

Ginseng, Asian

Panax ginseng C.A. Meyer (syn. *P. schinseng* T. Nees)

[Fam. *Araliaceae*]

OVERVIEW

Asian ginseng is one of the most economically important medicinal herbs in world trade. In the U.S., ginseng ranks second in total sales in food, drug, and mass market retail stores with sales in 2000 totaling \$62.5 million. The medical use of ginseng dates back thousands of years, though the first written account of its use appears in *Shen-nung pen-ts'ao-ching*, the first *Chinese Materia Medica*, believed to have been compiled during the Late Han Dynasty in the first century C.E. Ginseng has remained an important medicine in the health care systems of China, Japan, and Korea and has also become a leading product in European and U.S. herbal supplements.

PRIMARY USES

- Adaptogen and general tonic
- Increased athletic performance and endurance (although several more recent studies have not resulted in positive outcomes for performance enhancement)
- Immunomodulatory effects

OTHER POTENTIAL USES

- Non-insulin dependent diabetes mellitus
- Menopausal symptoms
- Aphrodisiac; erectile dysfunction and fertility
- Improved cognitive function and mental performance (although the effects on psychological wellbeing in normal healthy young adults were not confirmed in a later study)
- Possible reduction of risk of gastric cancer, as well as cancer of the, lungs, ovaries, larynx, esophagus, and pancreas
- Maintained CD4+ T-cell counts and delayed resistance to zidovudine in HIV positive patients taking Korean red ginseng combined with zidovudine
- Improved pulmonary function in treatment of severe, chronic respiratory disease; additive effect of antibiotic treatment for respiratory tract infection



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TRADITIONAL CHINESE MEDICINE (TCM)

INDICATIONS

White Ginseng (Renshen)

Prostration with impending collapse marked by cold limbs and faint pulse; diminished function of the spleen with loss of appetite; cough and dyspnea due to diminished function of the lung; thirst due to impairment of body fluid; diabetes caused by internal heat; general weakness with irritability and insomnia in chronic diseases; impotence or frigidity; heart failure and cardiogenic shock.

Red Ginseng (Hongshen)

Collapse tendency due to asthenia; cool limbs and weak pulse; *qi* (vital force) cannot control blood; uterine bleeding; cardiac failure and cardiogenic shock.

NOTE: In TCM, the terms “spleen” and “lung” do not correlate to the western system of anatomy, but are part of a system of classification defined by their functions and relationships. Also, in TCM, herbs are rarely used as monopreparations and almost always used in combinations; it is therefore difficult to attribute the traditional uses of ginseng to the pharmacology of this herb alone as the actions of other herbs used in classic formulas may have an additive or synergistic effect.

PHARMACOLOGICAL ACTIONS

RED GINSENG ROOT: long-term, immunomodulating effect in human immunodeficiency virus (HIV) patients; improves parameters of rigidity and tumescence in erection, early detumescence, libido, and satisfaction.

STANDARDIZED EXTRACT: increases natural killer cell activity; immunomodulatory effects; reduces plasma total cholesterol and triglycerides and elevated HDL levels.

POWDERED ROOT: significantly increases mean platelet count.

DOSAGE AND ADMINISTRATION

Ginseng can generally be used up to three months, with a repeated course of treatment possible.

DRIED ROOT, POWDERED: 1–2 g daily for up to three months.

DECOCTION: 3–9 g dried root simmered in 720–960 ml water for approximately 45 minutes.

INFUSION: 150–250 ml boiling water poured over 1–2 g fine cut or powdered root, steeped covered for 10 minutes, then strained.

FLUID EXTRACT: 1–6 ml daily [1:2 (*g/ml*)].

DRY EXTRACT: 2, 100 mg capsules daily taken with liquid at breakfast or 1 capsule with breakfast and 1 capsule with lunch [standardized to 4% ginsenosides].

CONTRAINDICATIONS

No known contraindications according to the Commission E and the World Health Organization (WHO). The *British Herbal Compendium* (BHC) contraindicates ginseng for patients with acute illnesses, hypertension, or who use excessive amounts of stimulants, particularly caffeine-containing beverages.

PREGNANCY AND LACTATION: No known restrictions according to the American Herbal Products Association and the Commission E, but controlled, long-term safety studies are lacking. The BHC contraindicates ginseng in pregnancy, even though ginseng is not teratogenic *in vivo*. NOTE: In Traditional Chinese Medicine (TCM), ginseng root is included in prescriptions given during pregnancy, labor, and postpartum.

ADVERSE EFFECTS

None known. Although a few adverse effects have been reported in the literature, given the long and safe history of use, widespread modern use, and clinical trials, most authoritative experts conclude that Asian ginseng is not associated with serious adverse effects if taken at the recommended dosages.

DRUG INTERACTIONS

Two cases of interaction between ginseng and phenelzine, a monoamine oxidase inhibitor, have been reported, although the clinical significance of this interaction is not yet known. Diabetic patients may need to adjust their insulin dosages because ginseng may reduce blood glucose levels slightly. Positive synergistic effects of ginseng combined with zidovudine in HIV patients have been reported. In one case report, an interaction with warfarin resulted in a subtherapeutic decrease in clotting time (International Normalization Ratio). The BHC cautions against using ginseng with stimulants, including excessive amounts of caffeine.

CLINICAL REVIEW

More than 60 clinical studies on ginseng have been published with most using a dry extract (G115[®]) standardized to 4% total ginsenosides at a daily dosage of 200 mg. The drug-to-extract ratio is approximately 5:1 (*w/w*) so that 200 mg of extract corresponds to about 1 g of dried root. Of 29 clinical studies on Asian ginseng root that included a total of 12,037 participants, all but five demonstrated positive effects for indications including cancer prevention, diabetes, immune support, fatigue, menopause, and circulation. Five double-blind, placebo-controlled (DB, PC) trials investigated the ergogenic and anti-fatigue effects of ginseng extract on physical performance. Six DB, PC studies examined the effect of ginseng on psychological functions. Ginseng's immunomodulatory activity is the subject of three DB, PC studies. One DB, PC study investigated the effect of ginseng on newly diagnosed non-insulin-dependent diabetes. Ginseng's effect on erectile dysfunction and fertility in men was the focus of two studies. A review in a popular newsletter has raised issues regarding the design and results of some of these studies.

In a meta-analysis of studies on the general effectiveness of Asian ginseng on physical performance in young healthy volunteers, nine of the 16 clinical trials reviewed concluded that the “ginseng” preparation used in the trials had a positive effect. However, the analysis has been criticized because it did not differentiate between five different types of “ginseng.” Another review of 16 clinical trials involving ginseng's effect on exercise performance in athletes and other healthy subjects was criticized for statistical and design problems and for methodological problems such as inadequate sample size and lack of DB, PC paradigms. These studies were conducted on ginseng combined with other ingredients (e.g., herbs, vitamins) and, in some cases, did not specify dose, duration, or specific parameters of the ginseng preparation. The authors of this review concluded that future trials should rectify design flaws so that a reasonable conclusion can be made about the effect of ginseng on physical performance. Another paper suggests that increasing dosage levels to be consistent with those used historically in TCM and in recent pharmacological experiments in animals would produce more positive outcomes in clinical trials measuring the ergonomics and other activities of ginseng.



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OVERVIEW

Asian ginseng is one of the most economically important medicinal herbs in world trade; in the U.S., ginseng ranks second in total sales in food, drug, and mass market retail stores with sales in 2000 totaling \$62.5 million. Ginseng root is indigenous to northern mountainous regions of China, Korea, and parts of the Russian Federation. In Asia, the medical use of ginseng dates back thousands of years, and it has remained an important drug in the health care systems of China, Japan, and Korea.

PRIMARY USES

May increase athletic performance and endurance; immunomodulating effects; fatigue.

OTHER POTENTIAL USES

Non-insulin dependent diabetes mellitus; menopausal symptoms; erectile or fertility problems; improves cognitive function and mental performance; possibly reduces risk of gastric, lung, ovarian, larynx, esophagus, and pancreas cancers; improves lung function; increases antibiotic effect for respiratory tract infection.

DOSAGE

Ginseng can generally be used for up to three months followed by a repeated course of treatment.

DRIED ROOT, POWDERED: 1–2 g daily for up to three months.

DECOCTION: Simmer 3–9 g dried root in 720–960 ml water for approximately 45 minutes.

INFUSION: Pour 150–250 ml boiling water over 1–2 g finely cut or powdered root, steep covered for 10 minutes, then strain.

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.



FLUID EXTRACT: 1–6 ml daily [1:2 (g/ml)].

DRY EXTRACT: Take 2, 100 mg capsules daily with liquid at breakfast; or 1 capsule with breakfast and 1 capsule with lunch [standardized to 4% ginsenosides].

CONTRAINDICATIONS

Consult with a healthcare provider before using Asian ginseng in cases of acute illnesses, high blood pressure (hypertension), and when using large amounts of stimulants like caffeine-containing beverages.

PREGNANCY AND LACTATION: No known restrictions although some authorities say that ginseng root should not be used during pregnancy. In Traditional Chinese Medicine, ginseng root is used during pregnancy, labor, and postpartum, in combinations containing other herbs.

ADVERSE EFFECTS

None known.

DRUG INTERACTIONS

Patients taking phenelzine (an MAO inhibitor), warfarin (an anticoagulating drug), or zidovudin (an HIV drug) should consult with a healthcare provider before using ginseng. Diabetic patients may need to adjust their insulin dosages because ginseng may lower blood glucose levels. Use with caution when taking with significant amounts of stimulants such as coffee, sugar, and caffeine-containing teas.



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OVERVIEW

Asian ginseng is one of the most economically important medicinal herbs in world trade (Iqbal, 1993; Ma, 1999). In the U.S., ginseng ranks second in total sales in food, drug, and mass market retail stores with sales in 2000 totaling \$62.5 million (Blumenthal, 2001). The U.S. Department of Commerce (USDOC) tracks ginseng imports due to the herb's significant economic value. The U.S. imports over 1 million pounds of cultivated Asian ginseng roots annually mainly from China, Hong Kong, and Korea (USDOC, 2000). The quantity and value of finished ginseng consumer products imported into the U.S. from Europe and Asia are significant. In Germany, ginseng is one of the few economically important herbal drugs listed separately in the *Foreign Trade Statistics*. A considerable amount of ginseng is value-added (i.e., processed into finished products) in Germany, and then exported mostly to France, Italy, and Argentina (Lange and Schippmann, 1997). A recent study by the American Botanical Council's Ginseng Evaluation Program, found that the quality control regarding standardized ginseng products was reasonably consistent over five separate lots of 13 different products (Hall *et al.*, 2001).

Asian ginseng (*Panax ginseng*) is indigenous to northern mountainous regions of China and Korea and far eastern regions of the Russian Federation (Blumenthal *et al.*, 2000). Though Asian ginseng is cultivated in China, Japan, Korea and Russia (Siberia), the Republic of Korea, and China are the main producers and exporters of the herb (Iqbal, 1993).

In Asia, the medical use of ginseng dates back thousands of years, though the first written account of its use appears in *Shen-nung pen-ts'ao-ching*, the first *Chinese Materia Medica*, believed to have been compiled during the Late Han Dynasty in the first century C.E. (Hu, 1977). Ginseng has remained an important medicine in the health care systems of China, Japan, and Korea (JSHM, 1993; PPRC, 1997). Asian ginseng has also become integrated into European medicine (Morant and Ruppanner, 2001; Blumenthal *et al.*, 2000; DAB, 1999; ÖAB, 1990; Ph.Eur., 2001). In Sweden, ginseng represents the top-selling category of all registered natural remedies (Tunón, 1999). An extensive review of the detailed chemistry, mechanisms of action, pharmacology, therapeutics, and related information on *P. ginseng* was recently published, stating that since 1960 more than 4,000 research articles have been published in the scientific literature

covering Asian ginseng (Court, 2000). Another review has focused on the ginsenosides, the primary active constituents, and includes biological effects noted in pharmacological and clinical studies on ginsenosides from ginseng root and aerial parts (leaves, flowers, fruits) (Chen *et al.*, 2002).



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DESCRIPTION

White ginseng root (also referred to in the literature by its pharmaceutical name, *Radix Ginseng*) consists of the mature dried root of *Panax ginseng* C.A. Meyer [Fam. *Araliaceae*], collected in autumn and dried in the sun (PPRC, 1997). Before drying, the root is washed, and the rhizomes are removed (JSHM, 1993). White ginseng root contains no less than 0.4% of combined ginsenosides Rg1 and Rb1, calculated with reference to the dried root (Ph.Eur., 2001), or no less than 1.5% of total ginsenosides calculated as ginsenoside Rg1 (Blumenthal *et al.*, 1998; DAB, 1999). Red ginseng root (*Radix Ginseng Rubra*) is produced by steaming the raw root at 98–100°C for two to three hours (Kim *et al.*, 2000), then drying. The concentration of the major ginsenosides (Rb1, Rb2, Rc, Rd, Re, Rf, Rgl) are slightly higher in white ginseng than red ginseng (Yun, 1996).

PRIMARY USES

- Adaptogen and general tonic (Amato *et al.*, 2000; Court, 2000)

Fatigue and physical performance

- Increased athletic performance and endurance (Le Gal, 1996; Van Schepdael, 1993; Cherdrunsi and Rungroeng, 1995), (although several more recent studies have not resulted in positive outcomes for performance enhancement [Bahrke and Morgan, 1994, 2000])

Immunology

- Immunomodulatory effects (Scaglione *et al.*, 1990, 1996; Srisurapanon *et al.*, 1997)

OTHER POTENTIAL USES

Diabetes

- Non-insulin dependent diabetes mellitus (Sotaniemi *et al.*, 1995)

Gynecology

- Menopausal symptoms (Wickland *et al.*, 1994; Reinold 1990)

Male Reproductive Health

- Aphrodisiac (Amato *et al.*, 2000); erectile dysfunction and fertility (Salvati *et al.*, 1996; Choi *et al.*, 1995)

Mental Health

- Improved cognitive function and mental performance (Sørensen *et al.*, 1996; Smith *et al.*, 1995; Rosenfeld, 1989; Von Ardenne *et al.*, 1987; D'Angelo *et al.*, 1986; Fulder *et al.*, 1984; Dorling, 1980; Johnson *et al.*, 1980), although the effects on psychological well-being in normal healthy young adults were not confirmed in a later study (Cardinal and Engels, 2001).

Oncology

- Possible reduction of risk of gastric cancer, as well as cancer of the lungs, ovaries, larynx, esophagus, and pancreas (Kakizoe, 2000; Yun and Choi, 1998; Yun and Choi, 1995; Yun and Choi, 1990)
- Maintained CD4+ T-cell counts and delayed resistance to zidovudine in HIV + patients taking Korean red ginseng combined with zidovudine (Cho *et al.*, 2001).

Respiratory System

- Improved pulmonary function in treatment of severe, chronic respiratory disease (Gross *et al.*, 1995); additive effect of antibiotic treatment for respiratory tract infection (Scaglione *et al.*, 2001, 1994)

Ginseng root extracts and/or isolated ginsenosides have been studied clinically for the following indications with some positive results: general quality of life, adaptogenic activity and physical stress, anti-aging effects, aphrodisiac effects, memory and intellectual skills, diabetes, various types of cancers, angiocardioopathy and other cardiovascular parameters, hepatitis, peptic ulcer, aplastic anemia, atherosclerosis, and others (Court, 2000; Chen *et al.*, 2003).

TRADITIONAL CHINESE MEDICINE (TCM)

INDICATIONS

White Ginseng (Renshen)

Prostration with impending collapse marked by cold limbs and faint pulse; diminished function of the spleen with loss of appetite; cough and dyspnea due to diminished function of the lung; thirst due to impairment of body fluid; diabetes caused by internal heat; general weakness with irritability and insomnia in chronic diseases; impotence or frigidity; heart failure and cardiogenic shock (PPRC, 1997).

Red Ginseng (Hongshen)

Collapse tendency due to asthenia; cool limbs and weak pulse; *qi* (vital force) cannot control blood; uterine bleeding; cardiac failure and cardiogenic shock (PPRC, 1997).

NOTE: In TCM, the terms “spleen” and “lung” do not correlate to the Western system of anatomy, but are part of a system of classification defined by their functions and relationships. Also, in TCM, herbs are rarely used as monopreparations and almost always used in combinations (Kaptchuk, 1983); it is therefore difficult to attribute the traditional uses of ginseng to the pharmacology of this herb alone as the actions of other herbs used in classic formulas may have an additive or synergistic effect.

DOSAGE

Internal

Crude Preparations

DRIED ROOT, POWDERED: 1–2 g daily for up to three months (Blumenthal *et al.*, 1998).

DECOCTION: 3–9 g dried root simmered in 720–960 ml water for approximately 45 minutes (PPRC, 1997).

INFUSION: 150–250 ml boiling water poured over 1–2 g fine cut or powdered root, steeped covered for 10 minutes, then strained (Blumenthal *et al.*, 1998, 2000).

FLUID EXTRACT: 1:2 (*g/ml*): 1–6 ml daily (Bone, 1998).

NOTE: The German Commission E specifies cut root for teas, powder, or equivalent preparations (Blumenthal *et al.*, 1998). In an infusion of coarsely powdered root, the yield of total ginsenosides at 10 minutes steeping time is 64%, and the yield is 73% at 15 minutes. If decocted, the yield of ginsenosides is 69% at 5 minutes and 77% at 15 minutes. A cold maceration will yield 71% at 60 minutes (Meyer-Buchtela, 1999).

Standardized Preparations

DRY EXTRACT: Standardized to 4% ginsenosides, 2x100 mg capsules daily taken with liquid at breakfast, or 1 capsule with breakfast and 1 capsule with lunch (Morant and Ruppner, 2001). NOTE: Much of the pharmacological and clinical research conducted on the leading 4% standardized ginseng extract (G115®) suggests that 200 mg of this extract, yielding 8 mg ginsenosides per day, is an optimal dose (Soldati, 2000). However, a review of historical literature and recent pharmacological investigations conducted in Asia suggests that significantly higher doses (3–9 g of dried root, equivalent to as much as 80–240 mg ginsenosides per day) are possibly warranted (Dharmananda, 2002).

DURATION OF ADMINISTRATION

According to the German Commission E, ginseng can generally be used up to three months, with a repeated course of treatment possible (Blumenthal *et al.*, 1998).

CHEMISTRY

Ginseng root contains up to 40 dammarane- and oleanane-type saponins, polyacetylene derivatives, and polysaccharides (Chen *et al.*, 2003; Court, 2000; Fukuda *et al.*, 2000; Tang and Eisenbrand, 1992). Saponins are believed to be the primary active components of ginseng, with characteristic dammarane-type saponins divided into two major groups based on their aglycones; (1) 20(S)-protopanaxadiol: ginsenosides Rb1, Rb2, Rc, and Rd; and (2) 20(S)-protopanaxatriol: ginsenosides Re, Rf, Rg1, and Rg2 (Kwon *et al.*, 2000). Ginsenoside Ro is an oleanane-type saponin (WHO, 1999). Ginseng also contains alkaloids, phenols, amino acids, polypeptides, proteins, and other constituents (Court, 2000).

Raw (white) ginseng root contains 0.56–0.95% ginsenoside Rb1, 0.52–0.74% ginsenoside Rb2, 0.48–0.72% ginsenoside Rc, 0.26–0.46% ginsenoside Rd, 0.38–0.64% ginsenoside Re, 0.11% ginsenoside Rf, 0.39–0.61% ginsenoside Rg1 and 0.13% ginsenoside Rg2 (Chuang *et al.*, 1995; Kim *et al.*, 2000; Kwon *et al.*, 2000) 0.005% volatile oil (Yen, 1992).

Steamed (red) ginseng root, depending on the temperature used during steaming, contains 0.12–0.5% ginsenoside Rb1, 0.1–0.44% ginsenoside Rb2, 0.17–0.57% ginsenoside Rc, 0.14–0.27% ginsenoside Rd, 0.02–0.3% ginsenoside Re, 0.1–0.12% ginsenoside Rf, 0.22–0.35% ginsenoside Rg1,

0.2–0.3% ginsenoside Rg2, 0.24–1.32% ginsenoside Rg3, 0.15–0.64% ginsenoside Rg5, 0.14–0.23% ginsenoside F4 (Kim *et al.*, 2000). Ginsenosides Rg3, Rg5, and F4, do not occur in white ginseng and are formed as a product of the steaming process.

A high-performance liquid chromatography-tandem mass spectrometry method was developed to distinguish between *P. ginseng* (Asian ginseng) and *P. quinquefolius* (American ginseng). This method differentiates between American ginseng containing 24(R)-pseudoginsenoside F11 in excess of 0.1% (*w/w*) in the dried root and Asian ginseng containing trace levels of less than 0.00001% (Wenkui *et al.*, 2000).

Ginsenosides are quite stable: They were identified in 1,200 year-old root samples from Japan (Court, 2000).

PHARMACOLOGICAL ACTIONS

Pharmacological studies on Asian ginseng are numerous and are summarized in recent publications (Chen *et al.*, 2003; Court, 2000; Tang and Eisenbrand, 1992).

Human

Red ginseng root

Demonstrated a long-term, immunomodulating effect in human immunodeficiency virus (HIV) patients (Cho *et al.*, 1997); improved parameters of rigidity and tumescence in erection, early detumescence, libido, and satisfaction (Choi *et al.*, 1995).

Standardized extract

Increased natural killer cell activity (Scaglione *et al.*, 1996); showed significant immunomodulatory effects (Scaglione *et al.*, 1990); reduced plasma total cholesterol and triglycerides, and elevated HDL levels (Yamamoto *et al.*, 1983).

Powdered root

Significantly increased mean platelet count (Chang *et al.*, 1980).

Animal

Increased resistance in coldness test and immobilization test in rodents (Blumenthal *et al.*, 1998); increased oxidative capacity of the skeletal muscle in rats (standardized extract) (Ferrando *et al.*, 1999); demonstrated hormone-like and cholesterol-lowering effects, promoted vasodilation, acted as anxiolytic, and antidepressant (Choi *et al.*, 1995; Chong *et al.*, 1988); prevented cancer-causing effects of DMBA, urethane, and aflatoxin in newborn mice (Yun *et al.*, 1993); inhibited alcohol-induced amnesia in rats (Lee *et al.*, 2000); enhanced thermogenic capacity (Wang and Lee, 2000); enhanced energy metabolism (Avakian *et al.*, 1984); protected against irradiation damage (Takeda *et al.*, 1981, 1982); reduced injuries and inflammation caused by eccentric muscle contractions in rats (de Oliveira *et al.*, 2001); Ginseng Total Saponin (GTS) fraction inhibited striatal dopamine release stimulated by local infusion of nicotine in male rats (Shim *et al.*, 2000).

In vitro

ANTI-TUMOR: Isolated ginsenoside Rg3 demonstrated anti-proliferation activity in human prostate cancer cell line (Liu *et al.*, 2000); isolated ginsenosides have shown antitumor effects in human and mouse tumor cells (Molnar *et al.*, 2000).

BRONCHO-RELAXING: Ginsenosides induced relaxation of human bronchial smooth muscle via stimulation of nitric oxide generation, mainly from airway epithelium and cyclic GMP synthesis, possibly explaining the anti-asthmatic effect of ginseng (Kawatani *et al.*, 2000).

TRADITIONAL CHINESE MEDICINE (TCM)

ACTIONS

According to the concepts inherent in TCM, the actions of ginseng are explained in terms of TCM's energetics model as follows:

White Ginseng (Renshen)

Reinforces vital energy (*qi*), remedies collapse and restores normal pulse, benefits the spleen and lung, promotes production of body fluid, calms the nerves (PPRC, 1997). NOTE: "spleen" in TCM is not the specific anatomical organ known in Western medicine; in TCM, "organs" are discussed with reference to their functions and relationships to other organs, substances and other body parts. In most cases, the term "spleen" in TCM refers to the entire digestive system.

Red Ginseng (Hongshen)

Replenishes vital essence (*jing*), promotes blood circulation and relieves collapse, reinforces *qi* and stanches bleeding (PPRC, 1997).

MECHANISM OF ACTION

- Some research suggests that ginseng acts through both the hypothalamus-pituitary-adrenal axis and partly through its immunomodulatory activity (WHO, 1999).
- *In vitro*, isolated ginsenosides have shown a chemical structure-dependent immunomodulating effect by enhancing the activity of natural killer cells and ADCC (antibody-dependent cell-mediated cytotoxicity) activities, the effect being structure-dependent (Molnar *et al.*, 2000).
- For male impotence, ginseng saponins appear to depress blood prolactin levels, causing increased libido (WHO, 1999), suggesting that ginseng may have an effect at different levels of the hypothalamus-pituitary-testes axis (Salvati *et al.*, 1996).
- Based on animal experiments, pretreatment with either ginseng extract or its isolated saponins block methamphetamine- or cocaine-induced behavioral activity. Ginseng Total Saponins (GTS) inhibits striatal dopamine release stimulated by local infusion of nicotine, suggesting that ginseng may act on presynaptic nicotinic acetylcholine receptors (nAChRs), or receptor-operated Na⁺ channels in dopaminergic nerve terminals, though not on voltage-sensitive ion channels (Shim *et al.*, 2000).
- Red ginseng total saponin's (RGTS) inhibition of alcohol-induced amnesia in rats is dependent on catecholaminergic but not serotonergic neuronal activity (Lee *et al.*, 2000).
- Depressant and stimulant effects on the central nervous system by the two main ginsenosides, Rb1 and Rg1, (Chong and Oberholzer, 1988) indicate that the pharmacological actions of individual ginsenosides may work in opposition. In rats with selective hippocampal lesions, red ginseng ameliorates learning and memory deficits through its effect on the CNS which may be partly due to its effects on hippocampal formation (Zhong *et al.*, 2000).

CONTRAINDICATIONS

The Commission E and World Health Organization (WHO) report that there are no known contraindications for Asian ginseng (Blumenthal *et al.*, 1998; WHO, 1999). The *British Herbal Compendium* (BHC) contraindicates ginseng in acute illnesses, hypertension, and with use of stimulants, particularly caffeine-containing beverages (Bradley, 1992).

PREGNANCY AND LACTATION: No known restrictions are noted by the American Herbal Products Association (McGuffin *et al.*, 1997) and the Commission E (Blumenthal *et al.*, 1998), but controlled, long-term safety studies have not been conducted. The BHC contraindicates ginseng in pregnancy. The WHO monograph states that the safety of ginseng use during pregnancy has not been established, but it has been shown that ginseng is not teratogenic *in vivo* (WHO, 1999). **NOTE:** In TCM, ginseng root is included in prescriptions given during pregnancy, labor, and postpartum (Hu, 1977).

ADVERSE EFFECTS

There is some confusion about the relative safety of Asian ginseng in the scientific literature. After evaluating various reports published prior to 1991, the Commission E determined that there was not sufficient basis for supporting definitive adverse reactions, concluding that there were none known (Blumenthal *et al.*, 1998). One paper suggests that the relative safety of ginseng is supported by the contention that the dose required to produce adverse effects is about 1,000 times the normal effective dose (Chandler, 1988).

The WHO states, “Various researchers who studied *Radix Ginseng* extracts using conventional toxicological methods in five different animal models reported no acute or chronic toxicity of the extract. On the basis of *Radix ginseng*’s long use, and the relative infrequency of significant demonstrable side-effects, it has been concluded that the use of *Radix Ginseng* is not associated with serious adverse effects if taken at the recommended dose” (WHO, 1999). The BHC states that “Numerous studies have confirmed the safety of Ginseng; no significant toxicity or drug interactions have been reported.” (Bradley, 1992). Another leading manual for professionals (Newall *et al.*, 1996) cites a report from Japan in which Asian ginseng was administered to more than 500 people in the course of two studies with no adverse side effects reported. There is considerable difficulty in evaluating individual case reports on ginseng due to a lack of information on dose, duration, species of ginseng (reports sometimes inadequately refer to “ginseng” without citing the specific type or species) and other simultaneous medication (Newall *et al.*, 1996).

Despite the relative safety of Asian ginseng, reports surface in the literature regarding potential adverse reactions. Many writers continue to uncritically cite an uncontrolled study (Siegel, 1979) in which 133 people reportedly using some form of “ginseng” (type or identity not determined) were studied for potential adverse reactions. About 10% (14) reported hypertension, nervousness, irritability, insomnia, morning diarrhea, and related symptoms, which the author labeled as the “Ginseng Abuse Syndrome” (GAS). All subjects reporting these symptoms were determined to have taken abnormally large amounts of “ginseng” (up to 15 g per day), many with concomitantly large levels of caffeine, prompting the author to suggest a potential ginseng-caffeine synergy. The study has been discredited for being uncontrolled, for not having confirmed the identity of the purported ginseng products ingested, and because most of the symptoms of GAS are also associated with consumption of large amounts of caffeine (Blumenthal, 1991).

Other adverse effects are reported. WHO cites two cases of mydriasis, disturbance in accommodation, and dizziness that were reported from ingestion of relatively large doses (3–9g) of an unspecified ginseng product (Lou *et al.*, 1989). There is one report of vaginal bleeding resulting from the vaginal application

of a “ginseng face cream” (Hopkins *et al.*, 1988). The composition of the cream was not analyzed to determine the identity of the purported ginseng contents and what level of ginseng may have been present; it is probable that other cosmetic ingredients in the preparation, intended and approved for safety in facial dermal application, but not for mucous epithelia, were responsible. The WHO discusses reports suggesting potential estrogen-like effects in premenopausal and postmenopausal women after use of ginseng. Seven cases of mastalgia as well as increased libido in premenopausal women have been reported; however, subsequent pharmacological studies on a standardized ginseng extract suggest that there is no interaction of ginseng constituents with either cytosolic estrogen receptors isolated from mature rat uterus or progesterone receptors from human myometrium. Additionally, clinical studies on a standardized ginseng extract show that ginseng does not alter male and female hormone levels (WHO, 1999).

DRUG INTERACTIONS

The Commission E reported none known (Blumenthal *et al.*, 1998). The WHO monograph cites two cases of ginseng interaction with phenelzine, a monoamine oxidase inhibitor, although the clinical significance of this interaction has yet to be determined. Diabetic patients may need to adjust insulin dosage because ginseng may reduce blood glucose levels slightly (WHO, 1999). Positive synergistic effects of ginseng combined with zidovudine in HIV patients have been reported (Cho *et al.*, 1994). There is one case report of an interaction with warfarin resulting in a subtherapeutic decrease in clotting time (International Normalization Ratio) (Morreale and Janetsky, 1997). However, in a recent study on rats, the pharmacokinetics and pharmacodynamics of warfarin were not significantly altered with the addition of a decoction of ginseng (2 g/kg), twice daily over five days (Zhou *et al.*, 1999). The BHC cautions against using ginseng with stimulants, including excessive caffeine (Bradley, 1992). A freeze-dried hot water extract of ginseng reduced blood alcohol levels 35.2% 40 minutes after the last drink of alcohol (Brinker, 2001). Case reports and pharmacological studies suggest that ginseng saponins can alleviate some of the adverse effects of glucocorticoid drugs (e.g., prednisolone) without significantly compromising the anti-inflammatory effect of the drug (Chen *et al.*, 2003). In a clinical study ginseng extract (100 mg 2x daily) increased bacterial clearance from lungs in acute attacks of chronic bronchitis when combined with amoxicillin and clavulanic acid more than when the antimicrobial drugs were used (Brinker, 2001).

TRADITIONAL CHINESE MEDICINE (TCM)

DRUG INTERACTIONS

According to the *Chinese Pharmacopoeia*, ginseng is incompatible with the root and rhizome of hellebore (*Veratrum nigrum* and presumably other species of *Veratrum*); however, the nature of this incompatibility is not explained (PPRC, 1997). **NOTE:** *Veratrum* species are not found in herbal products in the North American market.

AMERICAN HERBAL PRODUCTS ASSOCIATION (AHPA) SAFETY RATING

CLASS 2D: Contraindicated in hypertension (McGuffin *et al.*, 1997).

REGULATORY STATUS

AUSTRIA: Official in the *Austrian Pharmacopoeia* (ÖAB, 1990) (Meyer-Buchtela, 1999; Wichtl and Bisset, 1994).

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 an over-the-counter (OTC) 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 an OTC homeopathic drug with premarket authorization and assignment of a DIN (Health Canada, 2001).

CHINA: Both white and red (steamed) dried root are official drugs in the *Pharmacopoeia of the People's Republic of China* (PPRC, 1997).

EUROPEAN UNION: Dried root containing not less than (NLT) 0.4% of combined ginsenosides Rg1 and Rb1 is official in the *European Pharmacopoeia* (Ph.Eur., 2001). The homeopathic mother tincture and dilutions thereof are also allowed in veterinary medicinal products for all food-producing animal species (EMEA, 1999).

FRANCE: Official in the *French Pharmacopoeia* (Ph.Fr.X) (WHO, 1999). Traditional Herbal Medicine for self-medication with specific indications (Bradley, 1992; Goetz, 1999).

GERMANY: Dried root containing a minimum of 1.5% ginsenosides, official in the *German Pharmacopoeia* (DAB, 1999). Dried main and lateral root, and root hairs containing a minimum of 1.5% ginsenosides, used for preparation as tea, powder, or equivalent galenical preparations, is an approved nonprescription drug of the Commission E monographs (Blumenthal *et al.*, 1998).

JAPAN: Dried root with rootlets removed is official in the *Japanese Pharmacopoeia*, and powdered root is official in the *Japanese Herbal Medicine Codex* (JSHM, 1993).

REPUBLIC OF KOREA: Quality standards for ginseng extracts are published in the Korean Food Standard Code (KMHW, 1999; Kwon *et al.*, 2000; Lee *et al.*, 1999), which maintains specific guidelines for manufacturing and for ginseng product approvals (KMHW, 2000). All herbal drugs must meet the requirements of the *Korean Pharmacopoeia*, the National Institute of Health, and the Ministry of Public Health and Social Affairs (WHO, 1998).

RUSSIAN FEDERATION: Official in the *State Pharmacopoeia of the Union of Soviet Socialist Republics* (Ph USSR X) (Bradley, 1992; Reynolds *et al.*, 1989).

SWEDEN: Classified as Natural Remedy for self-medication requiring advance application for marketing authorization. A *Panax ginseng* monograph is published in the Medical Products Agency (MPA) "Authorized Natural Remedies," which lists five registered monopreparations (e.g., Gericomplex® and Ginsana®) with the approved indication: "Traditionally used as a tonic in case of decreased performance such as fatigue and sensation of weakness" (MPA, 1999 & 2001; Tunón, 1999). Food, if no therapeutic claims are made.

SWITZERLAND: Official in the *Swiss Pharmacopoeia* (Ph.Helv.) (Meyer-Buchtela, 1999; WHO, 1999). Positive classification (List D) by the *Interkantonale Kontrollstelle für Heilmittel*, and corresponding sales Category D with sale limited to pharmacies and drugstores, without prescription (Morant and Ruppanner, 2001; Ruppanner and Schaefer, 2000; WHO, 1998).

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

U.S.: Dietary supplement (USC, 1994). Asian ginseng root and powdered Asian ginseng root, powdered Asian Ginseng extract, and ginseng tablets are official in the *U.S. National Formulary* (USP, 2002). A monograph for Asian ginseng root, dry extract, in capsules is in development (USPC, 2000).

CLINICAL REVIEW

More than 60 clinical studies on ginseng have been published with most using a dry extract (G115®) standardized to 4% total ginsenosides at a daily dosage of 200 mg. Its drug-to-extract ratio is approximately 5:1 (*w/w*) so that 200 mg of extract corresponds to about 1 g of dried root (Bone, 1998).

Twenty-nine studies are outlined in the table, "Clinical Studies on Asian Ginseng," including a total of 12,037 participants. All but five of these studies (Engels and Wirth, 1997; Engels *et al.*, 1996; Srisurapanon *et al.*, 1997; Sørensen *et al.*, 1996; Smith *et al.*, 1995) demonstrated positive effects for indications including cancer prevention, diabetes, immune support, fatigue, menopause, and circulation. The table includes 15 double-blind, placebo-controlled (DB, PC) studies. Five of these investigated the ergogenic and anti-fatigue effects of ginseng extract on physical performance (Cherdrungsi and Rungroeng, 1995; Engels *et al.*, 1996; Engels and Wirth, 1997; Le Gal *et al.*, 1996; Van Schepdael, 1993). Six DB, PC studies examined the effect of ginseng on psychological functions (D'Angelo *et al.*, 1986; Dorling, 1980; Forgo *et al.*, 1981; Fulder *et al.*, 1984; Johnson *et al.*, 1980; Sørensen *et al.*, 1996). Ginseng's immunomodulatory activity is the subject of three DB, PC studies (Scaglione *et al.*, 1990, 1997; Srisurapanon *et al.*, 1997). One DB, PC study investigated the effect of ginseng on newly diagnosed non-insulin-dependent diabetes (Sotaniemi *et al.*, 1995). Ginseng's effect on erectile dysfunction and fertility in men was the focus of two studies (Choi *et al.*, 1995; Salavati *et al.*, 1996).

A review in a popular newsletter has raised issues regarding the design and results of some of these studies (Schardt, 1999). A recent meta-analysis questioned the general effectiveness of Asian ginseng on physical performance in young, healthy volunteers (Vogler *et al.*, 1999). The meta-analysis acknowledged that nine of the 16 clinical trials reviewed concluded the "ginseng" preparation used in the trials had a positive effect. However, this review has been criticized because the authors included five different types of "ginseng": Asian, American, Japanese (*P. japonicus*), Vietnamese (*P. vietnamensis*) and eleuthero (also known as Siberian ginseng) (*Eleutherococcus senticosus*). Such reviews should focus on a homogeneous substance or in this case, one species of an herb, especially since the reviewers themselves acknowledged the chemical differences among the species (Hoegler, 2001a).

In another review (Bahrke and Morgan, 2000), researchers examined 16 clinical trials involving athletes and other healthy subjects who tested ginseng's effect on exercise performance. Criticizing the current level of ginseng research, the review's authors discussed statistical and design problems, and methodological problems such as inadequate sample size and lack of DB, PC paradigms. Studies were conducted on ginseng combined with other ingredients (e.g., herbs, vitamins), and in some cases did not specify dose, duration, or specific parameters of the ginseng preparation. The authors of this review concluded that future trials should rectify design flaws so that a reasonable conclusion can

be made about the effect of ginseng on physical performance. Another paper suggests that increasing dosage levels to be consistent with those used historically in TCM and in recent pharmacological experiments in animals would produce more positive outcomes in clinical trials measuring the ergonomic and other activities of ginseng (Dharmananda, 2002).

BRANDED PRODUCTS*

Dansk Droge Ginseng tablets: Dansk Droge A/S / Industrigrenen 10 / 2635 / Ishøj / Copenhagen / Denmark / Tel: +43-56-5656 / Fax: +43-56-5600. 100 mg or 200 mg ginseng root (ginseng composition not stated).

G115®: Pharmaton Natural Health Products / P.O. Box 368 / Ridgefield, CT 06877 / U.S.A. / Tel: 800-451-6688 / Fax: 203-798-5771 / www.pharmaton.com / Email: askpharmaton@rdg.boehringer-ingelheim.com.

Gerimax® Ginseng extract: Dansk Droge A/S / Industrigrenen 10 / 2635, Ishøj, Copenhagen / Denmark / Tel: +43-56-5656 / Fax: +43-56-5600. Internal composition of tablet not disclosed in study.

Ginsana® G115 capsules: Pharmaton Natural Health Products. One capsule contains 100 mg of standardized (4% total ginsenosides) ginseng root extract G115®. Dry extract is approximately 5:1 (w/w) so that 200 mg extract corresponds to about 1 g of dried root.

Pharmaton® capsules: Pharmaton Natural Health Products. One capsule contains 40 mg of standardized (4% total ginsenosides) ginseng root extract G115®, 26 mg dimethyl aminoethanol bitartrate, 4,000 I.U. vitamin A, 2 mg vitamin B1, 2 mg vitamin B2, 1 mg vitamin B6, 1 mcg vitamin B12, 60 mg vitamin C, 400 I.U. vitamin D, 10 mg vitamin E, 15 mg niacinamide, 2.8 mg copper sulphate monohydrate, 3.1 mg manganese sulphate monohydrate.

PKC 167/79: Pharmaton S.A. / CH-6903 / Lugano / Switzerland / Tel: +41-91-610-3111. Each capsule contains 100 mg of ginseng extract derived from an aqueous solution. Investigational product only, not available.

*American equivalents, if any, are found in the Product Table beginning on page 398.

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Clinical Studies on Asian Ginseng (*Panax ginseng* C.A. Meyer)

Cancer Prevention

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Yun and Choi, 1998	Cancer prevention	P, CC n=4,587 (mean age 55.5 years)	5 years (1987–92)	Varied	Ginseng root soup (boiled 3 hours), fresh ginseng root extract, and other dosage forms	Intake of ginseng correlated with an overall 60% reduction in risk of dying of any type of cancer compared to non-users. Fresh ginseng extract showed the strongest protective effect, with 69% risk reduction compared to non-users. The risk of gastric and lung cancers was also reduced significantly (67% and 70% protection, respectively).
Yun and Choi, 1995	Cancer prevention	E, CC n=3,974 case control study on 1,987 pairs (average ages men=53.2 years, women=49.8 years)	67 weeks	Varied	Red ginseng root, white ginseng root powder, dried white ginseng extract, fresh white ginseng extract (brands not stated)	Relative risk of cancer in ginseng group was 50% lower than for non-users. Red ginseng users had the lowest risk. Subjects taking ginseng for one year decreased the rate of cancer incidence by 36% compared to 69% in those who used ginseng for 5 years or more. In those who had used ginseng less than 50 times in their lifetime the reduction was 45%, while those who had used ginseng over 500 times had a 72% reduction. Most protective against cancer of the ovaries, larynx, esophagus, pancreas, and stomach. No significant effect on breast, cervical, bladder, or thyroid cancer.
Yun and Choi, 1990	Cancer prevention	E, CC n=1,810 905 pairs, (average ages, men=51 years, women=48 years)	5 years	Varied	Red ginseng root, white ginseng root powder, dried white ginseng extract, fresh white ginseng extract (brands not stated)	Of the cases, 62% had history of ginseng intake compared to 75% of controls; 0.56 odds ratio (OR) ($p<0.01$) of cancer in relation to ginseng intake. A dose-response relationship was observed. The higher the ginseng intake, the lower the risk of cancer. The extract and powder were found to be the most effective forms in reducing the OR.

Diabetes

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Sotaniemi et al., 1995	Non-insulin-dependent diabetes mellitus (type 2)	DB, PC, R, MC n=36 type II diabetic patients; 3 parallel groups. Average age of 100 mg group=59 years, and 200 mg group=57 years	2 months	1 tablet/day containing 100 mg ginseng/day or 200 mg ginseng/day or placebo	Dansk Droge tablets containing 100 mg ginseng root or 200 mg ginseng root (ginseng composition not stated)	Compared with baseline, both ginseng groups experienced significant improvement ($p<0.05$) in physical performance, mood, reduced fasting blood glucose levels, serum aminoterminal propeptide (PIIINP) of type 2 procollagen concentration; also experienced lowered glycated hemoglobin. But no improvement in memory or sleep. Hemoglobin A1c (HbA1c) significantly improved ($p<0.05$) in patients receiving 200 mg ginseng daily.

Fatigue/Ergogenic Effects

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Engels and Wirth, 1997	Maximal aerobic exercise	DB, PC n=36 healthy men, mean age 37 years, 3 parallel groups	8 weeks	2 or 4 capsules/day containing 100 mg extract each or placebo	Ginsana® G 115, 100 mg ginseng extract standardized to 4% ginsenosides	No significant effect on oxygen consumption, respiratory exchange ratio, blood lactic acid concentration, or heart rate ($p>0.05$). Study does not support claims that ginseng extract is an ergogenic aid to support submaximal and maximal aerobic exercise.
Engels et al., 1996	Athletic performance parameters	DB, PC, R n=19 healthy women, 21–35 years, 2 parallel groups	8 weeks	2 capsules/day containing 100 mg extract each or placebo	Ginsana® G 115	Athletic performance parameters measured included maximal work performance, oxygen uptake, respiratory exchange rate, blood lactate, and heart rate during graded cycle ergometry test to exhaustion. No significant intergroup differences in any of the measured parameters ($p>0.05$).
Le Gal et al., 1996	Functional fatigue	DB, PC, R n=232 age 25–60 years	42 days	1 capsule containing 40 mg ginseng extract G 115, 2x/day or placebo	Pharmaton® capsules	Compared to placebo, ginseng group noticed improvements in tested parameters including fatigue score at 21 days, but no significant differences noted until day 42 ($p=0.023$).

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Clinical Studies on Asian Ginseng (*Panax ginseng* C.A. Meyer) (cont.)

Fatigue/Ergogenic Effects (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Cherdrungsi and Rungroeng, 1995	Maximal oxygen uptake, leg muscle strength, body fat, resting heart rate	DB, PC n=41 healthy students, 4 parallel groups	2 months	150 mg extract, 2x/day with exercise or placebo with exercise	Asian ginseng extract (extract composition not stated)	Body fat significantly decreased in both ginseng groups compared with baseline (p<0.05): subjects in the ginseng group without exercise improved maximal oxygen uptake, resting heart rate, and leg strength compared with the placebo group without exercise (p<0.05).
Van Schepdael, 1993	Effect on physical capacity and endurance	DB, PC, CO n=43 male triathletes	20 weeks during training	1 capsule containing 100 mg extract, 2x/day	Ginsana® G 115	During first 10-week period, no significant changes were observed. In the second 10-week period, ginseng treatment appeared to prevent loss of physical fitness determined by measurement of oxygen uptake and oxygen pulse.

Immunology

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Cho et al., 1997	HIV	O, C n=26 HIV-infected patients	40–57 months with follow-up period of 41–69 months	5,400 mg/day	Korean red ginseng root powder (brand not stated)	Markers including CD4+ T-cells, serum beta2-microglobulin, soluble CD8 antigen (sCD8), and ICD p24 antigen were measured every 6 months and compared to control group. The sCD8 significantly decreased (p<0.01) in ginseng group. Study suggests that Korean red ginseng has definite long-term, immunomodulating effect without side effects on HIV-infected patients.
Srisurapanon et al., 1997	Immunomodulation parameters	DB, PC n=20 healthy men, age range 21–22, 2 parallel groups	2 months	3 capsules containing 100 mg extract/day	Ginsana® G 115	No significant intergroup differences in any tested parameters including total and differential leukocyte count, lymphocyte subpopulations CD3, CD4, CD8, CD4/8 ratio, CD19, CD25.
Scaglione et al., 1996	Immune response to flu vaccine	DB, PC, R, MC n=227 volunteers, mean age 48 years	3 months with an influenza vaccine at week 4	1 capsule containing 100 mg extract, 2x/day or placebo	Ginsana® G 115	Ginseng group experienced a significant immune response to flu vaccine with a significant rise in antibody levels and number of natural killer (NK) cells. Compared to placebo, ginseng group had significantly fewer (p<0.0001) cases of common cold or influenza. Antibody titres (p<0.0001) and NK cell activity (p<0.0001) significantly higher in ginseng group.
Scaglione et al., 1990	Immuno-modulatory effects	DB, PC, Cm n=60 healthy volunteers, 3 parallel groups	8 weeks	One, 100 mg capsule G115, 2x/day or one, 100 mg capsule PKC 167/79, 2x/day or placebo	Ginsana® G115 vs. PKC 167/79 (an aqueous ginseng extract) vs. placebo	After 8 weeks, blood samples from both ginseng groups showed significant increase in intracellular killing of polymorphonuclear leukocytes, phagocytosis, and total number of T3 and T4 lymphocytes compared with baseline and placebo, though a more significant and earlier response was seen in the G115 group. Authors concluded that ginseng extract stimulates the human immune system and that the standardized extract was more effective than the aqueous extract.

Menopausal Symptoms

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Wickland et al., 1994	Quality of life of post-menopausal women	R, PC n=NA	4 months	1 capsule containing 100 mg extract, 2x/day or placebo	Ginsana® G 115	No major impact on vasomotor symptoms. Significantly superior to placebo in enhancing aspects of well-being: vitality, alertness, mood, and relieving somatic symptoms.
Reinold, 1990	Menopausal symptoms	O, PC n=49	3 months	1 capsule containing 100 mg extract, 2x/day or placebo	Ginsana® G115	Good to very good effects on headache, dizziness, adynamia, asthenia, depression, and sleep disturbances. Unwanted side effects did not arise from taking the preparation. No changes observed in speculum exams and cytological smears from the cervix and vaginal wall.

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Clinical Studies on Asian Ginseng (*Panax ginseng* C.A. Meyer) (cont.)

Psychomotor Response/Circulatory System

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Sørensen and Sonne, 1996	Effect on cognitive functions	DB, PC, R n=112 healthy volunteers (> 40 years), 2 parallel groups	8–9 weeks	400 mg extract/day or placebo	Gerimax®	Ginseng group had non-significant tendency to faster speed of simple reactions and significantly improved abstract thinking skills compared with placebo (p<0.02). No significant differentiation in concentration, memory, or subjective experience.
Smith et al., 1995	Effect on mood and perception	PC n=19 women, 2 parallel groups	2 months	1 capsule containing 100 mg extract, 2x/day or placebo	Ginsana® G115	No significant intergroup differences in tested parameters including mood profile and rating of perceived exertion after submaximal and maximal ergometer exercise.
Rosenfeld, 1989	Psycho-physical asthenia, depressive syndrome and neurological disorder	PC n=50 24 men, 26 women (mean age 39.7 years)	56 days, 2 week wash-out or placebo	1 capsule containing 100 mg extract, 2x/day or placebo	Ginsana® G115	G115® led to clinical improvement evidenced by the positive results of the psychometric tests used: Toulouettes (changes in total scores) (p<0.01); Wechsler-Bellevue test (intelligence and cognition function) (p<0.01); SCAG questionnaire (p<0.01).
Von Ardenne and Klemm, 1987	Oxygen status of human body in the elderly	C n=6 (venous), n=10 (arterial)	1 month	1 capsule containing 100 mg extract, 2x/day or placebo	Ginsana® G115	Increase in the resting pO ₂ uptake and O ₂ transport to the organs and tissues of the body from 100% before treatment to 129% after.
D'Angelo et al., 1986	Psychomotor performance	DB, PC n=32 healthy male volunteers (20–24 years old)	3 months	1 capsule containing 100 mg extract, 2x/day or placebo	Ginsana® G115	Compared to baseline, ginseng and placebo group experienced favorable effects on attention, processing, integrated sensory-motor function, and auditory reaction time. Significant intergroup differences (p<0.05) in favor of ginseng compared to placebo in mental arithmetic test.
Fulder et al., 1984	Mental performance	DB, PC, CO n=49 with depression and reduced abilities associated with elderly senescence	20 days (10 days ginseng, 10 days placebo, with 3-week wash-out period between)	1,500 mg dried root/day or placebo	Korean red ginseng root (brand not stated)	Small improvements were noted in mood and well-being. Based on analog scales, subjects reported increased energy and alertness, but slightly worse sleep and reduced happiness. However, highly significant improvements were seen in the most objective and accurate tests of the trial: reactivity, speed, and coordination at the tapping test, and the visual, auditory, and disjunctive reaction timer. The authors concluded that ginseng can increase function in senile individuals.
Forgo et al., 1981	Effect on mental and physical functions	DB, PC n=120 60 men, 60 women, Divided by sex (male vs. female) and age, 30–39 years vs. 40–60 years)	3 months	1 capsule containing 100 mg extract, 2x/day or placebo	Ginsana® G115	Significant difference between groups in favor of ginseng in self-assessment for women, ages 30–39 years (p=0.01). Significant changes in reaction capacity, pulmonary function, and self-assessment in patients ages 40–60 years. No significant difference in tests for mood, well-being, or general health.
Dörfling, 1980	Effects on physical and mental performance	DB, PC n=60 22–80 years	90 days	1 capsule containing 100 mg extract, 2x/day or placebo	Ginsana® G115	Improvements in reaction time to visual and auditory stimuli, coordination, respiratory quotients, and length of recovery phase.
Johnson et al., 1980	Effect on mental performance	DB, PC, Cm n=38	30 days	Approximately 2 g/day	Asian red ginseng root, or American ginseng root or eleuthero root (Siberian ginseng)	All 3 types of ginseng improved proofreading performance, while only Asian and American improved mood-fatigue. None significantly affected mathematical performance or final grade performance, nor did they affect urinary concentrations of catecholamines.

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Clinical Studies on Asian Ginseng (*Panax ginseng* C.A. Meyer) (cont.)

Reproductive System, Male

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Salvati et al., 1996	Fertility in men	O, C n=66 20 normal controls; 30 with idiopathic low sperm count, 16 with low sperm count due to varicocele	3 months	4,000 mg extract/day	Brand not stated	After 3 months, all 3 groups showed a rise in sperm count, total testosterone, sperm motility, free testosterone, and dihydrotestosterone (DHT) levels. Normal control subjects showed lowest increases. Prolactin levels fell in all 3 groups.
Choi et al., 1995	Erectile dysfunction	PC, Cm n=90 patients with erectile dysfunction	3 months	3 groups: 1,800 mg/day extract or 25 mg/day trazodone or placebo	Red ginseng extract (brand not stated), vs. trazodone or placebo	Compared to trazodone and placebo, ginseng caused significant improvements ($p<0.05$) in parameters of rigidity and tumescence in erection, early detumescence, libido, and patient satisfaction. No significant changes found in frequency of coitus, premature ejaculation, or morning erection.

Respiratory System

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Scaglione et al., 2001	Acute bacterial attacks of chronic bronchitis (ACB)	R, Cm, PS n=75 (44 completed study) patients with acute attacks of chronic bronchitis (ages >18 years)	9 days	Initially 875 mg amoxicillin and 125 mg clavulanic acid 2x daily for 9 days then one group received antibiotic with 100 mg standardized ginseng extract G115 2x daily, the other group received antibacterial treatment only.	Ginsana® G115	Both groups responded positively to treatment. In ginseng group, bacterial clearance was significantly faster than in the subjects receiving antibacterials alone. Statistically significant differences between treatment groups were observed on days 4, 5, 6, and 7 ($p=0.0049$, $p=0.0104$, $p=0.0175$, $p=0.0182$, respectively). Borderline trend seen on day 8 ($p=0.0554$). Log rank test showed significant difference after analysis of time to clearance of infection ($\chi^2=6.2127$, $p=0.0127$). The authors concluded that due to the sample size, definitive conclusions could not be drawn, but the study suggests that patients with ACB may heal faster if ginseng is given with antibacterial treatment.
Gross et al., 1995	Severe chronic respiratory diseases	C, PS n=120 patients with severe chronic respiratory disease (mean age 67 years)	3 months	1 capsule containing 100 mg extract, 2x/day or placebo	Ginsana® G115	Improvement demonstrated in pulmonary functions, oxygenation capacity and walking capacity. Forced vital capacity increased from 32.1% to 72.8% ($p<0.05$), forced expiratory volume from 34.75% to 47.3% ($p<0.05$), and peak expiratory flow from 37.5% to 47.2% ($p<0.01$). Distance walked in 6 minutes increased from 600 m to 1,123 m.
Scaglione et al., 1994	Chronic bronchitis	SB, PC n=40 patients with smoker's chronic bronchitis	2 months	1 capsule containing 100 mg extract/12 hours or placebo	Ginsana® G115	Intracellular killing of alveolar macrophages increased significantly by the eighth week in the treatment group but not in the control group. The study concluded G115 restored and increased the activity of alveolar macrophages in patients with chronic bronchitis ($p<0.001$).

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