st Century*. Ottawa, ON: Agriculture and Agri-Food Canada; 2000–02–07.
Xiao-fan Z, Liscum G. *Chinese Medicinal Teas*. Boulder, CO: Blue Poppy Press, Inc.; 1996;269–70.
Yen K. *The Illustrated Chinese Materia Medica—Crude and Prepared*. Taipei, Taiwan: SMC Publishing Inc.; 1992;53.
Yoshikawa M, Murakami T, Yashiro K, *et al*. Bioactive saponins and glycoside. XI. Structures of new dammarane-type triterpene oligoglycosides, quinquenosides I, II, III, IV, and V, from American ginseng, the roots of *Panax quinquefolium* L. *Chem Pharm Bull* (Tokyo); 1998;46(4):647–54.
Yuan C, Attele A, Wu J, Liu D. Modulation of American ginseng on brainstem GABAergic effects in rats. *J Ethnopharm* 1998a;62(3):215–22.
Yuan C, Attele A, Wu J, *et al. Panax quinquefolium* L. inhibits thrombin-induced endothelin release *in vitro*. *Am J Chin Med* 1999;27(2–3):331–8.
Yuan C, Wu J, Lowell T, Gu M. Gut and brain effects of American ginseng root on brainstem neuronal activities in rats. *Am J Chin Med* 1998b;26(1):47–55.
Zheng Y, Zhang C, Li X, Guo S. A comparison between Chinese *Panax quinquefolius* and imported *Panax quinquefolius*—analysis of composition of essential oil in *Panax quinquefolius*. [in Chinese]. *Yao Hsueh Hsueh Pao* 1989;24(2):118–21.

Clinical Studies on American Ginseng (*Panax quinquefolius* L.)

Athletic Performance

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Morris *et al.*, 1996	Ergogenic response of ginseng to intense exercise	PC, CO n=8	1 week	8 or 16 mg/kg body weight	American ginseng root purified extract vs. placebo (brand not stated)	No significant intergroup differences in any measured parameters (oxygen uptake, heart rate, time to exhaustion, mean lactate concentration, rating of perceived exertion during submaximal ergometer exercise).
Goode *et al.*, 1993	Sub-maximal and maximal performance as measured by oxygen consumption and ventilation	R, PC n=39 (mean age 22.5 years)	90 days	3 capsules per day of 330 mg; 2 with breakfast and 1 at supper	American ginseng root extract, encapsulated (brand not stated) vs. placebo (wheat flour)	Significant reduction ($p<0.01$) in ventilation during submaximal exercise in post-test results compared to pretest values for entire ginseng group and compared to no significant change in placebo group. Increased ability to consume oxygen, especially in those who were less fit (not significant).

Diabetes

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Vuksan *et al.*, 2001	Postprandial glycemia in healthy individuals	R, PC, CO, Cm n=12	1 day	16 treatments: 2 capsules (1 g), 4 capsules (2 g), 6 capsules (3 g) or placebo at 40, 20, 10, or 0 minutes before 25 g oral glucose challenge	Chai-Na-Ta® capsules containing 500 mg 3-year old, dried and ground American ginseng root vs. placebo capsules (corn flour)	Ginseng reduced postprandial glycemia in nondiabetic subjects. Ginseng significantly lowered glycemia over last 45 minutes of test after doses of 1, 2, or 3 g compared to placebo ($p<0.05$). No significant differences among three doses. Glycemia in last hour of test and area under the curve significantly lower when ginseng was administered 40 minutes before challenge than when administered 20, 10, or 0 minutes before challenge ($p<0.05$). Reductions were time-dependent and not dose-dependent, even though one of the doses (3 g) is relatively higher than normal.
Vuksan *et al.*, 2000a	Postprandial glycemia in nondiabetic individuals and individuals with type 2 diabetes mellitus	R, DB, PC n=19 (mean age nondiabetics 34 years; mean age diabetics 62 years)	4 weeks	3 g/day, 40 minutes before or w/25 g oral glucose	Chai-Na-Ta® Ontario-grown American ginseng root capsules vs. placebo (corn flour)	Type 2 diabetes mellitus subjects: ginseng significantly ($p<0.05$) lowered incremental glycemia; 22% ± 17% with glucose challenge and 19% ± 22%, 40 minutes before glucose challenge. Nondiabetic subjects: ginseng significantly ($p<0.05$) lowered incremental glycemia 18% ± 31% when taken 40 minutes before glucose challenge, but no difference when taken with glucose challenge.
Vuksan *et al.*, 2000b	Postprandial glycemia in individuals with type 2 diabetes mellitus	R, PC, CO n=10 type 2 diabetic indviduals (6 males, 4 females) (age 63± 2 years)	16 doses (at least 3 day washout between each dose)	3, 6, 9 g ginseng or placebo, 120, 80, 40, or 0 minutes before receiving glucose challenge	Chai-Na-Ta® Ontario-grown American ginseng root encapsulated or placebo (corn flour)	Treatment with 3, 6, 9 g American ginseng significantly lowered incremental glycemia ($p<0.05$). Reductions, however, occurred independent of the dose used. This effect was seen irrespective of the time of administration.

Psychomotor Response

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Johnson *et al.*, 1980	Effect of whole ginseng on mental performance	DB, PC, Cm n=38 dental students 4 arms: Arm 1: n=8 males, 1 female Arm 2: n=5 males Arm 3: n=13 males, 1 female Arm 4: n=10 males (approximately 25 years old)	Over 32 days	All arms: Approximately 2 g/dose, 8–14 doses over 30 days	4 arms: Arm 1: Asian red ginseng root (*Panax ginseng*) Arm 2: North American white ginseng root (*P. quinquefolius*) Arm 3: Eleuthero (a.k.a., Siberian ginseng) root (*Eleutherococcus senticosus*) Arm 4: Placebo	Both species of ginseng and eleuthero improved proofreading error detection, while only Korean and American ginseng improved mood-fatigue. None significantly affected mathematical performance and final grade performance, or the urinary concentrations of catecholamines.

KEY: C – controlled, **CC** – case-control, **CH** – cohort, **CI** – confidence interval, **Cm** – comparison, **CO** – crossover, **CS** – cross-sectional, **DB** – double-blind, **E** – epidemiological, **LC** – longitudinal cohort, **MA** – meta-analysis, **MC** – multi-center, **n** – number of patients, **O** – open, **OB** – observational, **OL** – open label, **OR** – odds ratio, **P** – prospective, **PB** – patient-blind, **PC** – placebo-controlled, **PG** – parallel group, **PS** – pilot study, **R** – randomized, **RC** – reference-controlled, **RCS** – retrospective cross-sectional, **RS** - retrospective, **S** – surveillance, **SB** – single-blind, **SC** – single-center, **U** – uncontrolled, **UP** – unpublished, **VC** – vehicle-controlled.