

# Ginseng: Fact Versus Myth

**WILLIAM HAMILTON**, Pharm.D.

Assistant Professor, Creighton University School of Pharmacy and Allied Health Professions, Omaha, NE

**WILLIAM KIRCHAIN**, Pharm.D.

Associate Professor, Philadelphia College of Pharmacy, Philadelphia, PA

**H**erbalists claim that preparations of ginseng improve overall physical and mental performance, regulate brain function and raise resistance to stress.<sup>1</sup> Known as atale-kule to the Cherokee, it was used for headaches, premenstrual syndrome and other menstrual-associated complaints.<sup>2</sup> Traditional Chinese textbooks describe near-mythical qualities such as restoring balance to one's life force, increasing longevity, improving memory, stopping convulsions, and increasing happiness.<sup>3</sup>

Ginseng is one of the most frequently used herbs reported in a study of customers visiting health food stores.<sup>4</sup>

## COMMON NAMES

*Panax ginseng* C. A. Meyer [Fam. Araliaceae] is also referred to as Korean ginseng or Chinese ginseng.<sup>3,5</sup> Used extensively in Asia, it is the subject of numerous historical anecdotes and subjective publications.<sup>6</sup> Another major species is *Panax quinquefolius* L., commonly referred to as American ginseng. A third variety—Siberian ginseng—is not a species of *Panax*. The preferred name is eleuthero (*Eleutherococcus senticosus* Maxim.)<sup>6</sup> American and Korean ginseng contain a complex mixture of triterpenoid saponins classified into panaxosides, ginsenosides and chikusetsusaponins.<sup>7</sup> Ginsenoside RB-1 must be hydrolyzed by intestinal bacteria to be absorbed.<sup>8</sup>

## REPORTED USES

Herbalists classify ginseng as an "adaptogen," a term with no allopathic equivalent. These are substances that "enhance endurance for physical and mental work and increase nonspecific resistance to stress...in physiologically adverse habitats."<sup>9</sup>

Claims for ginseng include improved concentration, increased stamina, improved erectile function, cardiovascular protection, decreased

## Few herbs carry the history and therapeutic promise of ginseng. Is the promise fulfilled?

blood pressure, anti-stress activity, and better athletic performance. Ginseng is also believed to protect the liver, reduce radiation effects, improve blood sugar in diabetics, and help to prevent cancer.

**Improved Concentration and Anti-stress Activity:** Studies have shown mixed results with respect to memory and anti-stress responses in rats. Ginseng standardized extract (G115) and American ginseng produce modest positive improvements in standardized tests of memory in animal models.<sup>10,11</sup> In a double-blind study evaluating quality-of-life parameters, a multivitamin product was compared to a multivitamin with ginseng extract G115. The 12-week study involved 501 outpatients. Results, assessed by a standardized questionnaire, indicated that ginseng was effective in improving quality of life.<sup>12</sup>

**Improved Athletic Performance:** Most claims of improved athletic performance are not supported by scientific evidence.<sup>13</sup> Ginseng is promoted for "accelerating the restorative processes after intensive activity and increasing the body's resistance to unfavorable external influences."<sup>14</sup> Investigations of *Panax ginseng* and

*Eleutherococcus senticosus* on various physiologic measurements failed to support either supplement as a reliable aid to athletic performance.<sup>15-18</sup>

### Improved Erectile Function:

American ginseng has shown positive effects on male copulatory behavior in male rats.<sup>19</sup> Reproductive performance was studied in two generations of rats using ginseng extract G115. Results revealed no significant differences in physiologic or reproductive parameters in two generations.<sup>20</sup> In a separate study, Korean red ginseng (*Panax ginseng*) was compared to placebo and trazodone. Choi HK, et al.,<sup>21</sup> noted increased "penile rigidity and girth, libido and patient satisfaction ( $p < 0.05$ )" in a group of 90 men. Ginseng has been shown to enhance the conversion of L-arginine to nitrous oxide.<sup>22</sup>

### Cardiovascular Protection:

American ginseng has an inhibitory effect on low density lipoprotein oxidation in hyperlipidemic-prone rats.<sup>23</sup> In an animal model, *Panax ginseng* enhanced release of nitric oxide from endothelial cells, which appeared partially responsible for its cardioprotective effects.<sup>24</sup> An extract of ginseng root has been shown to inhibit high-threshold, voltage-dependent calcium channels.<sup>25</sup> When added to a cardioplegic solution, ginsenosides were claimed to have protective effects in a human trial of 30 mitral valvular surgical patients.<sup>26</sup> A study of 45 patients

with class IV congestive heart failure compared red ginseng alone and in combination with digoxin to digoxin alone. A synergistic benefit was suggested for the treatment of congestive heart failure with ginseng in combination with digoxin.<sup>27</sup> Another study of red ginseng on blood pressure in 26 subjects showed decreased systolic blood pressure ( $p = 0.03$ ) and a trend to lowering diastolic blood pressure ( $p = 0.17$ ).<sup>28</sup>

**Liver Protection:** One animal study suggests a possible liver-protective effect with ginseng. Ginseng significantly decreased AST and ALT levels in dexamethasone-treated rats.<sup>29</sup> A preparation containing a standardized ginseng extract, trace elements and vitamins was compared to placebo in 24 elderly outpatients with toxin-induced (alcohol and drugs) chronic liver disease. No significant difference in these parameters was observed.<sup>30</sup>

**Cancer Preventative:** An animal model evaluating the ability of red ginseng to protect against a papilloma induced by 7,12-dimethylbenz[ $\alpha$ ]anthracene showed a significant benefit.<sup>31</sup> Ginseng showed inhibition of some lung metastasis. It was not effective in preventing the invasion of melanoma and fibrosarcoma cells.<sup>32</sup> Ginsenoside Rh2 inhibits the growth of B16 melanoma cells. Oral but not intraperitoneal treatment with Rh2 resulted in induction of apoptotic cells in the tumor, in addition to augmenting natural killer activity in spleen cells from tumor-bearing nude mice.<sup>33</sup> American ginseng root extract has been evaluated in breast cancer cell lines. Results indicate an exhibition of estrogen-like effects on certain estrogen receptor-positive breast cancer cells. This induction of pS2 expression appears to promote a protective role against breast cancer.<sup>34</sup>

A Korean study compared the cancer risk to the reported intake of ginseng. A decreased risk of some types of cancer was associated with groups ingesting fresh ginseng extract, white ginseng extract, white ginseng powder and red ginseng. Benefit increase correlated with the frequency and duration of ginseng use. There was no attempt to sort out other health-promoting behaviors and other risk factors beyond smoking, however.<sup>35</sup> Cancers that did not appear

to benefit in this study included female breast, uterine cervix, urinary bladder and thyroid gland. In Korea, stomach cancer is the most frequently reported neoplasm. There appears to be a correlation with people who have the highest consumption of broiled meats and fish, especially salted and fermented products. Ginseng, mung bean pancake, tofu spinach, cabbage and sesame oil appear to decrease this risk.<sup>36</sup>

**Reduced Effect from Radiation:** Eleuthero has shown protection against the effects of radiation in rats.<sup>37</sup>

**Improved Blood Sugar in Diabetics:** Sotaniemi, Haapakoski, and Rautio<sup>38</sup> generated interest in the impact of ginseng on type 2 diabetes mellitus. In an 8-week, double-blind, placebo-controlled study of 36 newly diagnosed patients, ginseng (100 or 200 mg) reduced fasting blood glucose and body weight, and improved psychophysical performance.



**Adaptogen-Anti-aging:** Traditional anti-aging products are being studied extensively in China. Chen and Li<sup>39</sup> reviewed 386 traditional effective anti-aging medications. Ginseng heads that list, but the authors of the review classify the results of most studies as preliminary and suggest further investigations. One animal study in mice investigated four different ginseng infusions for up to 96 days. The comparison of eleuthero, Chinese and American ginseng showed no differences in stamina or longevity between them. The researchers concluded that ingesting adaptogenic glycosides did not significantly affect the survival of mice under major environmental stress.<sup>40</sup> In another animal model, *Panax ginseng* alone and combined

with a multivitamin was found effective for developing resistance to physical stress.<sup>9</sup> A small, double-blind, controlled study of geriatric inpatients found no identifiable effect of ginseng in length of hospital stay or in the functional outcomes measured.<sup>41</sup> Another double-blind study investigated the effect of ginseng extract G115 added to a multivitamin in 501 outpatients under environmental stress. They found a significant increase in the quality-of-life index.<sup>12</sup>

**Immunity:** A study of 20 young Thai males on the effects of prolonged administration of standardized ginseng extract on peripheral blood leukocytes and lymphocyte subsets. Two equal groups, one supplemented with ginseng and one taking placebo, were used. The treatment group received two capsules daily of standardized ginseng extract 150 mg per capsule for 8 weeks. No significant differences were seen in total and differential leukocyte counts or lymphocyte subpopulations between the two subject groups.<sup>42</sup> In Milan, Italy, a two-arm, randomized, placebo-controlled, double-blind investigation looked at whether ginseng supplementation increased the protective effect of influenza vaccination. Volunteers (227) received daily oral capsule doses of either placebo or 100 mg of a standardized ginseng extract for a period of 12 weeks, within which they received an anti-influenza polyvalent vaccination at week 4. There were 42 cases of influenza or common cold in the placebo group, versus 15 cases in the ginseng group. The difference was highly significant ( $p = 0.001$ ). Antibody titers and natural killer cell activities were twice as high in the ginseng group versus placebo ( $p = 0.0001$ ). Insomnia was reported to be a common adverse event.<sup>43</sup> Polymorphonuclear leukocyte chemiluminescence increased in a rat model.<sup>44</sup> A comparison of wild and cultured *Panax ginseng* measured pan T cells, helper T cells, and cytotoxic T cells. Results indicate a positive effect in mice from wild *Panax ginseng*. Cultures did not show the same change in mitogenic activity.<sup>45</sup> Eleutherococcus senticosus extract (Eleukokk) showed a pronounced increase in T lymphocytes in a double-blind human study of 36 healthy volunteers.<sup>46</sup>

## SPECIAL CONSIDERATIONS

Several weeks are recommended for full benefits to be realized. Although lifetime use may be common in Asia, there are no long-term clinical studies to evaluate risk or benefit. References suggest limiting therapy at various durations (TABLE 1).

## ADVERSE REACTIONS

Hypertension was noted as part of a "ginseng abuse syndrome" described by Siegel.<sup>47,48</sup> The report relied on patient accounts of unverified but reportedly high-dose ginseng use and concurrent caffeine use in a group of psychiatric patients. Of the 133 patients studied, elevated blood pressure developed in 14 patients using *Panax ginseng* and 8 patients using *Eleutherococcus senticosus*. Ginseng has not been confirmed in other studies to cause an abuse syndrome.<sup>49</sup> The German Commission E monographs and the PDR for Herbal Medicines list high blood pressure as a contraindication to using *Eleuthero*, but not *Panax ginseng*.

This contrasts with the PDR and

REFERENCE	Suggested Duration of Therapy	
	<i>Panax ginseng</i>	<i>Eleutherococcus senticosus</i>
Professional's Handbook of Complementary & Alternative Medicines	Continual	3 weeks
The Complete German Commission E Monographs	3 months, a repeated course is feasible	3 months, a repeated course is feasible
PDR for Herbal Medicines	3-4 weeks	None listed
Herbal Medicinals: A Clinician's Guide	A 2-week break every 2 months	A 2-week break every 2 months
Therapeutic Monographs of (American Botanical Council)	Short-term for young and healthy. Long-term for older and unhealthy.	Up to 3 months, or a course 1 month with 2 months off, then repeat
Nutritional Herbology	Only in response to specific stress	Only as needed in response to stress
The Pharmacology of Chinese Herbs	None listed	None listed

Medications	Action
Warfarin, heparin, aspirin and NSAIDs	Avoid concomitant use or monitor carefully
MAOIs	Avoid concomitant use
Oral hypoglycemics, insulin	Monitor blood sugar
Vitamins B1, B2, C	Increase vitamin dose
Estrogens or corticosteroids	Avoid concomitant use (possible additive effects)
Digoxin	Avoid concomitant use or monitor closely

Chest pain	Nausea
Diarrhea	Nervousness
Epistaxis	Palpitations
Headache	Pruritus
Hypertension	Skin eruptions (with ginseng abuse)
Impotence	Vaginal bleeding
Insomnia	Vomiting
Mastalgia	

Source: Based on reference 60

Commission E monographs, which indicate no known side effects. Many of these reactions are extensions of the possible effects of ginseng. Pharmacist's Letter makes a good case for the possible disparity in adverse effects as secondary to the adulteration and mislabeling common with ginseng products.<sup>50</sup>

**Unusual Side Effects:** A regular ginseng user experienced the symptoms of Stevens-Johnson syndrome (painful erosions in mouth and urogenital mucosa, corneal ulceration and purpuric macules) after taking two pills a day for three days to help recover from a cold. It is possible that a contaminant such as a nonsteroidal anti-inflammatory could have been present. Consideration should be given to any change in blood pressure, and hypertensive patients should not use ginseng without medical supervision and frequent monitoring. Extremely high doses should be avoided. Any unusual symptoms associated with recent additions to therapy should be evaluated.

## Interactions and Cautions: The

Commission E monographs and the PDR for Herbal Medicines list no known interactions with ginseng. The Professional's Handbook suggests caution in patients using antidiabetic agents and insulin because of hypoglycemic effects. The combination of monamine oxidase inhibitors (parnate, selegiline, etc.) and ginseng is reported to cause headache, tremors and mania. *Eleuthero* may increase the excretion of some B vitamins and vitamin C.<sup>60</sup> McRae reported elevated digoxin levels following the addition of *eleuthero* to a patient with constant levels for many years.<sup>52</sup>

One animal study on the non-saponin fraction from the roots of *Panax ginseng* demonstrated inhibition of platelet aggregation.<sup>53</sup> Anticoagulation was also described after 30 days of *eleuthero* administration in rats.<sup>54</sup> A probable interaction between warfarin and ginseng was reported.<sup>55</sup> A patient had a reduction in the international normalized ratio (INR) following the addition of ginseng. The INR returned to previous levels following discontinuation of the ginseng. Mastalgia has been reported in a woman after using ginseng powder for 3 weeks.<sup>49</sup> A case of postmenopausal bleeding attributed to the use of topical ginseng has been reported.<sup>56</sup> TABLE 2

provides some cautions for ginseng or *eleuthero* therapy.

## DOSAGE

The dry root is usually dosed at 0.5-3 g daily. Commercial ginseng extract products range from 100-600 mg standardized to a percent of ginsenosides daily, in one or two equal doses.

## COMBINATION PRODUCTS

A combined preparation (60 mg *Ginkgo biloba* + 100 mg ginseng), standardized of 24% ginkgo flavone glycosides and 4% ginsenosides, was studied for its effect on blood pressure in 10 healthy medical students. Systolic blood pressure was decreased both for the large-dose (120 mg *Ginkgo biloba* + 200 mg ginseng) and low-dose administration (60 mg *Ginkgo biloba* + 100 mg ginseng). Diastolic blood pressure and heart rate decreased only in the high dosage group.<sup>57</sup> A combination of *Ginkgo biloba* and ginseng produced a modest improvement in cognitive function in a short-term, double-blind, placebo-controlled study of 64 otherwise healthy volunteers (aged 40-65 years) with neurasthenia.<sup>58</sup> ■

References available upon request to MSP.

<b>Case 1.</b> TC is a 23-year-old male in good physical condition. He is considering using ginseng to improve his workouts and physical conditioning.
<b>Case 2.</b> FX is a 34-year-old female seeking advice for supplements to help prevent cancer. Her older sister was just diagnosed with breast cancer and she is concerned about her own risk. She has Type 2 diabetes mellitus.
<b>Case 3.</b> GB is a 59-year-old man complaining of fatigue. He goes home at night after work with just enough energy to eat and sit on the couch for the rest of the evening. He is 28 pounds over his ideal body weight and is being treated for mild hypertension with a low dose of an angiotensin II receptor antagonist. His average blood pressure with treatment is 132 systolic over 84 diastolic. He wants to have more energy so he can try an exercise program.

<b>Case 1.</b> It is recommended not to incorporate ginseng into TC's supplement plan. Proper diet and consistency in training are the two most significant factors in any physical conditioning program. Ginseng has not been shown to add to these two factors in any substantial way.
<b>Case 2.</b> Studies in both areas are extremely limited. Korean ginseng is not helpful for breast cancer prevention. However, one study demonstrated a benefit, in vitro, from American ginseng. It will be much more important for FX to have a complete work-up for the HER2 genotype and other inherited risks for breast cancer. Based on results of this work-up, she may be a candidate for tamoxifen or early mammography. Regarding her type 2 diabetes mellitus, one human study using <i>Panax ginseng</i> demonstrated improvement in blood glucose. One approach could be to try <i>Panax ginseng</i> with the consent of her physician for 8 weeks while she monitors blood sugars daily.
<b>Case 3.</b> GB could benefit from improved immunity, improved mental function, and the adaptogenic effects possible with ginseng. Although physical performance appears not to be improved with ginseng, increased energy is a historical use. The World Health Organization (WHO) Guidelines for the Assessment of Herbal Medicines considers "historical use of a substance [as] a valid form of information on safety and efficacy, in the absence of scientific documentation to the contrary." <sup>59</sup> If GB believes that ginseng could help him, and his physician consents, treatment can begin. His dose should start at the low range, with biweekly monitoring for changes in blood pressure during the first two months of treatment.