Ginseng and Immune Function

General Information:

- **Active component[s]:** Ginsenosides and water-soluble polysaccharides.
- **Source material:** Root of *Panax ginseng or Panax quinquefolius* [American ginseng].

  Note: Only use of the root of cultivated American ginseng due to endangerment.
- **Dosage route:** Oral.
- **Directions of use:** Prepare dried root as decoction.
- **Duration of use:** Consult a health care practitioner for use of *Panax ginseng* beyond 3 months (NHPD, 2009b).
- **Target Population:** Adults.
- **Risk Information:**
  - According to TCM, do not use *Panax ginseng* in cases of yin deficiency with heat signs, heat excess, or in the absence of significant qi deficiency (NHPD, 2009b).
  - Some people may experience insomnia, anxiety, or headaches, in which case, discontinue use (NHPD, 2009b).
  - There have been reports of hypertension, gastrointestinal disturbances, insomnia and nervousness, confusion and depression (Siegel, 1979).
  - Consult a health care practitioner prior to use if you are taking blood thinners, digoxin, antidepressants or have diabetes (NHPD, 2009a; NHPD, 2009b).
  - Consult a health care practitioner prior to use of *Panax ginseng* if you are pregnant or breastfeeding (NHPD, 2009b).
  - Avoid if you have a known allergy to *Panax* species (NHPD, 2009a, b).

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HUMAN HEALTH INDICATIONS:

Recommended Use or Purpose	Dosage Range
General	**Glucose levels, Mild sedative, Nervousness, and Immune System** Preparation: Dry, Powder, Decoction, Infusion and Non-Standardised Extracts 0.5-12g/day, dried powdered root **Traditional Chinese Medicine:** Prepare dried root as decoction 2.4-9g/day, root
Traditionally used in Herbal Medicine to help maintain a healthy immune system (NHPD, 2009a; NHPD, 2009b)	

GINSENG AND IMMUNE FUNCTION

The term "ginseng" has been used when referring to 3 different species of the Araliaceae family including Asian or Korean ginseng [*Panax ginseng*], American ginseng [*Panax quinquefolius* L.], and Siberian ginseng [*Eleutherococcus senticosus*]. *Panax ginseng* and *Panax quinquefolius* L. are perennial medicinal herbs from the same genus and are considered "true" ginseng (Block and Mead, 2002). *Panax ginseng* is a native to China and Korea (Xiang et al., 2008) while *Panax quinquefolius* L. is native to eastern forests of North America (Cruse-Sanders and Hamrick, 2004).

The name *Panax* was derived from the Greek words *pan* [all] and *akos* [healing] literally translating to all-healing while the Chinese word translates to "the essence of man". Documented use of ginseng dates back as far as 4000 years, and has been associated with enhanced well-being and favourable modification of illness. Ginseng has also been termed a general tonic used to maintain homeostasis as well as an adaptogen indicating it is a substance reputed to increase resistance to physical, chemical and biological stressors (Block and Mead, 2002; Carabin et al., 2000; Choi et al., 2008). The historical use of ginseng has led to the sale of natural health products containing ginseng for the treatment and prevention of common colds and the flu in modern society. Additionally, the Natural Health Products Directorate [NHPD] has issued monographs for both American and Panax ginseng recognizing their uses in traditional Chinese medicine and specifically American ginseng to help maintain a healthy immune system (NHPD, 2009).

The bioactive compounds of ginseng providing beneficial effects to immune function have been identified as saponin glycosides [ginsenosides] and water-soluble polysaccharides (Biondo et al., 2008). It is believed that ginsenosides function as antioxidants protecting immune cells against oxidative damage (Block and Mead, 2002; Zhang et al., 1996). However, a considerable amount of research attributes the immunological effects of ginseng to the water-soluble polysaccharides though the specific mechanisms of action of are not established (Vohra et al., 2008).

The results of pre-clinical research have demonstrated a wide range of effects indicating increased immune function (Jie et al., 1984; Kin et al., 1990; Lee et al., 1997; Wang et al., 2001, 2004). In spite of

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this, increased immune function *in vitro* may not translate to prevention or treatment of disease *in vivo.* Therefore several human trials have been performed to determine the clinical effects of ginseng supplementation. The effects of proprietary and non-proprietary extracts of both American and Panax ginseng root on immune function, focusing particularly on beneficial effects related to influenza and the common cold have been investigated and are described below.

Sixty healthy volunteers [age 18-50] were administered 200 mg/day of standardized *Panax ginseng* extract [G115], 200 mg/day of aqueous Panax ginseng extract [PKC 167/79], or placebo for 8 weeks. Venous blood samples taken at baseline, and weeks 4 and 8 were obtained and utilized to measure changes in parameters of leukocyte function. Eight weeks of treatment resulted in significant increases in chemotaxis, phagocytosis, blastogenesis, number of total lymphocytes and T4 cells were observed in both ginseng extract treatment groups. It is of interest to note however, that subjects treated with the standardized extract [G115] tended to experience significantly stronger beneficial effects [chemotaxis, phagocytosis, and blastogenesis], which were elicited earlier [at the fourth week for phagocytosis and T4 cell numbers] than the changes observed in the PKC 167/79 group. These results indicate the efficacy of both ginseng extracts for the enhancement of immune function as well as the superiority of effect of the standardized extract over the non-standardized aqueous extract (Scaglione et al., 1990).

Further to these results, a randomized, double-blind, placebo-controlled multi-centered study investigated the effects of the administration of 200 mg/day of *Panax ginseng* extract [Ginsana G115] for 12 weeks on immune function. Two hundred and twenty-seven subjects [mean age 48 and 48.5 for G115 and placebo respectively] were enrolled in the study with 114 subjects in the G115 group and 113 in the placebo group. An influenza vaccine was administered to all subjects on the fourth week of the study. Following 12 weeks of treatment, only 15 individuals in the ginseng treatment group experienced cases of the common cold or influenza compared to 42 in the placebo group. This indicates a significant decrease in frequency of influenza or common cold as a result of ginseng intake. Statistically significant improvements were also observed in the ginseng treatment group with respect to NK activity and antibody titers as determined by *ex vivo* testing of serum samples. However, 8 subjects in the ginseng treatment group compared to 1 in the placebo group experienced adverse events [nausea, vomiting, epigastralgia, anxiety and insomnia] which were determined to be significantly higher by Sieda et al [2009]. Nevertheless, these results indicate that ginseng treatment gave rise to a lower frequency of influenza or common cold, an increase in antibody titers, and natural killer cell activity (Scaglione et al., 1996).

A randomized, non-blinded comparative pilot study compared the effects antibacterial treatment alone to antibacterial treatment and ginseng extract on patients with acute bacterial attacks of chronic bronchitis [a cough present on most days for a minimum of 3 consecutive months over 2 or more successive years]. Subjects were administered 1750 mg/day amoxicillin and 250 mg/day clavulgaric acid for the first 9 days of the study following which they underwent randomization to either continue with antibacterial treatment, or receive 200 mg/day *Panax ginseng* extract G115 in addition to antibacterial treatment for an additional 9 days. Bronchial samples were obtained each morning throughout the study by protected expectoration and analyzed for bacterial count [number of colony forming units]. Forty-four of the 75 patients included in the trial were evaluable. On days 4, 5, 6, and 7, the ginseng treatment group was found to have a significantly lower bacterial count compared to the control group. Moreover, individuals treated with ginseng in addition to antibacterials experienced a shorter time to clearance of infection that individuals receiving antibacterial treatment alone. These results indicate that ginseng

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extract may potentially serve as an ancillary treatment to antibacterials for individuals experiencing acute bacterial attacks of chronic bronchitis (Scaglione et al., 2001).

With respect to American ginseng, a publication pooling results of 2 randomized, double-blind, trials investigated the effects of treatment with of American ginseng extract [CVT-E002] compared to placebo for the prevention of acute respiratory illness [ARI] and influenza in generally healthy elderly patients [age 60^{+}]. The studies were 8 and 12 weeks in length, and administered 200 mg twice daily of CVT-E002 [400mg/day] or placebo to residents of assisted living facilities during the flu season. The ginseng extract provided was standardized to 80% poly-furanosyl-pyranosyl-saccharides and 10% protein. Peripheral blood samples, antibody titers, laboratory safety data were measured at baseline, week 4, and after the final week of supplementation. Standardized symptom monitoring was performed twice weekly, and all adverse events were reported. Neither study demonstrated statistical significance as a low incidence of ARI led to insufficient power to detect differences with respect to incidence of ARI, and severity and duration of symptoms. After pooling of data however, a significant decrease in relative risk of acute respiratory illness was detected. Adverse events were reported did not differ significantly between groups. These results indicate that supplementation with American ginseng extract may prevent the incidence of ARI in elderly subjects (McElhaney et al., 2004).

Forty-three [43] healthy elderly patients [age 65^{+}] were randomized, in a double-blind fashion to 4 months of treatment with either a placebo [n=21] or 400 mg/day of CVT-E002 ginseng extract [n=22] to observe any potential effects for the prevention of acute respiratory illness. On a daily basis, subjects were required to record any adverse events and the presence of symptoms of upper respiratory tract infections including fever, sore throat, cough, nasal congestion, chills, headache, fatigue or aches/pains. Following 4 weeks of treatment, subjects received the influenza vaccine. No significant differences between groups with respect to duration of symptoms or adverse events after 2 months of treatment. However after 4 months of treatment, a significantly fewer proportion of subjects administered ginseng extract [32%] experienced colds compared to subjects administered placebo [62%]. This translated to a 48% decrease in relative risk of respiratory symptoms and 55% decrease in duration of respiratory symptoms. The incidence of adverse events reported by both groups was similar indicating a lack of effect in this regard and safety of ginseng intake at these levels. Overall, these results indicate that treatment with 400 mg/day of CVT-E002 may prevent acute respiratory illness in healthy seniors (McElhaney et al., 2006).

Another randomized, double-blind, placebo-controlled study involving 323 subjects administered 400 mg/d CVT-E002 or placebo for 4 months to measure its ability for the prevention of upper respiratory tract infections. Subjects were asked to complete a daily log scoring the severity of cold-related symptoms [sore throat, runny nose, sneeze, nasal congestion, malaise, fever, headaches, hoarseness, ear-aches, and cough] on a 4-point scale. A symptom score of 14 over 2 days was defined as a cold [as per modified Jackson criteria]. Statistical analysis revealed a significantly lower mean number of colds, number of recurring colds, symptom score, and number of days cold symptoms were experienced in the ginseng treatment group compared to placebo. Therefore, the use of ginseng may provide protection against the development of cold and decrease the severity of symptoms upon their occurrence (Predy et al., 2008).

To corroborate the reports of clinical trials reporting the efficacy of North American and Asian ginseng extracts for the reduction of the incidence, duration and severity of the common cold and its symptoms, a systematic review of the literature was performed. Data was compiled from 5 randomized, controlled trials administering ginseng extracts as the primary active ingredient to elderly and middle-aged subjects [n=747] (McElhaney et al., 2006; McElhaney et al., 2004; Predy et al., 2005; Scaglione et al., 1996). While

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one trial reported a significant reduction in number of colds and two trials showed significant shortened duration of colds, amalgamation of data from the 5 studies found only an *in*significant 30% decrease the incidence of colds and acute respiratory infections. In addition to these findings, this report also noted that more well-designed studies reported more conservative effects of treatment compared to studies of lower quality. This variation with respect to the efficacy of ginseng for immune function may be due to differences in standardardization or lack of standardization of ginseng root as a result of differences in method of extraction, handling, and seasonal variation (Vohra et al., 2008). Thus while there are a number of studies which indicate a benefit of ginseng on immune function, more work needs to be done in order to define mechanism and identify dose.

Safety and Toxicity:

Safe doses of ginseng have been administered safely as extract at doses up to 6 g/day (Kim and Park, 2003), and as dry ginseng root between 0.5 and 2g daily of (Ernst et al., 2002). In terms of long-term administration, 3g/day of ginseng capsules were administered for two years. At this level, subjects experienced such side effects as hypertension, gastrointestinal disturbances, insomnia and nervousness. Subjects in the same study taking very high levels [15 g/day] of ginseng reported symptoms of confusion and depression (Siegel, 1979). It has therefore been suggested that 1g of dry root daily should not be exceeded for long-term administration (Ernst et al., 2002).

Cautions, Warnings, Contraindications and Interactions

Consult a health care practitioner prior to use if you have a pre-existing medical condition, are taking prescription medication, or are pregnant or breastfeeding.

For additional information from the clinical literature regarding interactions, please refer to the following tables:

Drug	Interaction with Ginseng
Alcohol	Panax ginseng increases the clearance of alcohol (Lee et al., 1987).
Anti-platelet agents **Anti-coagulants** **Pentazocine**	Panax ginseng potentiates the effects of various drugs including anti-coagulants such as warfarin (Lee et al., 2008), the anti-platelet activity of NSAIDs such as aspirin, and pentazocine (Mitra et al., 1996).
Antidiabetic agents	Ginseng can reduce blood glucose levels (Reay et al., 2005; Sotaniemi et al., 1995) and therefore the use of both in combination use may lead to additive effects.
Phenelzine	Panax ginseng should not be combined with monoamine oxidase inhibitors such as phenelzine, as it may lead to headache, tremor and mania (Jones and Runikis, 1987).

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Natural Health Products [NHP] Substances	Interaction with Ginseng
Ginkgo biloba	Ginseng is often combined with Ginkgo biloba in formulas. When used in combination, they may cause decreases in systolic blood pressure and/or decreases in diastolic blood pressure (Kiesewetter et al., 1992).

Food	Interaction with Ginseng
Coffee **Soda** **Tea**	Controversy exists to whether caffeine and stimulants such as coffee, soda and tea are safe to consume with ginseng, as there have been rare reports of the interaction causing insomnia and headaches (Carabin et al., 2000; Fugh-Berman, 2000).

You might also be interested in our reports on:

- ✓ Ginseng and Cardiovascular Health
- ✓ Ginseng and Glucose Levels
- ✓ Ginseng and Mood
- ✓ Ginseng and Physical Performance

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