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Panax Ginseng

SCIENTIFIC NAME
Panax ginseng, synonym Panax schinseng

FAMILY
Araliaceae

CAUTION: Panax ginseng should not be confused with American Ginseng, Blue Cohosh, Canaigre, Codonopsis, Eleuthero, or Panax Notoginseng, which are sometimes referred to as ginseng. It should also not be confused with Ashwagandha, which is used as an adaptogen.

Other Common Names

- Asian Ginseng, Asiatic Ginseng, Chinese Ginseng, Chinese Red Ginseng, Ginseng, Ginseng Asiatique, Ginseng Blanc, Ginseng Blanc de Corée, Ginseng Chinois, Ginseng Coréen, Ginseng Coréen Rouge, Ginseng de Corée, Ginseng Japonais, Ginseng Oriental, Ginseng Panax, Ginseng Radix Alba, Ginseng Root, Ginseng Rouge, Ginseng Sino-coréen, Ginseng Tibétain, Guigai, Hong Shen, Insam, Japanese Ginseng, Jen-Shen, Jinsao, Jintsam, Korean Ginseng, Korean Ginseng Root, Korean Panax, Korean Panax Ginseng, Korean Red Ginseng, Korean White Ginseng, Manchurian Ginseng, Mandragore de Chine, Ninjin, Ninzin, Oriental Ginseng, Panax Coréen, Panax Ginseng Blanc, Racine de Vie, Radix Ginseng Rubra, Red Chinese Ginseng, Red Ginseng, Red Kirin Ginseng, Red Korean Ginseng, Red Panax Ginseng, Ren Shen, Renshen, Renxian, Sheng Shai Shen, Tibetan Ginseng, White Ginseng, White Panax Ginseng.

Overview

Panax is a genus of slow-growing, deciduous plants that includes 13 different species (89741). While many of these species may be referred to as "ginseng," typically the term "ginseng" is associated with the species Panax ginseng (3122,89741). Panax ginseng grows in Korea, northeastern China, and far-eastern Siberia (3122). It has been used as a calming agent in traditional Chinese Medicine (TCM) and as an "adaptogen" (3122,8600,8604,89738). Adaptogenic herbs are used with the intention of helping the body resist physiological and psychological stress.

Safety

LIKELY SAFE ...when used orally and appropriately, short-term. Panax ginseng seems to be safe when used for up to 6 months (8813,8814,17736,89741,89743,89745,89746,89747,89748,103044)(103477,114980,114981,114984,114985). Panax ginseng sprout extract has also been used with apparent safety in doses up to 450 mg daily for up to 12 weeks (114983).

POSSIBLY UNSAFE ...when used orally, long-term. There is some concern about the long-term safety due to potential hormone-like effects, which might cause adverse effects with prolonged use (12537). Tell patients to limit continuous use to less than 6 months.

There is insufficient reliable information available about the safety of Panax ginseng when used topically.

CHILDREN: **LIKELY UNSAFE** ...when used orally in infants. Use of Panax ginseng in newborns is associated with intoxication that can lead to death (12). There is limited reliable information available about use in older children (24109,103049); avoid using.

PREGNANCY: **POSSIBLY UNSAFE** ...when used orally. Ginsenoside Rb1, an active constituent of Panax ginseng, has

teratogenic effects in animal models (10447,24106,24107); avoid using.

LACTATION: Insufficient reliable information available; avoid using.

Adverse Effects

General: Orally, Panax ginseng is generally well tolerated when used for up to 6 months. There is some concern about the long-term safety due to potential hormone-like effects.

Topically, no adverse effects have been reported when ginseng is used as a single ingredient. However, a thorough evaluation of safety outcomes has not been conducted.

Most Common Adverse Effects:

Orally: Insomnia.

Serious Adverse Effects (Rare):

Orally: Anaphylaxis, arrhythmia, ischemia, Stevens-Johnson syndrome.

- ### Cardiovascular

  Panax ginseng may cause hypertension, hypotension, and edema when used orally in high doses, long-term (3353). However, single doses of Panax ginseng up to 800 mg are not associated with changes in electrocardiogram (ECG) parameters or increases in heart rate or blood pressure (96218). There is a case report of menometrorrhagia and tachyarrhythmia in a 39-year-old female who took Panax ginseng 1000-1500 mg/day orally and also applied a facial cream topically that contained Panax ginseng. Upon evaluation for menometrorrhagia, the patient also reported a history of palpitations. It was discovered that she had sinus tachycardia on ECG. However, the patient was a habitual consumer of coffee 4-6 cups/day and at the time of evaluation was also mildly anemic. The patient was advised to discontinue taking Panax ginseng. During the 6 month period following discontinuation the patient did not have any more episodes of menometrorrhagia or tachyarrhythmia (13030). Also, a case of transient ischemic attack secondary to a hypertensive crisis has been reportedly related to oral use of Panax ginseng (89402).

- ### Dermatologic

  Orally, Panax ginseng may cause itching or an allergic response consisting of systemic rash and pruritus (89743,89760,104953,114984,114985). Skin eruptions have also been reported with use of Panax ginseng at high dosage, long-term (3353). Uncommon side effects with oral Panax ginseng include Stevens-Johnson syndrome (596).

  In one case report, a 6-year-old male with a previous diagnosis of generalized pustular psoriasis, which had been in remission for 18 months, presented with recurrent pustular lesions after consuming an unspecified dose of Panax ginseng. The patient was diagnosed with pityriasis amiantacea caused by subcorneal pustular dermatosis. Treatment with oral dapsone 25 mg daily was initiated, and symptoms resolved after 4 weeks (107748). In another case report, a 26-year-old female presented with itchy exanthem and oval erythematous lesions on the face, neck, and abdomen after consuming a decoction containing Panax ginseng, aconite, ginger, licorice, Cassia cinnamon, goldthread, and peony 400 mL twice daily for 1 week. Pityriasis rosea-like eruption was suspected, but the patient refused topical or oral antihistamines or corticosteroids. The patient continued taking the decoction but with Panax ginseng and aconite removed. After 6 days, symptoms began to resolve, and by 17 days symptom improvement was significant (114986). It is unclear if this reaction was due to Panax ginseng, aconite, the combination, or some other factor. Pityriasis rosea typically resolves spontaneously.

Topically, when a specific multi-ingredient cream preparation (SS Cream) has been applied to the glans penis, mild pain, local irritation, and burning have occurred (2537).

- **Endocrine**

  The estrogenic effects of ginseng are controversial. Some clinical evidence suggests it doesn't have estrogen-mediated effects (10981). However, case reports of ginseng side effects such as postmenopausal vaginal bleeding suggest estrogenic activity (590,591,592,10982,10983).

  In a 12-year-old Korean-Japanese male, enlargement of both breasts with tenderness in the right breast (gynecomastia) occurred after taking red ginseng extract 500 mg daily orally for one month. Following cessation of the product, there was no further growth or pain (89733). Swollen and tender breasts also occurred in a 70-year-old female using Panax ginseng orally (590).

- **Gastrointestinal**

  Orally, Panax ginseng can cause decreased appetite (3353), constipation, diarrhea, dyspepsia (3353,89734,103477,112841,114980,114985), abdominal pain (89734,87984,112841,114985), and nausea (589,87984). However, these effects are typically associated with long-term, high-dose usage (3353). Some evidence suggests that fermented Panax ginseng is more likely to cause abdominal pain and diarrhea when compared with unfermented Panax ginseng (112841).

- **Genitourinary**

  Amenorrhea has been reported with oral use of Panax ginseng (3353).

  Topically, when a specific multi-ingredient cream preparation (SS Cream) has been applied to the glans penis, sporadic erectile dysfunction and excessively delayed ejaculation have occurred (2537). Less commonly, patients can experience vaginal bleeding (591,592,3354,23630).

- **Hepatic**

  It is unclear if Panax ginseng is associated with adverse hepatic effects. Cholestatic hepatitis has been reported in a 65-year old male following oral use of a combination product containing Panax ginseng and other ingredients (Prostata). However, it is unclear if this adverse effect was due to Panax ginseng, other ingredients, or the combination (598). An elevation in liver enzymes has been rarely reported in clinical research (114985).

- **Immunologic**

  A case of anaphylaxis, with symptoms of hypotension and rash, has been reported following ingestion of a small amount of Panax ginseng syrup (11971).

- **Neurologic/CNS**

  Orally, one of the most common side effects to Panax ginseng is insomnia (589,89734,111336,114985). Headache (594,23638,112840,114985), vertigo, euphoria, and mania (594) have also been reported. Migraine and somnolence occurred in single subjects in a clinical trial (87984). In a case report of a 46-year-old female, orobuccolingual dyskinesia occurred following oral use of a preparation containing black cohosh 20 mg and Panax ginseng 50 mg twice daily for menopausal symptoms. The patient's condition improved once the product was stopped and treatment with baclofen 40 mg and clonazepam 20 mg daily was started (89735).

Effectiveness

POSSIBLY EFFECTIVE

Cognitive function. In middle-aged individuals, but not young adults, oral Panax ginseng seems to improve abstract thinking, attention, arithmetic skills, and reaction time. Any benefit to memory seems to be dependent on the inclusion of ginkgo.

Details: Some clinical evidence shows that taking Panax ginseng orally can improve abstract thinking, attention, mental arithmetic skills, and reaction times in healthy, middle-aged people; however, Panax ginseng does not seem to improve these outcomes in young adults (2064,23596,23599,23608,23609,54374). While Panax ginseng alone does not seem to improve memory (2064), there is some evidence that a combination of Panax ginseng (G115) and ginkgo leaf (GK501) extract 80-320 mg daily for 12 weeks can improve memory in otherwise healthy people or people with neurasthenia 38-66 years of age (8591,9759,87984,88046). In clinical trials, various doses have been used. These include a specific Panax ginseng extract (G115, Pharmaton SA, Lugano) 200-400 mg once daily or in two divided doses for up to 12 weeks, or 200-960 mg administered as a single dose (8591,23596,23599,23608,23609,54374,88046). Another extract (Gerimax Ginseng Extract; Dansk Droge A/S Ishoj) 400 mg daily for 8 weeks has also been used (2064).

Erectile dysfunction (ED). Oral Panax ginseng seems to improve sexual function in people with ED.

Details: Taking Panax ginseng orally for 8 weeks seems to improve sexual function in adults with ED (8813,23637,23638,89747). Doses used in clinical research have included extract from the juice and pulp of 4 year-old Panax ginseng berry 700 mg twice daily (89747), tissue-cultured mountain ginseng extract 1000 mg twice daily (23638), and Korean red ginseng, a type of Panax ginseng, 1000-2700 mg daily (8813,112840).

Panax ginseng has also been studied in adults with symptoms of ED that are associated with an enlarged prostate. A small clinical study in adult males with moderate lower urinary tract symptoms shows that taking a specific extract of Korean red ginseng (RXGIN, Jung Kwan Jang), a type of Panax ginseng, 1000 mg daily for 12 weeks improves symptoms of sexual dysfunction including erectile function, sexual desire, orgasmic function, and intercourse satisfaction when compared with placebo. However, there was no improvement reported in overall satisfaction. Most symptoms of ED except sexual desire had not significantly improved by 6 weeks, suggesting that longer durations of at least 12 weeks may be needed for Panax ginseng to significantly improve ED symptoms (112840).

Additionally, Panax ginseng has been evaluated in combination with other ingredients. A moderate-sized, open-label clinical study in adults with mild-to-moderate ED shows that taking a specific combination supplement (Icarifil, Anvest Health S.p.A) containing Panax ginseng 150 mg, L-carnitine, L-citrulline, tribulus, and other ingredients daily for 3 months improves patient-reported erectile function when compared to baseline. Additionally, taking the supplement with tadalafil improves some, but not all, patient-reported assessments of erectile function when compared with taking tadalafil alone (114989). It is unclear if this effect is due to Panax ginseng, other ingredients, or the combination. Additionally, the interpretation of these results is limited by poor methodology, including the use of per-protocol analysis and lack of a placebo group.

Influenza. Oral Panax ginseng seems to modestly reduce the risk of developing influenza. However, it might not reduce the severity or duration of symptoms.

Details: Some preliminary clinical research shows that taking a specific Panax ginseng extract (G115) 200 mg daily, beginning 4 weeks prior to influenza vaccination and continuing for 8 weeks thereafter, can decrease the relative risk of getting the flu or common cold by 65% when compared with placebo (589). Also, clinical research in healthy adults shows that taking Panax ginseng extract 1 gram three times daily for 12 weeks reduces the relative risk of developing an acute influenza infection by 45% when compared with placebo. However, taking Panax ginseng does not seem to affect symptom duration or severity (89746).

Multiple sclerosis-related fatigue. Oral Panax ginseng seems to reduce fatigue and improve quality of life in patients with multiple sclerosis.

Details: Clinical research shows that taking Panax ginseng 250 mg twice daily for 3 months improves symptoms of fatigue and quality of life when compared with placebo in female patients with relapsing-remitting multiple sclerosis (RRMS). Females taking Panax ginseng experienced a 75% reduction in fatigue, compared with no change in the

placebo group; quality of life was increased by 19.9 points in the Panax ginseng group, compared with only 4.2 in the placebo group (89745).

Sexual arousal. Oral Panax ginseng, alone or in combination with other ingredients, seems to improve sexual arousal in postmenopausal adults or females with sexual dysfunction.

Details: Taking Korean red ginseng, a specific form of Panax ginseng, 3 grams daily for 8 weeks seems to improve sexual arousal and satisfaction when compared with placebo in postmenopausal adults (23630). Also, other preliminary clinical research shows that taking a specific combination product (ArginMax for Women, Daily Wellness Company) containing ginkgo leaf extract, Panax ginseng root extract, damiana leaf extract, L-arginine, multivitamins, and minerals for 4 weeks can improve sexual satisfaction when compared with placebo in females who are self-reported to have sexual dysfunction (23635,46933). It is unclear if this effect is due to Panax ginseng, other ingredients, or the combination.

POSSIBLY INEFFECTIVE

Athletic performance. Most research shows that oral Panax ginseng does not improve athletic performance.

Details: Taking Panax ginseng 0.4 to 3 grams daily orally for up to 8 weeks, or as a single dose 200 mg one hour prior to exercise, does not improve aerobic exercise capacity (1427,4230,4231,23646,23647,89737,114981). Higher doses of Panax ginseng also do not seem to improve athletic performance. A small study in young athletes shows that taking Panax ginseng 100 mg/kg (about 5-7 grams, standardized to 10% ginsenosides) daily in three divided doses for 8 days does not improve squat exercise performance, although it might modestly improve perceived exertion, when compared with placebo (103045). Similarly, a small clinical study in adult male recreational athletes shows that taking Panax ginseng extract 500 mg daily for 14 days does not improve 10-kilometer running times when compared with placebo (114981).

INSUFFICIENT RELIABLE EVIDENCE to RATE

Aging. Although there has been interest in using oral Panax ginseng for aging, there is insufficient reliable information about the clinical effects of Panax ginseng for this condition.

Anthracycline cardiotoxicity. It is unclear if oral Panax ginseng protects against anthracycline cardiotoxicity.

Details: A very small clinical study in adults with non-metastatic HER-2 negative breast cancer being treated with anthracycline-based chemotherapy in Iran shows that taking Panax ginseng rhizome powder 1000 mg daily starting on the first day of doxorubicin administration until one week after completion of the eighth doxorubicin cycle improves left ventricular ejection fraction (LVEF) by 1% when compared with placebo, which was associated with a 7% reduction in LVEF. Treatment with Panax ginseng also reduces the incidence of chemotherapy-related cardiac dysfunction when compared with placebo, an effect that endured over a 6-month follow up period. However, Panax ginseng did not improve the cardiac biomarker high-sensitive cardiac troponin I or transthoracic echocardiographic measurements of left atrium diameter, left ventricular end-systolic diameter, or left ventricular end-diastolic diameter when compared with placebo (112817).

Attention deficit-hyperactivity disorder (ADHD). Oral Panax ginseng has only been evaluated in combination with other ingredients; its effect when used alone is unclear.

Details: A small low-quality study in children with ADHD aged 6-12 years shows that taking Panax ginseng extract 3 mg with omega-3 fatty acids 500 mg daily for 12 weeks improves overall symptoms, reduces errors of commission, and improves reaction time when compared with baseline (103049). The validity of this study was limited by the lack of a comparator group. Also, it is unclear if these changes are due to Panax ginseng, omega-3 fatty acids, or the combination.

Age-related cognitive decline. It is unclear if oral Panax ginseng is beneficial in age-related cognitive decline.

Details: Clinical research in patients over 50 years of age with memory impairments shows that taking standardized ginseng extract (G115) in combination with vitamins, minerals, and dimethylaminoethanol bitartrate may

improve memory when compared to baseline (23600). The validity of this finding is limited by the lack of a comparator group. Also, it is unclear if these changes are due to Panax ginseng, other ingredients, or the combination.

Allergic rhinitis (hay fever). It is unclear if oral Panax ginseng is beneficial in allergic rhinitis.

Details: A small clinical study in adults with allergic rhinitis shows that taking Panax ginseng (Korean Ginseng Corporation) 3 mg/kg daily for 4 weeks improves rhinorrhea, nasal itch, and eye itch when compared to baseline (103047). The validity of this study is limited because it did not report statistical comparisons between the treatment and control groups.

Alzheimer disease. Some preliminary clinical studies suggest that oral Panax ginseng might improve cognitive performance in patients with this condition.

Details: Clinical research shows that taking Panax ginseng root 4.5 to 9 grams daily for 12 weeks can improve cognitive performance in patients with Alzheimer disease when compared with control (23611,23612). The validity of this finding is limited by the lack of patient and caregiver blinding.

Androgenic alopecia. Topical Panax ginseng has only been evaluated in combination with other ingredients; its effect when used alone is unclear.

Details: A small clinical study in patients with androgenic alopecia shows that applying 1 mL of a topical combination product (Hirsuit hair tonic, Dermcor Pharmaceutical) containing Panax ginseng extract, biochanin A (from red clover), acetyl tetrapeptide-3, Salvia officinalis oil, and other ingredients, twice daily for 24 weeks, is similarly effective to minoxidil 3% solution for increasing hair count and mass (105672). It is unclear if the benefit is due to Panax ginseng, other ingredients, or the combination.

Anxiety. Although there has been interest in using oral Panax ginseng for anxiety, there is insufficient reliable information about the clinical effects of Panax ginseng for this condition.

Aplastic anemia. Although there has been interest in using oral Panax ginseng for aplastic anemia, there is insufficient reliable information about the clinical effects of Panax ginseng for this condition.

Asthma. Although there has been interest in using oral Panax ginseng for asthma, there is insufficient reliable information about the clinical effects of Panax ginseng for this condition.

Benign prostatic hyperplasia (BPH). It is unclear if oral Panax ginseng is beneficial for treating lower urinary tract symptoms.

Details: A small clinical study in adults with moderate lower urinary tract symptoms shows that taking a specific extract of Korean red ginseng (RXGIN, Jung Kwan Jang), a type of Panax ginseng, 1000 mg daily for 12 weeks reduces serum prostate-specific antigen (PSA) and improves most prostate symptoms including residual urine sensation, frequency, intermittency, urgency, weak stream, straining, and nocturia after 6 and 12 weeks when compared with placebo. However, there was no improvement in maximum urinary flow rate or post-void residual volume when compared with placebo (112840).

Breast cancer. It is unclear if oral Panax ginseng is beneficial in breast cancer.

Details: Observational research in Chinese patients with breast cancer suggests that regular use of ginseng, including either Panax ginseng or American ginseng, is associated with higher quality of life scores and a lower risk of overall mortality, breast cancer-related mortality, and breast cancer recurrence when compared with patients who do not take ginseng (14466). However, ginseng users were also significantly more likely to have been treated with tamoxifen. Another small clinical study in adults with non-metastatic breast cancer undergoing anthracycline-based chemotherapy in Iran shows that taking Panax ginseng 1 gram daily starting on the first day of chemotherapy until 1 week after completion of the final cycle at 7 or 10 weeks improves social, emotional, and functional measures of health-related quality of life but does not improve physical well-being when compared with placebo (112823).

Bronchitis. It is unclear if oral Panax ginseng is beneficial in bronchitis.

Details: One small clinical study shows that taking a specific Panax ginseng extract (G115) 100 mg twice daily for 9 days might be beneficial when used adjunctively for treating acute exacerbations of chronic bronchitis. Panax ginseng, combined with antibiotic therapy, might reduce bronchial bacterial counts more than antibiotic therapy alone (8814).

Cancer. It is unclear if oral Panax ginseng is beneficial in preventing cancer. However, it might increase quality of life in some cancer patients.

Details: Observational research has found that taking ginseng orally might decrease the incidence of cancer, specifically breast, stomach, lung, liver, ovarian, and skin cancer (2063,3122). But evidence from large-scale clinical research shows that taking Panax ginseng 1 gram once weekly for 3 years does not reduce the risk of cancer development (23622). However, some clinical research suggests that Panax ginseng may slow cancer progression or improve quality of life in patients already diagnosed with cancer. One clinical study shows that taking sun ginseng, a form of Panax ginseng that has been heat treated, 3000 mg daily orally for 12 weeks can improve quality of life for cancer patients (23643). Evidence from a case series suggests that giving Panax ginseng (also called Cultivated Wild Ginseng Pharmacopuncture) 20 mL daily by intravenous infusion for up to 13 cycles lasting 2-4 weeks each may attenuate the progression of advanced non-small cell lung cancer in some patients (23619,23620).

Cancer-related fatigue. It is unclear if oral Panax ginseng is beneficial in cancer-related fatigue.

Details: Preliminary clinical research shows that taking Panax ginseng 400 mg twice daily for 4 weeks reduces fatigue in 63% of adults with cancer-related fatigue when compared to baseline. Panax ginseng also reduces pain and improves appetite and overall quality of life when compared to baseline. The lack of a control group limits the validity of these findings (96217). Another clinical study in patients with colorectal cancer receiving the mFOLFOX-6 chemotherapy regimen shows that taking Panax ginseng 2000 mg daily for 16 weeks improves fatigue as measured on the brief fatigue inventory (BFI) when compared with placebo. However, when evaluated on the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scale, no benefit was seen (103048).

Chronic fatigue syndrome (CFS). It is unclear if oral Panax ginseng is beneficial in patients with severe CFS.

Details: A nonblinded, observational study in patients with severe CFS, most of whom also have fibromyalgia, shows that taking Panax ginseng daily for one month improves patient reports of energy, overall wellbeing, mental clarity, sleep, pain, and stamina when compared with baseline. Patients took Panax ginseng either as capsules (Terry Naturally HRG80 Red Ginseng Energy capsules; EuroPharma, Inc) 200-400 mg daily or chewable tablets (Terry Naturally HRG80 Red Ginseng Energy chewable tablets; EuroPharma, Inc) 100-200 mg daily. There were no dose- or formulation-dependent differences between groups (107746). The validity of these findings is limited by the lack of randomization and placebo-control; additionally, the majority (89%) of patients included in this study were female.

Chronic kidney disease (CKD). It is unclear if oral Panax ginseng prevents CKD.

Details: A cross-sectional study in Korea suggests that supplemental Panax ginseng or American ginseng use is associated with a higher prevalence of CKD when compared with no supplemental ginseng use. However, no association was found when adjusting the results for potential confounders (112810). The applicability of these results is limited by a lack of subgroup analysis on the type of supplemental ginseng.

Cognitive impairment. It is unclear if oral Panax ginseng is beneficial for the prevention or treatment of cognitive impairment. Most research has evaluated Panax ginseng in combination with other ingredients.

Details: Preliminary clinical research in elderly patients with mild cognitive impairment shows that taking a specific combination product (Memo, Pharco Pharmaceuticals), which contains natural lyophilized royal jelly 750 mg, standardized ginkgo leaf extract 120 mg, and standardized Panax ginseng root extract 150 mg, orally for 4 weeks improves memory when compared with placebo (89712). It is unclear if these benefits are due to Panax ginseng, other ingredients, or the combination.

A moderate-sized clinical study in older adults with subjective memory impairment shows that taking a specific Panax ginseng sprout extract (ThinkGIN, BTC Corporation) 450 mg daily for 12 weeks improves performance on some verbal and visual memory tests and cognitive function as measured with MoCA-Korean version when compared with placebo (114983).

Common cold. It is unclear if oral Panax ginseng is beneficial in preventing the common cold.

Details: Preliminary clinical research shows that taking a specific Panax ginseng extract (G115) 200 mg daily orally beginning 4 weeks prior to influenza vaccination and continuing for 8 weeks thereafter can decrease the relative risk of getting the flu or common cold by 65% when compared with placebo (589).

Congestive heart failure (CHF). It is unclear if oral Panax ginseng is beneficial in CHF.

Details: A small clinical study in adults with CHF shows that Panax ginseng 2 grams daily, with or without digoxin 0.25 mg once daily for 15 days, seems to improve heart function according to New York Heart Association (NYHA) classification when compared to baseline. Ginseng might also improve hemodynamics and may work synergistically with digoxin (4243). The validity of these findings is limited by the lack of a comparator group.

Constipation. It is unclear if oral fermented Panax ginseng is beneficial for constipation.

Details: An observational study in healthy postmenopausal adults aged 50 years and older in Korea suggests that taking fermented red ginseng 20 mL before meals daily for 3 weeks normalizes stool consistency and increases the frequency of bowel movements when compared to baseline (112837). The validity of these effects is limited by the observational study design, lack of a comparator group, and insufficient blinding.

Chronic obstructive pulmonary disease (COPD). Oral Panax ginseng has primarily been evaluated in combination with other ingredients for improving symptoms of COPD; its effect when used alone is unclear. Taking Panax ginseng doesn't seem to prevent exacerbations.

Details: A meta-analysis of clinical trials in patients with stable COPD shows that taking Panax ginseng, usually in combination with other ingredients as part of TCM formulations, significantly improves pulmonary function tests and quality of life when compared with placebo after 3-6 months of treatment. These formulations improve COPD symptoms by approximately 53% when compared with placebo. However, they only modestly improve forced expiratory volume in one second (FEV1) (17736). In contrast, Panax ginseng might not reduce the risk of COPD exacerbations. A clinical study in patients with moderate to very severe COPD shows that taking Panax ginseng 200 mg does not reduce the rate of acute COPD exacerbations over 12 months (103044).

Depression. It is unclear if Panax ginseng is beneficial in depression.

Details: In adults with treatment-resistant major depressive disorder, a small clinical study shows that taking Panax ginseng 2 grams daily in addition to current antidepressant medications for 6 weeks produces remission in 39% of patients and decreases scores on the Montgomery-Asberg Depression Rating Scale by a mean of 44% when compared with baseline (104954). The reliability of these findings is limited by the lack of a control group, randomization, blinding, and an intention-to-treat analysis, as well as a high drop-out rate.

Diabetes. Research on the use of oral Panax ginseng for improving glycemic control in patients with diabetes is inconclusive and conflicting.

Details: A meta-analysis of 6 small clinical trials in patients with type 2 diabetes using Panax ginseng for 4-24 weeks and 3 small trials using American or unidentified ginseng for 4-8 weeks, shows that taking these ingredients modestly reduces fasting blood glucose, but does not affect glycated hemoglobin (HbA1c) or insulin levels, when compared with control (105689). This analysis is limited by publication bias, as well as the heterogeneity and imprecision of the included trials. Another meta-analysis of 5 clinical studies in healthy adults and adults with a variety of metabolic disorders including diabetes and prediabetes shows that taking Panax ginseng 200 mg up to 8 grams daily for 4 to 24 weeks does not improve fasting blood glucose, 2-hour postprandial blood glucose, HbA1c, or insulin levels when compared with placebo. However, Panax ginseng might improve glucose AUC in these individuals. Subgroup analysis

further suggests that the beneficial effect of Panax ginseng on glucose AUC is greater in adults with diabetes than those with prediabetes (112838).

Individual small studies have shown modest glycemic benefit with fermented Panax ginseng 2.7 grams daily for 4 weeks or non-fermented Panax ginseng 6 grams daily for 8-12 weeks (23627,89740), and other studies have shown no benefit with Korean red ginseng extract or Korean black ginseng 2-8 grams daily for 4-6 weeks (17734,112839). It is unclear if the effects of Panax ginseng may be dose- or product-dependent.

Panax ginseng has also shown some glycemic benefit when used in combination with other ingredients. Panax ginseng extract 750 mg (standardized to 30% ginsenosides) has been used in combination with American ginseng extract 1500 mg (standardized to 10% ginsenosides), viscous fiber 10 grams, and ground white chia seeds 60 grams daily for 24 weeks (105673). It is unclear if this benefit is due to Panax ginseng, other ingredients, or the combination.

Diabetic neuropathy. It is unclear if oral Panax ginseng is beneficial in diabetic neuropathy.

Details: A small clinical study in patients with diabetic neuropathy shows that taking Panax ginseng extract powder 1 gram daily for 24 weeks seems to improve sensory perception of electric currents, a marker for severity of diabetic neuropathy, when compared with baseline (103051). The validity of this study was limited by the lack of statistical comparison between treatment and placebo groups.

Exercise-induced muscle damage. Although there has been interest in using oral Panax ginseng for exercise-induced muscle damage, there is insufficient reliable information about the clinical effects of Panax ginseng for this condition.

Fatigue. Most clinical research shows that oral Panax ginseng can reduce fatigue in adults with idiopathic chronic fatigue. However, not all research agrees.

Details: Some clinical research in patients with idiopathic chronic fatigue or self-reported fatigue shows that taking Panax ginseng improves self-reported fatigue when compared with baseline or placebo (89743,23623,106665). A small clinical study in patients with idiopathic chronic fatigue shows that taking an ethanolic extract of Panax ginseng 1 gram twice daily for 4 weeks reduces self-reported fatigue by 66% and mental fatigue by 50% when compared with placebo (89743). Another clinical study in adults with chronic fatigue also shows that taking a specific combination product containing Panax ginseng (G115) 80 mg, vitamins, and minerals daily for 7 weeks alleviates fatigue symptoms in 20% more patients when compared with placebo (23623). However, not all research has been positive. A small clinical study in middle-aged patients with idiopathic chronic fatigue shows that taking Panax ginseng, steamed and aged for six years, 3 grams daily for 6 weeks is no different than placebo for reducing fatigue (103052). Notably, this clinical trial had a robust placebo effect.

Fibromyalgia. It is unclear if oral Panax ginseng is beneficial for fibromyalgia.

Details: Clinical research shows that taking Panax ginseng root extract 100 mg daily orally for 12 weeks does not improve pain, fatigue, sleep quality, anxiety, tender point count, or quality of life when compared with placebo in patients with fibromyalgia (89744).

A nonblinded, observational study in patients with fibromyalgia, most of whom also have severe chronic fatigue syndrome (CFS), shows that taking Panax ginseng daily for one month improves patient reports of energy, overall wellbeing, mental clarity, sleep, pain, and stamina when compared with baseline. Patients took Panax ginseng, either as a capsule (Terry Naturally HRG80 Red Ginseng Energy capsules; EuroPharma, Inc) 200-400 mg daily, or chewable tablet (Terry Naturally HRG80 Red Ginseng Energy chewable tablets; EuroPharma, Inc) 100-200 mg daily. There were no dose- or formulation-dependent differences between groups (107746). The validity of these findings is limited by the lack of randomization and placebo-control; additionally, the majority (89%) of patients included in this study were female.

Gallbladder disease. It is unclear if oral Panax ginseng is beneficial for gallbladder disease.

Details: Clinical research shows that taking Panax ginseng 7.5 grams as an adjuvant to the bile acids chenodeoxycholic acid (CDCA) 500 mg daily plus ursodeoxycholic acid (UDCA) 500 mg daily, divided into three doses

daily for 24 weeks, does not decrease the total volume of gallstones or increase gallstone dissolution when compared to use of bile acids alone (89748).

Gastritis. Although there has been interest in using oral Panax ginseng for gastritis, there is insufficient reliable information about the clinical effects of Panax ginseng for this condition.

Glaucoma. It is unclear if oral Panax ginseng is beneficial for glaucoma.

Details: A clinical crossover study in patients with glaucoma shows that taking oral Panax ginseng 1 gram three times daily for 4 weeks improves dry eye severity, daytime visual function, and eye pain when compared with placebo. In a sub-group of patients with early or moderate glaucoma, nighttime visual function was also improved (107744). The validity of this study is limited due to short duration of treatment.

Halitosis. It is unclear if oral Panax ginseng is beneficial for halitosis.

Details: Preliminary clinical research shows that taking Korean red ginseng, a type of Panax ginseng, 2.7 grams daily for 10 weeks helps reduce bad breath when compared with baseline, particularly in patients with bad breath caused by Helicobacter pylori (H. pylori) infection (23624). The validity of this finding is limited by the lack of a comparator group.

Hangover. It is unclear if oral Panax ginseng is beneficial for hangover.

Details: One small clinical study shows that drinking 100 mL of a drink containing Panax ginseng extract 0.321 mg/mL within 5 minutes of drinking 100 mL blended Scotch whiskey with 40% alcohol and eating a piece of cheese may reduce hangover symptoms by approximately 66% when compared with placebo in healthy males. Levels of alcohol in the blood also appear to be reduced (89742).

Hearing loss. It is unclear if oral Panax ginseng is beneficial for hearing loss.

Details: Preliminary clinical research in male textile workers exposed to continuous noise shows that taking Korean red ginseng, a type of Panax ginseng, 200 mg daily for 14 days reduces temporary hearing loss caused by noises at frequencies of 4, 6, or 16 kHz when compared with control. However, Panax ginseng may be slightly less effective than N-acetyl cysteine at preventing temporary hearing loss caused by noise at 4 kHz frequency (89739).

HIV/AIDS. It is unclear if oral Panax ginseng is beneficial for this condition.

Details: Preliminary clinical research in adults with HIV shows that taking Korean red ginseng, a particular form of Panax ginseng, along with highly active antiretroviral therapy (HAART) modestly increases CD4 count, but does not affect viral load, when compared with HAART alone (23625).

Hyperlipidemia. It is unclear if oral Panax ginseng is beneficial for hyperlipidemia.

Details: A meta-analysis of clinical studies in healthy adults and adults with a variety of metabolic disorders shows that taking Panax ginseng 200 mg to 8 grams daily for 4 to 24 weeks reduces total cholesterol by 7 mg/dL and low-density lipoprotein (LDL) cholesterol by 9 mg/dL but does not reduce triglycerides or increase high-density lipoprotein (HDL) cholesterol when compared with placebo (112838). However, a meta-analysis of up to 28 clinical studies in healthy adults and adults with a variety of metabolic disorders shows that taking Panax ginseng 300 mg to 6 grams daily for 3 to 32 weeks does not reduce total or LDL cholesterol or triglycerides or increase HDL cholesterol when compared with placebo (114985).

Hypertension. It is unclear if oral Panax ginseng is beneficial for hypertension.

Details: A meta-analysis of clinical studies in healthy adults and adults with a variety of metabolic disorders shows that taking Panax ginseng 200 mg to 8 grams daily for 4 to 24 weeks does not reduce systolic (SBP) or diastolic (DBP) blood pressure when compared with placebo. However, subgroup analysis suggests that Panax ginseng might modestly reduce SBP in people with prehypertension, hypertension, or metabolic syndrome (112838).

Smaller individual studies of various forms of Panax ginseng have been evaluated in patients with mild to severe hypertension with conflicting results. Some preliminary clinical research in patients with essential hypertension shows that taking Panax ginseng 4.5 grams daily in three divided doses, alone or with a beta-blocker or calcium channel blocker for 8 weeks, moderately decreases 24-hour SBP (23632). However, in patients with prehypertension or mild hypertension, taking protopanaxatriol-enriched Panax ginseng (Ginseol K-g1) 100 mg or 300 mg daily for 8 weeks does not reduce seated SBP or DBP when compared with placebo (89741).

Panax ginseng has also been evaluated in combination with American ginseng. Clinical studies in patients with hypertension with or without type 2 diabetes show that taking Panax ginseng 0.75 grams and American ginseng 1.5-2.25 grams enriched to contain 30% total ginsenosides daily for 12 weeks reduces central SBP by about 5 mmHg and 24-hour SBP by about 4 mmHg, but does not impact DBP, when compared with placebo or a control of wheat-bran (103046,107745). Patients receiving this combination also have greater reductions in daytime SBP, glycated hemoglobin, total cholesterol levels, and triglyceride levels when compared with control (107745). It is unclear if these effects are due to Panax ginseng, American ginseng, or the combination; additionally, it is unclear if enrichment with ginsenosides alters clinical effects.

Impaired glucose tolerance (prediabetes). It is unclear if oral Panax ginseng is beneficial for impaired glucose tolerance.

Details: In overweight adults with prediabetes, a small clinical study shows that taking hydrolyzed Panax ginseng extract, 320 mg three times daily before meals for 6 months, does not improve fasting blood glucose levels. However, compliance in this study was only 49% (104953). Additionally, a large, cross-over, clinical study in patients with prediabetes initiating a lifestyle intervention shows that taking a Chinese herbal medicine preparation containing Panax ginseng providing ginseng berry saponins 50 mg three times daily for 4 weeks improves 2-hour post-prandial glucose, but not fasting blood glucose, when compared with placebo (114980).

Panax ginseng has also been studied in combination with other ingredients. One clinical study shows that taking a combination of Korean red ginseng, a type of Panax ginseng, and cheonggukjang, a type of fermented soybean paste, 20 grams daily for 8 weeks can decrease fasting blood glucose levels by 17% in patients with prediabetes (23640). Also, taking fermented Panax ginseng 2.7 grams daily for 4 weeks reduces 2-hour postprandial glucose by about 17% and increases 2-hour postprandial insulin levels by about 44% when compared to baseline; when compared with placebo, these changes are significant (89740). It is unclear if these effects are due to Panax ginseng, other ingredients, or the combinations.

Inflammatory bowel disease (IBD). Although there has been interest in using oral Panax ginseng for Crohn disease and ulcerative colitis, there is insufficient reliable information about the clinical effects of Panax ginseng for these conditions.

Insomnia. Although there has been interest in using oral Panax ginseng for insomnia, there is insufficient reliable information about the clinical effects of Panax ginseng for this condition.

Liver disease. Although there has been interest in using oral Panax ginseng for liver diseases, there is insufficient reliable information about the clinical effects of Panax ginseng for these conditions.

Male infertility. It is unclear if oral Panax ginseng is beneficial for male infertility.

Details: Chronic prostatitis due to Chlamydia trachomatis infection is associated with reduced male fertility due to decreased sperm concentration and motility. Preliminary clinical research in adults with this condition shows that taking 25 mL of a specific product containing L-arginine 1660 mg, L-carnitine 150 mg, acetyl-L-carnitine 50 mg, and Panax ginseng 200 mg (Fertimev) along with prulifloxacin 600 mg daily for 6 months improves sperm concentration and sperm motility when compared to treatment with prulifloxacin alone (59006). It is unclear if this effect is due to Panax ginseng, other ingredients, or the combination.

Menopausal symptoms. Research on oral Panax ginseng for menopausal symptoms has yielded conflicting results.

Details: One clinical study in postmenopausal adults shows that taking Panax ginseng extract (G115) 200 mg daily orally for 16 weeks does not improve psychological well-being or reduce vasomotor symptoms such as hot flashes when compared with placebo (10981). However, several smaller clinical studies in postmenopausal adults demonstrate beneficial effects with higher doses of Panax ginseng. One study shows that taking Panax ginseng 1 gram (containing 30 mg ginsenosides) three times daily for 12 weeks reduces hot flashes and other symptoms, as measured by the Kupperman index and the Menopause Rating Scale (MRS), when compared with placebo (89749). Another study shows that taking an extract of Korean red ginseng, a specific form of Panax ginseng, 500 mg 4 times daily for 8 weeks improves fatigue severity scores by 21%, compared with 3% in those receiving placebo (106666). In premenopausal adults with menopausal symptoms following surgery for gynecologic cancer, taking Panax ginseng 1 gram three times daily for 12 weeks reduces the total symptom score on the MRS when compared with baseline. However, there was also a robust response in the placebo group, with no significant difference in symptom reduction between groups (104596).

Panax ginseng has also been evaluated for improving genitourinary syndrome and cognition after menopause. A small clinical trial in postmenopausal adults with genitourinary syndrome shows that taking a specific Panax ginseng supplement (Ruginseng, Ghaem Daru Pharmaceutical) 500 mg twice daily for 4 weeks does not affect vaginal maturation index or pH, but seems to improve patient-rated symptoms such as vaginal itching and burning, when compared with a lactose placebo (105670). This study was funded by the supplement manufacturer. In another clinical study, taking a specific combination product (Gincosan) containing Panax ginseng 200 mg and ginkgo 120 mg daily for 6-12 weeks does not improve cognition, memory, mood, anxiety, or sleep when compared with placebo (87767).

Metabolic syndrome. It is unclear if oral Panax ginseng is beneficial for metabolic syndrome.

Details: A meta-analysis of 23 clinical studies in healthy adults, menopausal adults, and adults with a variety of metabolic disorders shows that taking Panax ginseng 200 mg to 8 grams daily for 4 to 24 weeks reduces glucose area under the plasma concentration-time curve (AUC), total cholesterol, and high-density lipoprotein cholesterol, but does not improve other measures of blood glucose, insulin resistance, blood pressure, lipids, or anthropometric measures when compared with placebo (112838). Additionally, a small clinical study in adults with metabolic syndrome shows that taking Korean red ginseng, a specific form of Panax ginseng, 6 grams daily for 8 weeks modestly reduces systolic blood pressure from baseline, but not when compared with placebo. Additionally, Panax ginseng has no effect on anthropometric measurements, biochemical markers, or other vital signs when compared with placebo (106667).

Nausea and vomiting. Although there has been interest in using oral Panax ginseng for nausea and vomiting, there is insufficient reliable information about the clinical effects of Panax ginseng for these conditions.

Neuropathic pain. Although there has been interest in using oral Panax ginseng for neuropathic pain, there is insufficient reliable information about the clinical effects of Panax ginseng for this condition.

Nonalcoholic fatty liver disease (NAFLD). It is unclear if oral Panax ginseng is beneficial for NAFLD.

Details: A small clinical study in adults with NAFLD shows that taking Panax ginseng 2 grams (containing ginsenosides 4.5 mg/gram) daily for 30 days modestly reduces fatigue and plasma levels of alanine aminotransferase (ALT) and gamma-glutamyl transferase (GGT) when compared with placebo. All patients were also given milk thistle dried extract 450 mg (Legalon, Bukwang Pharmaceutical) daily and asked to exercise daily for at least 30 minutes (105671).

Oral cancer. It is unclear if topical Panax ginseng is beneficial for oral health in patients with oral cancer.

Details: A small clinical study in patients with oral cancer and poor oral hygiene shows that rinsing with a specific herbal mouthwash (Dr. Dental care liquid, Jangin Pharm Co., Ltd.) containing Panax ginseng 8 mL for 1 minute twice daily for 14 days reduces oral bacterial load and improves oral hygiene and gingival indices when compared with chlorhexidine or saline rinses (114987).

Osteoarthritis. It is unclear if oral Panax ginseng is beneficial for osteoarthritis of the hand.

Details: A small clinical study in postmenopausal adults with degenerative osteoarthritis of the hand shows that taking oral Korean red ginseng, a type of Panax ginseng, 1 gram three times daily for 12 weeks improves pain scores at rest, during daily activity, and at work or sport, and also improves disabilities of the arm, shoulder, and hand (DASH) score when compared with placebo (107747). The validity of this trial is limited due to the lack of objective outcome measures.

Pneumonia. Injectable Panax ginseng has only been evaluated in combination with other ingredients; its effect when used alone is unclear. Oral Panax ginseng has not been evaluated for this use.

Details: A meta-analysis of 20 small, low-quality randomized and non-randomized studies in older Chinese adults with severe pneumonia shows that administering an injection containing Panax ginseng extract 0.8 mg/mL and aconite extract 0.1 mg/mL in addition to standard treatment leads to improvement in symptoms such as fever, cough, and chest tightness in 77% of patients as compared with 61% of those who received standard treatment alone. This combination injection may also modestly reduce disease severity and the risk of mortality when compared with standard treatment alone. However, these outcomes were not evaluated in all studies, and dosing regimens were heterogenous (110472). Additionally, it is unclear whether these effects are due to Panax ginseng, aconite, or the combination.

Premature ejaculation. Oral Panax ginseng has primarily been evaluated in combination with other ingredients; its effect when used alone is unclear.

Details: Applying a multi-ingredient cream preparation containing Panax ginseng, angelica root, Cistanches deserticola, Zanthoxyl species, torlidis seed, clove flower, asiasari root, cinnamon bark, and toad venom (SS Cream) to the glans penis one hour prior to intercourse and washing off immediately before intercourse seems to improve ejaculatory latency in adults with premature ejaculation when compared with placebo (2537). It is unclear if this effect is due to Panax ginseng, other ingredients, or the combination.

Quality of life. It is unclear if oral Panax ginseng is beneficial for quality of life.

Details: While some research suggests that Panax ginseng might improve self-rated quality of life (6254,23644), other studies show no benefit (8601,10314). In studies showing benefit for quality of life, doses have included one capsule daily of a specific Panax ginseng extract (Pharmaton Capsules, Pharmaton Natural Health Products) for 12 weeks (6254) and Panax ginseng extract (G115) 40 mg twice daily for 12 weeks (23644).

Rheumatoid arthritis (RA). It is unclear if oral Panax ginseng is beneficial for improving symptoms of RA.

Details: A moderate-sized clinical study in patients with RA, Sjogren syndrome, or both shows that taking Panax ginseng 2000 mg daily for 3 months does not improve fatigue scores when compared with placebo (114984).

Sjogren syndrome. It is unclear if oral Panax ginseng is beneficial in patients with Sjogren syndrome.

Details: A moderate-sized clinical study in patients with RA, Sjogren syndrome, or both shows that taking Panax ginseng 2000 mg daily for 3 months does not improve fatigue scores when compared with placebo (114984).

Stress. It is unclear if oral Panax ginseng is beneficial for stress.

Details: A small clinical study in healthy patients with occupational stress shows that taking a specific Panax ginseng root preparation (HRG80) high in ginsenosides daily for 14 days modestly reduces perceived stress and improves attention and memory when compared with placebo. However, taking a standard Panax ginseng preparation with a lower quantity of ginsenosides was no better than placebo (103050). However, a moderate-sized clinical study in adult males shows that taking Panax ginseng 2000 mg daily for 8 weeks does not improve self-reported stress response when compared with placebo (114988).

Stroke. It is unclear if oral Panax ginseng prevents stroke.

Details: A small clinical study in adults with severe atherosclerosis in major intracranial arteries or extracranial carotid arteries at high risk for ischemic stroke shows that taking an extract of Korean red ginseng, a type of Panax ginseng, 1000 mg twice daily for 12 months does not prevent transient ischemic attack or ischemic stroke and does not improve neurological disability, cerebral blood flow, or the incidence of new ischemic brain lesions when compared with placebo (112835).

Traumatic brain injury (TBI). It is unclear if oral Panax ginseng is beneficial for asthenic syndrome due to TBI.

Details: A small study in adults with asthenic syndrome secondary to mild combat TBI shows that taking Panax ginseng improves autonomic nervous system functioning and asthenic symptoms when compared to baseline (112834). The validity of these effects is limited by a lack of a comparator group.

Vascular dementia. Oral Panax ginseng has only been evaluated in combination with other ingredients; its effect when used alone is unclear.

Details: A small clinical study in patients aged 60 years or older with vascular dementia shows that taking a supplement containing extracts of Panax ginseng, ginkgo, and saffron three times daily for 16 weeks modestly improves some cognitive function scores, caregiver assessed activities of daily living, and patient-reported quality of life when compared with placebo. However, these effects were not maintained after patients stopped taking the supplement (111336). Additionally, it is unclear if these effects are due to Panax ginseng, other ingredients, or the combination.

Wrinkled skin. It is unclear if oral Panax ginseng is beneficial for wrinkled skin.

Details: Preliminary clinical research shows that taking 3 grams of a combination of Korean red ginseng root with Torilus fructus and Corni fructus daily for 24 weeks may reduce wrinkles when compared with placebo. However, it does not seem to affect skin elasticity, moisture, thickness, or color (23645). It is unclear if this benefit is due to Panax ginseng, other ingredients, or the combination.

More evidence is needed to rate Panax ginseng for these uses.

Dosing & Administration

- **Adult**

  Oral:

  Panax ginseng is typically used in doses of 200 mg to 3 grams daily for up to 12 weeks. Doses of up to 9 grams have been used less often. When used for up to 16 weeks, doses of 2 grams daily have been used.
  See Effectiveness section for condition-specific information.

  Panax ginseng extract is sometimes standardized to ginsenosides. Concentrations of ginsenosides have ranged from 1% to 80% (10314,23611,23612,23646,54374,59006,89712,89744).

  Panax ginseng is thought to have stimulant effects. Theoretically, there may be an additive stimulant effect with the caffeine in foods and drinks, such as coffee and tea (589,594). Until more is known, avoid taking Panax ginseng with caffeine-containing foods and drinks.

  Topical:

  Research is limited; typical dosing is unavailable.

- **Children**

  Oral:

  Research is limited; typical dosing is unavailable.

- **Standardization & Formulation**

  In general, Panax ginseng is standardized to ginsenoside content, but the total content of ginsenosides can vary. Overall, the total ginsenoside content of Panax ginseng root or root extract can range from 1% to 80% (10314,23611,23612,23646,54374,59006,89712,89744). Extract from the pulp and juice of 4 year-old Panax ginseng berry has been standardized to contain 10% ginsenoside Re (89747). However, the contents of commercial preparations labeled as containing Panax ginseng can vary greatly; many contain little or no Panax ginseng (6,13).

  Panax ginseng is classified into one of three groups according to how processed: fresh, white, or red ginseng. Fresh ginseng is typically harvested when less than 4 years old and is used as-is. White ginseng is typically prepared by peeling and drying fresh ginseng that has been aged 4-6 years. Preparation of white ginseng does not involve steaming. Red ginseng is fresh ginseng that has typically been aged for at least 6 years. Red ginseng is prepared by steaming and drying fresh ginseng without peeling (3122,23637). There has been interest in using ginseng sprouts due to their shorter cultivation period, potentially higher content of ginsenosides, and more economically efficient production (114983).

  Panax ginseng ginsenoside content can be optimized through a variety of physical and chemical transformations. High temperature and pressure increases production of the ginsenosides Rg3, Rg5, Rg6, Rh2, Rh3, Rh4, and Rs3. These ginsenosides are usually absent or present in only small amounts in preparations of white or red ginseng (11006). Hydroponic cultivation of Panax ginseng by vertical-farming technology (FSSCC2 2000 certified standards) is said to increase the ginsenoside content by 2-3 fold (103050). Bioconverted formulations of Panax ginseng converts hydrophilic ginsenosides into hydrophobic ginsenosides Rg3, Rk1, Rg5, F2, and CK, increasing absorption speed, plasma ginsenoside concentration, total exposure, and bioavailability when compared with regular Panax ginseng (112832). Additionally, fermenting Panax ginseng increases peak concentrations, time to peak concentration, and area under the concentration-time curve (AUC) of ginsenosides compound K, compound O, compound Y, F2, Rh2, protopanaxadiol, and panaxatriol by up to 20-fold when compared with unfermented Panax ginseng (112841). Lastly, taking Panax ginseng with probiotics might increase plasma concentrations of some Panax ginseng ginsenosides (112831).

Interactions with Drugs

ANTICOAGULANT/ANTIPLATELET DRUGS

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = High • Occurrence = Unlikely • Level of Evidence = **B**

Although Panax ginseng has shown antiplatelet effects in the laboratory, it is unlikely to increase the risk of bleeding if used with anticoagulant or antiplatelet drugs.

Details

In vitro evidence suggests that ginsenoside constituents in Panax ginseng might decrease platelet aggregation (1522,11891). However, research in humans suggests that ginseng does not affect platelet aggregation (11890). Animal research indicates low oral bioavailability of Rb1 and rapid elimination of Rg1, which might explain the discrepancy between in vitro and human research (11153). Until more is known, use with caution in patients concurrently taking anticoagulant or antiplatelet drugs.

ANTIDIABETES DRUGS

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = Moderate • Occurrence = Probable • Level of Evidence = **B**

Theoretically, taking Panax ginseng with antidiabetes drugs might increase the risk of hypoglycemia.

Details

Clinical research suggests that Panax ginseng might decrease blood glucose levels (89740). Monitor blood glucose levels closely.

CAFFEINE

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = Moderate • Occurrence = Probable • Level of Evidence = **B**

Theoretically, taking Panax ginseng with caffeine might increase the risk of adverse stimulant effects.

Details

Panax ginseng has been shown to have stimulant effects (589,594). Theoretically, caffeine might have an additive effect on the stimulant effects of Panax ginseng.

CYTOCHROME P450 1A1 (CYP1A1) SUBSTRATES

Interaction Rating = **Minor** Be watchful with this combination.

Severity = Mild • Occurrence = Possible • Level of Evidence = **D**

Theoretically, Panax ginseng might decrease levels of drugs metabolized by CYP1A1.

Details

In vitro research shows that Panax ginseng can induce the CYP1A1 enzyme (24104).

CYTOCHROME P450 2D6 (CYP2D6) SUBSTRATES

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = Moderate • Occurrence = Possible • Level of Evidence = **B**

Theoretically, Panax ginseng might increase levels of drugs metabolized by CYP2D6. However, research is conflicting.

Details

There is some evidence that Panax ginseng can inhibit the CYP2D6 enzyme by approximately 6% (1303,51331). In addition, in animal research, Panax ginseng inhibits the metabolism of dextromethorphan, a drug metabolized by CYP2D6, by a small amount (103478). However, contradictory research suggests Panax ginseng might not inhibit CYP2D6 (10847). Until more is known, use Panax ginseng cautiously in patients taking drugs metabolized by these enzymes.

CYTOCHROME P450 3A4 (CYP3A4) SUBSTRATES

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = Moderate • Occurrence = Possible • Level of Evidence = **B**

Theoretically, Panax ginseng might increase or decrease levels of drugs metabolized by CYP3A4.

Details

Panax ginseng may affect the clearance of drugs metabolized by CYP3A4. One such drug is imatinib. Inhibition of CYP3A4 was believed to be responsible for a case of imatinib-induced hepatotoxicity (89764). In contrast, Panax ginseng has been shown to increase the clearance of midazolam, another drug metabolized by CYP3A4 (89734,103478). Clinical research shows that Panax ginseng can reduce midazolam area under the curve by 44%, maximum plasma concentration by 26%, and time to reach maximum plasma concentration by 29% (89734). Midazolam metabolism was also increased in animals given Panax ginseng (103478). Until more is known, use Panax ginseng cautiously in combination with CYP3A4 substrates.

ESTROGENS

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = Moderate • Occurrence = Possible • Level of Evidence = **D**

Theoretically, concomitant use of large amounts of Panax ginseng might interfere with hormone replacement therapy.

Details

Laboratory research and some case reports suggest that Panax ginseng can have estrogenic effects due to competition for estrogen receptors (590,591,592,6180,10982,10983,10984). The estrogenic activity is attributed to the ginsenoside constituents of Panax ginseng (10984).

FEXOFENADINE (Allegra)

Interaction Rating = **Minor** Be watchful with this combination.

Severity = Mild • Occurrence = Possible • Level of Evidence = **D**

Theoretically, Panax ginseng might decrease blood levels of oral or intravenous fexofenadine.

Details

Animal research suggests that taking Panax ginseng in combination with oral or intravenous fexofenadine may reduce the bioavailability of fexofenadine. Some scientists have attributed this effect to the ability of Panax ginseng to increase the expression of P-glycoprotein (24101).

FUROSEMIDE (Lasix)

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = Moderate • Occurrence = Possible • Level of Evidence = **D**

Theoretically, Panax ginseng might reduce the effects of furosemide.

Details

There is some concern that Panax ginseng might contribute to furosemide resistance. There is one case of resistance to furosemide diuresis in a patient taking a germanium-containing ginseng product (770).

IMATINIB (Gleevec)

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = High • Occurrence = Possible • Level of Evidence = **D**

Theoretically, Panax ginseng might increase the effects and adverse effects of imatinib.

Details

A case of imatinib-induced hepatotoxicity has been reported for a 26-year-old male with chronic myelogenous leukemia stabilized on imatinib for 7 years. The patient took imatinib 400 mg along with a Panax ginseng-containing energy drink daily for 3 months. Since imatinib-associated hepatotoxicity typically occurs within 2 years of initiating therapy, it is believed that Panax ginseng affected imatinib toxicity though inhibition of cytochrome P450 3A4. CYP3A4 is the primary enzyme involved in imatinib metabolism (89764).

IMMUNOSUPPRESSANTS

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = High • Occurrence = Possible • Level of Evidence = **B**

Theoretically, Panax ginseng use might interfere with immunosuppressive therapy.

Details

Panax ginseng might have immune system stimulating properties (3122).

INSULIN

Interaction Rating = **Moderate** Be cautious with this combination.

Severity = Moderate • Occurrence = Probable • Level of Evidence = **B**

Theoretically, taking Panax ginseng with insulin might increase the risk of hypoglycemia.

Details

Clinical research suggests that Panax ginseng might decrease blood glucose levels (89740). Insulin dose adjustments might be necessary in patients taking Panax ginseng; use with caution.

LOPINAVIR/RITONAVIR (Kaletra)

Interaction Rating = **Minor** Be watchful with this combination.
Severity = Insignificant • Occurrence = Unlikely • Level of Evidence = **B**

Although Panax ginseng has demonstrated variable effects on cytochrome P450 3A4 (CYP3A4), which metabolizes lopinavir, Panax ginseng is unlikely to alter levels of lopinavir/ritonavir.

Details

Lopinavir is metabolized by CYP3A4 and is administered with the CYP3A4 inhibitor ritonavir to increase its plasma concentrations. Panax ginseng has shown variable effects on CYP3A4 activity in humans (89734,89764). However, taking Panax ginseng (Vitamer Laboratories) 500 mg twice daily for 14 days did not alter the pharmacokinetics of lopinavir/ritonavir in 12 healthy volunteers (93578).

MIDAZOLAM (Versed)

Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Probable • Level of Evidence = **B**

Theoretically, Panax ginseng may increase the clearance of midazolam.

Details

Midazolam is metabolized by cytochrome P450 3A4 (CYP3A4). Clinical research suggests that Panax ginseng can reduce midazolam area under the curve by 44%, maximum plasma concentration by 26%, and time to reach maximum plasma concentration by 29% (89734). Midazolam metabolism was also increased in animals given Panax ginseng (103478).

MONOAMINE OXIDASE INHIBITORS (MAOIs)

Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Probable • Level of Evidence = **D**

Theoretically, Panax ginseng can interfere with MAOI therapy.

Details

Concomitant use of Panax ginseng with phenelzine (Nardil) is associated with insomnia, headache, tremors (617), and hypomania (618,23650).

NIFEDIPINE (Procardia)

Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Possible • Level of Evidence = **B**

Theoretically, taking Panax ginseng with nifedipine might increase serum levels of nifedipine and the risk of hypotension.

Details

Preliminary clinical research shows that concomitant use can increase serum levels of nifedipine in healthy volunteers (22423). This might cause the blood pressure lowering effects of nifedipine to be increased when taken concomitantly with Panax ginseng.

QT INTERVAL-PROLONGING DRUGS

Interaction Rating = **Moderate** Be cautious with this combination.
Severity = High • Occurrence = Possible • Level of Evidence = **B**

Theoretically, Panax ginseng has an additive effect with drugs that prolong the QT interval and potentially increase the risk of ventricular arrhythmias. However, research is conflicting.

Details

Clinical research shows that short-term use of Panax ginseng can increase the QT interval (4322,96218). However, no changes in QT interval have been identified with prolonged use (4322).

RALTEGRAVIR (Isentress)

Interaction Rating = **Moderate** Be cautious with this combination.
Severity = High • Occurrence = Possible • Level of Evidence = **D**

Theoretically, taking Panax ginseng with raltegravir might increase the risk of liver toxicity.

Details

A case report suggests that concomitant use of Panax ginseng with raltegravir can increase serum levels of raltegravir, resulting in elevated liver enzymes levels (23621).

SELEGILINE (Eldepryl)

Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Possible • Level of Evidence = **D**

Theoretically, Panax ginseng might increase or decrease levels of selegiline, possibly altering the effects and side effects of selegiline.

Details

Animal research shows that taking selegiline with a low dose of Panax ginseng extract (1 gram/kg) reduces selegiline bioavailability, while taking a high dose of Panax ginseng extract (3 grams/kg) increases selegiline bioavailability (103053). More research is needed to confirm these effects.

STIMULANT DRUGS

Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Possible • Level of Evidence = **D**

Theoretically, taking Panax ginseng with stimulant drugs might increase the risk of adverse stimulant effects.

Details

Panax ginseng has been shown to have stimulant effects (589,594).

WARFARIN (Coumadin)

Interaction Rating = **Moderate** Be cautious with this combination.
Severity = High • Occurrence = Unlikely • Level of Evidence = **B**

Panax ginseng might affect the clearance of warfarin. However, this interaction appears to be unlikely.

Details

There has been a single case report of decreased effectiveness of warfarin in a patient who also took Panax ginseng (619). However, it is questionable whether Panax ginseng was the cause of this decrease in warfarin effectiveness. Some research in humans and animals suggests that Panax ginseng does not affect the pharmacokinetics of warfarin (2531,11890,17204,24105). However, other research in humans suggests that Panax ginseng might modestly increase the clearance of the S-warfarin isomer (15176). More evidence is needed to determine whether Panax ginseng causes a significant interaction with warfarin.

Interactions with Supplements

ANTICOAGULANT/ANTIPLATELET HERBS AND SUPPLEMENTS: Theoretically, panax ginseng may have antiplatelet effects in some people; however, this is unlikely.

Details

In vitro evidence suggests that ginsenoside constituents in Panax ginseng might decrease platelet aggregation (1522,11891). However, research in humans suggests that ginseng does not affect platelet aggregation (11890). Theoretically, concomitant use with other herbs that inhibit platelet aggregation might increase the risk for bleeding. See other products with anticoagulant activity **here**.

HERBS AND SUPPLEMENTS WITH HYPOGLYCEMIC POTENTIAL: There is some evidence that Panax ginseng might lower blood glucose (23608,89740). Theoretically, concomitant use with herbs that lower blood glucose might increase the risk for hypoglycemia. See other products with hypoglycemic activity **here**.
QT INTERVAL-PROLONGING HERBS AND SUPPLEMENTS: Panax ginseng may increase the QT interval when used short-term.

Details
Clinical research shows that short-term use of Panax ginseng can slightly increase the QT interval, possibly increasing the risk of life-threatening ventricular arrhythmias (4322,96218). Using Panax ginseng with other herbs that prolong the QT interval might increase the risk for life-threatening ventricular arrhythmias (11355). See other products with this activity **here**.

Interactions with Conditions

AUTOIMMUNE DISEASES

Theoretically, Panax ginseng might exacerbate autoimmune diseases by stimulating disease activity; until more is known avoid or use with caution in patients with autoimmune diseases such as multiple sclerosis (MS), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), or others. Panax ginseng seems to stimulate immune function (3122).

BLEEDING CONDITIONS

Theoretically, Panax ginseng might increase bleeding; until more is known avoid in cases of hemorrhage or thrombosis. Panax ginseng has been reported to decrease blood coagulation (3122).

CARDIAC CONDITIONS

Theoretically, Panax ginseng might increase adverse cardiovascular effects; until more is known use with caution in patients with cardiac conditions. Panax ginseng can slightly increase the QT interval and slightly decrease diastolic blood pressure in healthy adults on the first day of therapy. However, there are no changes with prolonged use (4322).

HORMONE SENSITIVE CANCERS/CONDITIONS

Theoretically, Panax ginseng might increase the development of hormone-sensitive tumors; until more is known avoid in patients with hormone-sensitive conditions such as breast cancer, uterine cancer, ovarian cancer, endometriosis, and uterine fibroids. Preliminary evidence shows that Panax ginseng can have estrogenic effects (590,591,592,6180,10982,10983,10984). The estrogenic activity is attributed to the ginsenoside constituents of Panax ginseng (10984).

IMMUNOSUPPRESSION

Theoretically, taking Panax ginseng might interfere with immunosuppressive therapy; avoid use. Panax ginseng might have immune system stimulating properties (3122).

INSOMNIA

Theoretically, Panax ginseng might worsen insomnia; use with caution. High doses of ginseng have been associated with insomnia (597).

SCHIZOPHRENIA

Theoretically, Panax ginseng might worsen some symptoms; use with caution. High doses of ginseng have been associated with insomnia and agitation in people with schizophrenia (597).

Interactions with Lab Tests

DIGOXIN SERUM ASSAY

Taking Panax ginseng can result in false digoxin levels on some assays. Use of Panax ginseng falsely elevates serum digoxin concentrations when fluorescence polarization immunoassay (FPIA) or the Abbott Digoxin III assay are used, and falsely lowers digoxin concentrations when microparticle enzyme immunoassay (MEIA) is used (15585,15587,16417). This interference is due to the structural similarities of some ginsenosides to cardiac glycosides (15585,15587,16417). Interference does not occur when digoxin levels are measured with an enzyme multiplied immunoassay (EMIT), the Randox digoxin assay, a chemiluminescent assay (CLIA), the Roche Tina-Quant turbidimetric inhibition immunoassay, or the Beckman Synchron LX assay (15585,15587,16417).

Overdose

Presentation

There is limited information available about the presentation of overdose with Panax ginseng. In one case report, reversible cerebral arteritis occurred in a 28-year-old female who ingested dried ginseng extract 23 grams (595).

Treatment

There is insufficient reliable information available about the treatment of overdose with Panax ginseng.

Pharmacokinetics

Absorption: Ginsenosides seem to have a low oral bioavailability in humans and animal models (11153,17734). In human research, following ingestion of Panax ginseng or ginsenoside Re, the ginsenosides Re, Rb1, and Rb2 were not detectable in blood samples taken over 0.5-6 hours. However, ginsenosides may have been present at concentrations below the lower limit of detection (8 ng/mL) (17734).

Intestinal microflora transforms ginsenosides by deglycosylation, which seems to improve absorption by converting hydrophilic ginsenosides into hydrophobic ginsenosides. For example, ginsenosides Rb1, Rb2, and Rc are cleaved into ginsenoside compound K, which is better absorbed than its parent ginsenosides. The extent of intestinal deglycosylation of ginsenosides seems to vary significantly between individuals (59840,89884,105669,112831).

However, individual variation in ginsenoside absorption can be bypassed to increase ginsenoside absorption and enhance pharmacokinetic properties. Bioconverted formulations of Panax ginseng convert hydrophilic ginsenosides into hydrophobic ginsenosides Rg3, Rk1, Rg5, F2, and CK, increasing maximum concentration (Cmax), area under the concentration-time curve (AUC), bioavailability, and absorption and reducing time to peak concentration (Tmax) when compared with regular Panax ginseng formulations (112832). Fermenting Panax ginseng has similar pharmacokinetic effects on ginsenosides compound K, compound O, compound Y, F2, Rh2, protopanaxadiol, and panaxatriol when compared with unfermented Panax ginseng. Fermentation led to a 20-fold increase in peak concentrations of compound K and Rh-2 when compared with unfermented Panax ginseng. Additionally, ginsenosides CY and F2 that were below quantifiable levels in unfermented Panax ginseng were detected after fermentation (112841).

In humans, after oral administration of ginsenoside Rb1 and ginseng extracts, the time to maximum concentration of ginsenoside compound K occurs at about 10-11 hours, with a maximum concentration of about 1.7-28 ng/mL (89884,105669).

Elimination: In humans, consuming a single oral dose of Panax ginseng extract 2.95 grams results in a ginsenoside compound K half-life of about 10.2 hours. Consuming a single dose of ginsenoside compound K 600 mg results in a

half-life of about 8.7 hours (105669).

In rats, the distribution and elimination of Rg1 and Re were rapid after intravenous infusion, and the pharmacokinetic characteristics indicate a two-compartment model (11153). In rats, orally administered ginsenosides were mainly eliminated by first-pass biliary excretion (59840).

Mechanism of Action

General: The applicable part of Panax ginseng is the root. Panax ginseng contains several active constituents. The constituents thought to be of most importance are triterpenoid saponins, which are referred to collectively as ginsenosides or panaxosides. Numerous subtypes of ginsenosides have been identified from Panax ginseng and are structurally classified as protopanaxadiol, protopanaxatriol, or oleanane depending on the position of their sugar molecules (89788,89789,89790,89791,89792,89793,89794,103478,112832). Panax ginseng also contains the peptidoglycans, panaxans (12536) and water insoluble polyacetylenic constituents such as panaxynol, panaxydol, and panaxytriol (11005,89773). Other constituents include pectin, flavonoids, proteins, amino acids, alkaloids, fatty acids, saccharides, phytosterols, vitamins (thiamine, riboflavin, niacin, biotin, pantothenic acid, folic acid, B12), and minerals (manganese, copper, vanadium, cobalt, phosphorus, aluminum, nickel) (11,104955).

Alcohol clearance effects: In healthy males, Panax ginseng extract reduces hangover symptoms (89742). This is possibly due to improved alcohol clearance. Panax ginseng increases alcohol clearance in humans by 30% to 50%, likely by enhancing the metabolic activity of alcohol dehydrogenase (12191).

Anti-aging effects: In human research, Panax ginseng increases the copy number of mitochondrial DNA (mtDNA) when compared with placebo. A reduction in mtDNA copy number is considered a marker of biological aging (106666).

Anti-arthritis effects: Evidence from animal research suggests that a red ginseng saponin extract containing ginsenosides Rg3, Rk1, and Rg5 reduces symptoms of collagen-induced arthritis, including swelling and joint space narrowing. It is proposed that Panax ginseng attenuates arthritis by inhibiting the expression of matrix metalloproteinase-3, an enzyme that appears to correlate with arthritis progression, and reducing levels of inflammatory cytokines, including tumor necrosis factor-alpha and interleukin-1beta (89796).

Anti-asthmatic effects: There is evidence that ginsenosides can relax human bronchial smooth muscle in vitro by stimulating the release of nitrous oxide from airway epithelium, which may account for the potential anti-asthmatic effect of Panax ginseng (11007). Also, ginsan, a polysaccharide derived from Panax ginseng, has been shown to reduce airway hyperresponsiveness in an animal asthmatic model, possibly by reducing levels of some inflammatory cytokines and increasing levels of prostaglandin E2 (89767).

Antibacterial effects: Some people try ginseng for cystic fibrosis because there is preliminary evidence that it has activity against Pseudomonas aeruginosa lung infections. However, this effect has not yet been demonstrated in humans (3095,3096).

In animal research, mice treated with ginsan, a polysaccharide derived from Panax ginseng, prior to a bacterial challenge of Staphylococcus aureus were protected from sepsis. This protective effect may be due to early suppression of acute inflammatory responses and later enhancement of macrophage activity (89768).

Anti-cancer effects: Panax ginseng might have antitumor activity (3122). In human research, the potential anti-cancer effects of Panax ginseng have been shown in epidemiological (2063,3122) and preliminary clinical (23619,23620) research. Antineoplastic effects of ginseng have also been found in laboratory research; cell proliferation is inhibited in vitro and tumor size is reduced in animal models (89771,89772,89799,89800). The nature of this mechanism is poorly understood, but ginsenosides Rg3, Rg5, and Rh2 are active components that may prevent cancer, either singularly or synergistically (89797). Extracts of Panax ginseng decrease the production of tumor necrosis factor (TNF), diminish DNA strand breakage, and inhibit the formation of induced skin tumors in laboratory models (11006). There is conflicting research about the antioxidant and free radical scavenging activity of Panax ginseng; however, this may also play a role in its anti-cancer effects (4227,8602). Ginsenosides have been shown to inhibit tumor cell invasion and suppress sister chromatid exchanges in human lymphocytes (11006). The Panax ginseng constituent panaxydol seems to inhibit the

proliferation of various types of cancer cells by inhibiting cancer cell growth at the cell cycle G1 to S transition phase (11005). Also, intestinal metabolites of Panax ginseng constituents may interfere with tumor cell processes (89809,89811,89812,89813). In general, the anti-cancer effects of Panax ginseng and its constituents may be due to immunomodulating effects (89798), phase 2 enzyme induction (89808), inhibition of intra-cellular pathways involved in cancer progression (89802,89803,89804,89805,89806,89810), and stimulation of pathways involved in cell differentiation and apoptosis (89774,89775,89801,89804,89807).

Antidepressant effects: Panax ginseng is traditionally used for depression and anxiety. In laboratory research, Panax ginseng constituents have been shown to reduce depression and increase social interactions (89848,89849). A reduction in brain oxidative stress and downregulation of serum corticosterone levels may play a role (89849).

Antidiabetes effects: Animal research suggests that long-term Panax ginseng berry extract use with metformin might increase metformin concentrations in the liver without altering other pharmacokinetic parameters, thereby enhancing efficacy without increasing the incidence of adverse effects. When taken with metformin, Panax ginseng berry extract upregulates mRNA expression of organic cation transporter-1 (OCT1), which increases metformin uptake from the blood to hepatocytes. There is also reduced mRNA expression of multidrug and toxin extrusion-1 (MATE1), which inhibits the efflux of metformin into bile and therefore reduces biliary excretion of metformin. Higher hepatic metformin concentrations are associated with enhanced inhibition of gluconeogenesis, increasing metformin's efficacy in treating type 2 diabetes.

Additionally, Panax ginseng berry extract did not change kidney mRNA levels of OCT1, OCT2, MATE1, or MATE2-K, which are all implicated in the metformin's primary elimination pathway, renal excretion. The lack of effect on the kidneys suggests minimal toxic effects, namely lactic acidosis and fluid retention (112836).

Antiemetic effects: Panax ginseng is commonly used for gastritis and vomiting. Animal research suggests that Panax ginseng extract has antiemetic effects (89753,89815). The mechanism of action may be related to the constituent panaxatriol. In vitro, this constituent inhibits the recombinant serotonin type 3A receptor, which is believed to mediate nausea and vomiting (89751).

Anti-fatigue effects: In human research, the anti-fatigue effects of Panax ginseng are thought to be at least partially related to its antioxidant effects. Panax ginseng decreases serum reactive oxygen species and measurements of oxidation, and increases antioxidant status, although activities of antioxidant enzymes are not affected (89743). The antioxidant effects of Panax ginseng also played a role in anti-fatigue effects of Panax ginseng in an animal model (689). Additionally, a moderate-sized clinical study in adults shows that taking red ginseng capsules 1400 mg daily for 8 weeks decreases blood lactic acid and creatine phosphokinase levels after inducing exercise fatigue when compared with placebo. However, there was no effect on cortisol level. Researchers theorize that the reduction of creatine phosphokinase delays physical fatigue while the reduction in lactate prevents peripheral fatigue and the accumulation of tissue-damaging free radicals (112842).

Anti-fungal effects: Panaxagin, a protein isolated from unprocessed Panax ginseng root, seems to have antifungal activity, according to preliminary research. It appears to inhibit ribosomal activity of some fungi (8603).

Anti-inflammatory effects: Panax ginseng has been shown to reduce muscle injury and inflammation following exercise in laboratory (89770) and human (89738) research. The anti-inflammatory effects of Panax ginseng are likely related to the inhibitory effects of ginsenosides on inflammatory cytokines (89782,89817), inducible nitric oxide synthase (89817), and inflammatory eicosanoids (89817). However, a clinical study in healthy adults shows that taking Panax ginseng does not improve serum biomarkers associated with inflammation including high-sensitivity C-reactive protein or interleukin-6 (112839,114983).

Antioxidant effects: The antioxidant effects of Panax ginseng constituents are thought to play a role in its various clinical effects, including its anti-cancer and anti-inflammatory effects, as well as its ability to improve symptoms of fatigue and increase performance. Panax ginseng has antioxidant activity in human research (4227,89754,106666). This is thought to be due to ginsenoside content, which has the ability to activate antioxidant enzymes (89779,89820) and scavenge or suppress free radicals (89780,89818,89819).

Anti-platelet effects: Ginsenosides and other Panax ginseng constituents, such as panaxynol, seem to interfere with platelet activation, aggregation, and coagulation in vitro (1522,89736,89821,89822). Also, non-saponin constituents of

Panax ginseng inhibit the response of platelets to thrombin as well as platelet activation (1522,89758).

Anti-stress effects: Ginseng is widely used as a general tonic or "adaptogen" for fighting stress. There is some evidence that it might work against stress by affecting the hypothalamic-pituitary-adrenal (HPA) axis. Panax ginseng saponins seem to increase serum cortisol concentrations in animal models (3256,3257). Other clinical research in patients with increased stress shows that taking Panax ginseng daily for 2 months attenuates the decreases in serotonin and increases in cortisol occurring during stress when compared with placebo (114988).

Antiulcer effects: Ginseng is widely used as a general tonic or "adaptogen" for fighting stress. There is some evidence that it might work against stress by affecting the hypothalamic-pituitary-adrenal (HPA) axis. Panax ginseng saponins seem to increase serum cortisol concentrations in animal models (3256,3257). Other clinical research in patients with increased stress shows that taking Panax ginseng daily for 2 months attenuates the decreases in serotonin and increases in cortisol occurring during stress when compared with placebo (114988).

Anti-viral effects: A few studies indicate that ginseng may have antiviral activity in both humans and animals. Clinical research suggests that taking Panax ginseng reduces the frequency of developing an acute respiratory illness, such as the common cold or influenza (589,89746). Panaxagin, a protein isolated from unprocessed ginseng root, seems to have antiviral activity, according to preliminary research; it appears to inhibit HIV reverse transcriptase (8603). Also, Panax ginseng induces deletions in the HIV virus, coinciding with an increase in CD4 T cell counts and CD4:CD8 ratios (89826,89827). The anti-rotavirus effects of Panax ginseng appear to be due to pectic polysaccharide constituents, which may inhibit binding of the virus to cells (89825).

Auditory effects: In individuals exposed to continuous noise, preliminary clinical research suggests that taking Panax ginseng improves the hearing threshold at most frequencies tested (89739). In an animal model, Panax ginseng and compound K reduced threshold shifts, central auditory function damage, and cochlear functional and morphological deficits in noise-induced hearing loss in mice (89828). Although a mechanism is unclear, Panax ginseng may increase cell viability of auditory cells in an ototoxicity model, possibly by attenuation of increases in reactive oxygen species and resulting prevention of apoptosis (89776).

Blood pressure effects: There is contradictory evidence about the effects of Panax ginseng on blood pressure in patients with hypertension. It appears that, although taking Panax ginseng 4.5 grams may moderately decrease systolic blood pressure in patients with essential hypertension (23632), taking Ginseol K-g1 does not reduce blood pressure when compared with placebo in patients with prehypertension or stage I hypertension (89741). It is possible that these discrepant results are related to the types of ginsenosides in the products. The ginsenosides have a wide range of pharmacological activity and effects. In some cases, these isolated constituents seem to counteract each other's activity. For example, ginsenoside Rg1 raises blood pressure and ginsenoside Rb1 lowers blood pressure. In animal models ginsenosides had biphasic actions on vascular response and blood pressure (11,89763). Some of the blood pressure effects may be due to a relaxing effect on smooth muscle induced by certain ginsenosides (89763,89778,89829). Also, in vitro, Panax ginseng extract inhibited angiotensin-converting enzyme (ACE) activity, although nitric oxide (NO) production was not affected (89766).

Cardiovascular protective effects: In some human research, Panax ginseng appears to have negligible effects on cardiovascular function (4322). However, an intravenous formulation of ginseng seems to increase ejection fraction in patients with congestive heart failure. Ginseng might improve hemodynamics and might work synergistically with digoxin (4243,8604). Orally, ginseng improves coronary flow reserve in patients following myocardial infarction, possibly by increasing the number of angiogenic cells (89835). In healthy humans, Panax ginseng improves arterial stiffness (89882).

Cardioprotective effects have also been shown in laboratory research. In animal models, Panax ginseng reduced the susceptibility to arrhythmias (89833), improved heart function (89755,89834), and decreased infarction size (71225). Some of these benefits may be due to a relaxing effect on smooth muscle induced by certain ginsenosides (89763,89778,89829). Also, various constituents of ginseng have been shown to prevent the development of atherosclerosis through inhibition of signaling pathways in various cells, such as endothelial, vascular smooth muscle, cardiomyocytes, and dendritic cells (89830,89831,89832,89837,89883).

Some ginsenosides have structural similarities to cardiac glycosides and can interfere with measurement of serum digoxin levels by some assay methods (15585,15587). However, it is not clear whether Panax ginseng has any of the

pharmacological effects of cardiac glycosides.

Central nervous system effects: In human research, the anti-fatigue effects of Panax ginseng are thought to be at least partially related to its central nervous system effects. However, in some cases, ginsenosides seem to counteract each other's activity. For example, ginsenoside Rg1 acts as a central nervous system (CNS) stimulant and ginsenoside Rb1 acts as a CNS depressant (11). CNS-stimulating effects of Panax ginseng have been found in animal models (89839).

Cytochrome P450 effects: There is some evidence that a Panax ginseng root extract can mildly inhibit cytochrome P450 2D6 (CYP2D6) activity by approximately 6% in humans. However, contradictory research suggests Panax ginseng might not significantly inhibit CYP2D6. Panax ginseng appears to have no effect on CYP1A2 activity (1303,10847).

Dermatologic effects: Panax ginseng is part of an oral formulation used to reduce skin wrinkling in aging individuals (23645). It is also traditionally used for wound healing. Laboratory research suggests that effects on skin may be due to accelerated fibronectin synthesis in skin fibroblasts and in skin (89851,89852), as well inhibited collagen degradation (89878) and increased ceramide levels (89879). Anti-inflammatory effects in skin lesions of animal models have also been shown (89880,89881).

Gastrointestinal effects: An observational study in healthy postmenopausal adults aged 50 years and older in Korea shows that taking red ginseng fermented with Lactobacillus plantarum and L. brevis 20 mL before meals for 3 weeks normalizes stool consistency and increases the frequency of bowel movements. Fermented red ginseng is also associated with changes in 20 bacterial species which correlate with 16 metabolic pathways. Researchers theorize that the probiotics provided by the fermentation process or probiotics taken in addition to Panax ginseng facilitate the growth of certain bacterial species that enhance ginsenoside absorption through deglycosylation metabolism in the intestines (112831,112837).

Hepatoprotective effects: Ginseng may be beneficial for liver health. In humans, taking Panax ginseng improves levels of some liver enzymes in patients with elevated levels (103477). In addition, both Panax ginseng and its constituents have demonstrated protective effects against hepatic injuries in animal models (89853) possibly via antioxidant activity (89784,89785) and/or inhibition of inflammatory mediators (89785).

Hypoglycemic effects: Panax ginseng may affect blood glucose. The effect of Panax ginseng on blood glucose may vary with batches, plant parts, and preparation methods (12536). Panax ginseng might reduce or increase fasting blood glucose concentrations and test results (12536,23626,23629,89740). However, other research shows that Panax ginseng has no effect on blood glucose (23628). In human research, Korean red ginseng root lowers post-prandial blood glucose in healthy individuals with normal glucose levels; however, the rootlets with higher ginsenosides levels do not (89732). Also, preliminary evidence suggests that Panax ginseng might reduce tissue insulin resistance and changes in gene expression in type II diabetes (8605).

The effect of ginseng on glucose appears to be related in part to the mix of ginsenosides. Other non-ginsenoside constituents likely affect blood glucose as well. Panax ginseng and other ginsengs contain protopanaxadiol (PPD) ginsenosides, Rb1, Rb2, Rc, and Rd. They also contain protopanaxatriol (PPT) ginsenosides, Rg1, Re, and Rf. A higher ratio of PPD ginsenosides to PPT ginsenosides is related to greater blood glucose and insulin lowering potency of the ginseng product. Compared with American ginseng, Panax ginseng appears to have a lower PPD to PPT ratio and may have less blood glucose. Some research suggests Panax ginseng may actually increase postprandial blood glucose and lower preprandial insulin levels. However, ginsenoside content varies among batches, plant parts, and preparation methods (12536). Panax ginseng contains the peptidoglycans, panaxans, which have hypoglycemic effects in human research (12536). The malonyl-ginsenosides, found in Panax ginseng roots, also reduce blood glucose levels in an animal diabetic model (89814).

Immune effects: Panax ginseng might affect immune function. Both suppression and enhancement of humoral and cellular immunity have been reported in laboratory research due to ginseng extracts; discrepancy may arise from the difference in dose levels, composition, and duration of therapy (89855,89856,89857). Panax ginseng appears to stimulate natural-killer cell activity and possibly other immune-system activity. In animal research, ginseng has been shown to enhance cellular immune function by stimulating natural killer cell activity (10725,89857,89858) and increasing antibody production (89857). Panax ginseng has also been shown to stimulate the activity of macrophages in laboratory research (89859,89863), as well as lymphocytes in general in elderly humans (89861) and laboratory research (89862,89863). In

healthy adults, taking Panax ginseng 2 grams daily for 8 weeks increases T-cell, B-cell, and white blood cell counts when compared with placebo (104955).

Mechanisms of action likely relate to stimulation of inflammatory mediators (89859,89860,89863,89865) and production of nitric oxide (89859). The panaxanes have been implicated in some of the immunomodulatory effects of Panax ginseng (89863). The ginsenosides also play a role; however, different ginsenosides may modulate lymphocyte proliferation in a different manner (89864). Also, there is evidence to suggest that some of the ginsenosides, especially Rh1, may inhibit immune function and inflammatory mediator activity resulting in anti-allergic effects (89769,89795).

Lipid effects: Ginseng might lower lipid levels, but research is conflicting. In some human (12538,89759,102238,114981) and animal (89759,89867) research, Panax ginseng lowered serum cholesterol and/or triglyceride levels, possibly by increasing lipoprotein lipase activity, which enhances lipid metabolism (12538). However, other clinical research in humans shows that Panax ginseng red or black extracts do not change total cholesterol, triglycerides, high-density lipoprotein cholesterol, or low-density lipoprotein cholesterol when compared with placebo (112839). The conflicting results may be due to the differential effects of various ginsenosides. For example, ginsenoside Re has been shown to reduce cholesterol while Rb1 has been shown to increase it in laboratory research (89866).

Memory effects: Some clinical evidence shows that taking Panax ginseng orally can improve abstract thinking, attention, mental arithmetic skills, and reaction times in healthy, middle-aged people; however, Panax ginseng does not seem to improve these outcomes in young adults (2064,23596,23599,23608,23609,54374). While Panax ginseng alone does not seem to improve memory (2064), there is some evidence that a combination of Panax ginseng and ginkgo leaf extract can improve memory in otherwise healthy people or people with neurasthenia ages 38 to 66 years (8591,9759,87984,88046). In healthy individuals, Panax ginseng can directly modulate cerebroelectrical activity (89838).

The mechanism of action of Panax ginseng is likely related to its ginsenoside constituents. The ginsenoside Rb1 has been suggested to exert its memory effects by minimizing the inhibitory effects of beta-amyloid peptides, which are thought to play a role in memory degeneration (89840). However, neither Rb1 nor Rg1 reversed beta-amyloid-induced cell death (89841). Ginsenoside administration has also been shown to prevent memory impairment in various animal models (89842,89843,89844,89847), possibly by up-regulating plasticity-related proteins in the hippocampus (89842) or by reducing inflammatory signaling (89844). In one memory model, the ginsenosides Rg1 and Rb1 both improved memory; however, the mechanisms of action were considered to be different. Although both ginsenosides increased hippocampus levels of acetylcholine, only Rg1 inhibited acetylcholinesterase activity. Rb1 had a greater effect on maintaining serotonin levels (89846). Other authors suggest the glycemic properties of Panax ginseng may play a role in its cognitive enhancement (23608,23609).

Neuroprotective effects: In human research, Panax ginseng root can improve cognitive performance in patients with Alzheimer's disease (23611,23612) and in older adults with subjective memory impairment (114983). The neuroprotective effects of Panax ginseng may play a role in the improved performance in these patients. In laboratory research, ginsenosides have been shown to potentiate nerve growth factor and brain derived neurotrophic factor (11,89870) and might confer neuroprotection through nicotinic activity (3109). Ginsenosides have also been shown to inhibit tau hyperphosphorylation (89868). Ginsenosides may also protect against apoptosis of nerve cells (89869,89871) and inflammatory processes in microglial cells (89783). Clinical research shows that taking Panax ginseng sprout extract daily for 3 months decreases acetylcholinesterase levels in the blood (114983).

Respiratory effects: Panax ginseng is traditionally used for asthma. In human research, bronchodilation occurred in most healthy individuals tested (23599). In laboratory research, ginsenosides have been shown to induce a nitric oxide-mediated relaxation effect in bronchial smooth muscle (11007) and pulmonary endothelium (89778). This offers a possible mechanism for the above clinical effects of Panax ginseng. The constituent ginsan, has been shown to reduce fibrosis of pulmonary lung fibroblasts in vitro, possibly by inhibiting inflammatory cytokine activity (89872).

Sexual effects: Panax ginseng is commonly used to increase fertility and sexual arousal in both males and females. A multi-ingredient cream preparation containing Panax ginseng is thought to work in patients with premature ejaculation by increasing the penile vibratory threshold and reducing the amplitude of penile somatosensory evoked potentials (2537). Also, ginsenosides improved libido and erection ability in human research (89761). Panax ginseng has been shown to increase sperm counts in animals (89876,89877) and humans (89786). The constituent ginsenosides may have effects that enhance sexual function. Ginsenosides have been shown to enhance release of nitric oxide from rabbit corpus cavernosum in vitro (89873) and cause smooth muscle relaxation (89874). They have also been shown to

increase copulatory behavior in animal research (89875).

The hormonal effects of Panax ginseng are controversial. Some clinical evidence suggests it doesn't have estrogen-mediated effects such as increasing follicle-stimulating hormone (FSH), estradiol levels, or endometrial thickness (10981). However, case reports of ginseng side effects such as postmenopausal vaginal bleeding suggest estrogen activity (590,591,592,10982,10983). Panax ginseng extract has been shown to increase serum ceruloplasmin oxidase activity (a measure of estrogenic activity in the liver) in animal models when ovaries are removed (6180). In vitro research also shows estrogen activity. Studies on human breast cancer cells indicate that ginseng, specifically its constituent ginsonside-Rb1, acts as a phytoestrogen, possibly by binding and activating the estrogen receptor (10984,12537,89756). Panax ginseng may also affect levels of other hormones. In females, Panax ginseng increased dehydroepiandrosterone sulfate (DHEA-S) levels (3863). In both animal and human research, Panax ginseng increased levels of testosterone in the blood (89786,89787). Levels of follicle-stimulating hormone and luteinizing hormone may be increased in males (89786).

Ulcer protective effects: In peptic ulceration, Panax ginseng has shown inhibitory activity on Helicobacter pylori-induced hemagglutination in vitro (3121). In animal research, samgyetang, a soup made from chicken, Panax ginseng, garlic, jujube, and chestnuts, appears to offer protection from experimentally induced peptic ulcers (10249).

Weight loss effects: Panax ginseng is sometimes added to supplements intended for use in weight loss. Animal research in obese rats eating a high fat diet shows that receiving intraperitoneal injections of Panax ginseng constituents (ginsenosides Rb1, Rd, and Rg1) reduces body mass and weight when compared with no treatment. Theoretically, ginsenosides increase satiety by modulating hormones and neurotransmitters such as leptin and neuropeptide Y (102239).

Classifications

Antiplatelet Agents, Cytochrome P450 1A1 (CYP1A1) Inducers, Cytochrome P450 2D6 (CYP2D6) Inhibitors, Cytochrome P450 3A4 (CYP3A4) Inducers, Cytochrome P450 3A4 (CYP3A4) Inhibitors, Hypoglycemic Agents, Immunomodulators, QT Interval-Prolonging Natural Ingredients, Adaptogens, Stimulants (Cognitive), Testosterone Enhancers

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References

See Monograph References

Monographs are reviewed on a regular schedule. See our Editorial Principles and Process for details. The literature evaluated in this monograph is current through 9/12/2024. This monograph was last modified on 12/31/2024. If you have comments or suggestions, please tell the editors.