

Eleuthero

Eleutherococcus senticosus (Rupr. & Maxim.) Maxim.
(syn. *Acanthopanax senticosus* [Rupr. & Maxim.] Harms)

[Fam. *Araliaceae*]

OVERVIEW

Eleuthero root has been widely known in the U.S. as “Siberian ginseng.” It was first marketed in the U.S. in the late 1970s, and since become one of the top-selling herbal dietary supplements in the natural foods class of trade. It has been used in Traditional Chinese Medicine (TCM) for over two thousand years. From the 1940s through the 1960s, Soviet scientists conducted extensive clinical research on eleuthero in their search for a more abundant and economical alternative to Asian ginseng (*Panax ginseng*). Russian Olympic athletes, explorers, divers, sailors, and miners now use eleuthero as a preventive agent against stress-related illnesses.



Photo © 2003 stevenfoster.com

PRIMARY USES

- Herpes simplex type II infections
- Influenza complications (possible prevention)
- Fatigue; debility; declining work capacity and concentration; convalescence; chronic fatigue syndrome; supportive therapy during radiation or chemotherapy
- Functional asthenia
- Selective memory improvement

OTHER POTENTIAL USES

- Cholesterol reduction; atherosclerosis
- Insomnia and other anxiety-like conditions
- Chronic inflammatory conditions
- Visual perception enhancement

PHARMACOLOGICAL ACTIONS

Increases lymphocyte count; tonifying; anti-stress activity; immunomodulatory effect on cellular immune system; tranquilizes central nervous system; reduces heart palpitations and headaches due to high-altitude hypoxia syndrome.

DOSAGE AND ADMINISTRATION

Use for one to three months followed by a two-month break. A repeat course is feasible.

POWDERED ROOT: 2–3 g daily.

DECOCTION: 9–27 g daily.

INFUSION: Pour 150 ml of boiling water over 2–3 g, steep for 5–10 minutes.

FLUID EXTRACT: 2–4 ml, 1–3 times daily [1:1 (*g/ml*), 33% ethanol]; or 2–8 ml per day [1:2 (*g/ml*)]; or 2–3 g daily powdered or cut root aqueous alcoholic extract.

TINCTURE: 10–20 ml, 1–3 times daily [1:5 (*g/ml*)].

NATIVE EXTRACT: 300–450 mg, 3 times daily [20:1 (*w/w*)]; or 2–3 tablets (150 mg native extract per tablet), twice daily.

STANDARDIZED DRY EXTRACT: (>1% eleutheroside E), 100–200 mg, 3 times daily.

CONTRAINDICATIONS

Some authorities recommend that patients with high blood pressure (especially greater than 180/90) should consult a healthcare provider before using eleuthero. This is based solely on a 35-year old report in the Russian literature of a study on patients with rheumatic heart lesions. Eleuthero should not be used during the acute phase of infections, although it may be used concurrently with antibiotics for the treatment of dysentery.

PREGNANCY AND LACTATION: No known restrictions.

ADVERSE EFFECTS

No side effects have been documented for eleuthero in healthy individuals. In rare cases, mild, transient diarrhea and sleep disturbances (if taken close to bedtime) may occur. In patients with rheumatic heart disease, side effects such as pericardial pain, headaches, and elevated blood pressure have been reported.

DRUG INTERACTIONS

Mutual potentiation when administered with the radioprotector drug adeturone. Potentiates effect of antibiotics monomycin and kanamycin in treatment of *Shigella* dysentery and *Proteus* enterocolitis. May interact with concurrently administered antipsychotic drugs, barbiturates, or sedatives (speculative). May produce enhanced effect on insulin and antidiabetic therapy; therefore, blood glucose levels should be monitored closely in diabetics because of possible hypoglycemic action.

CLINICAL REVIEW

In 9 studies on eleuthero that included over 1,984 participants, all but one demonstrated positive effects for therapeutic indications, including immune response, stress, fatigue, and cardiovascular health. Four double-blind, placebo-controlled (DB, PC)

studies investigated the effects of eleuthero on concentration, selective memory, cognitive function and well-being, ergogenic parameters in athletes, immune protection against herpes simplex type II infection, and immunomodulatory measurements (e.g., T-cells) in healthy volunteers. A single-blind, PC study evaluated eleuthero's effects on work capacity, stamina, and fatigue in male athletes. In clinical studies on eleuthero extracts conducted in the former Soviet Union since the early 1960s, more than 2,100 normal and stressed human subjects were orally administered eleuthero root fluid extract, 33% ethanol. The studies examined the adaptogenic response of humans to adverse conditions such as heat, noise, motion, workload increase, and exercise. They also measured a significant improvement in auditory disturbances, increased mental alertness, work output, and quality of work under stress.



Eleuthero

Eleutherococcus senticosus (Rupr. & Maxim.) Maxim. (syn. *Acanthopanax senticosus* [Rupr. & Maxim.] Harms)
[Fam. Araliaceae]

OVERVIEW

Eleuthero root has been used in Traditional Chinese Medicine for thousands of years, and has been known as “Siberian ginseng.” Eleuthero is an “adaptogen,” a mild substance that produces a normalizing effect on the body. It was first marketed in the U.S. in the late 1970s, and has since become one of the top-selling herbal dietary supplements.

USES

Herpes simplex type II infections; decrease in occurrence of influenza complications; fatigue; chronic inflammation; debility; decreased work and concentration; chronic fatigue syndrome; convalescence; functional asthenia; supportive therapy during radiation or chemotherapy; atherosclerosis; selective memory improvement.

DOSAGE

Use for one to three months, followed by a two-month break.

INFUSION (TEA): Pour 150 ml of boiling water over 2–3 g, steep for 5–10 minutes.

FLUID EXTRACT: 2–4 ml, 1 to 3 times daily [1:1].

FLUID EXTRACT: 2–8 ml daily [1:2].

TINCTURE: 10–20 ml, 1 to 3 times daily [1:5].

NATIVE EXTRACT: 300–450 mg, 3 times daily.

STANDARDIZED DRY EXTRACT: (21% eleutheroside E), 100–200 mg, 3 times daily.

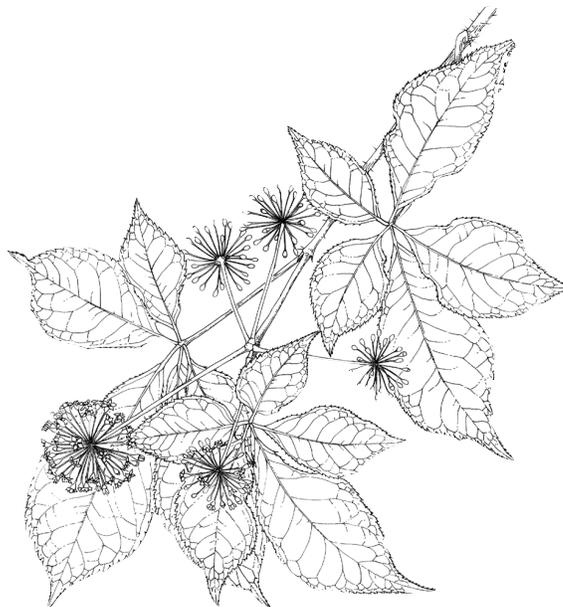
CONTRAINDICATIONS

Although the use of eleuthero is generally considered quite safe, some authorities recommend that patients with high blood pressure (especially greater than 180/90) should consult a healthcare provider before using eleuthero. It should not be used during the acute phase of infections, although it may be used concurrently with antibiotics for the treatment of dysentery.

PREGNANCY AND LACTATION: There are no known restrictions for usage during pregnancy or while breast-feeding.

Comments

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



ADVERSE EFFECTS

No significant adverse effects have been reported in healthy individuals. However, on rare occasions eleuthero may cause mild, brief diarrhea or insomnia if taken too close to bedtime. In individuals with rheumatic heart disease, side effects such as headaches, elevated blood pressure, and pain in the pericardium (the sac that encloses the heart) have been reported.

DRUG INTERACTIONS

Eleuthero may increase the effects of certain antibiotics, including monomycin and kanamycin, and the radioprotective drug adeturone. Eleuthero may interact with antipsychotic drugs barbiturates, and sedatives (although these interactions are only speculative, not reported). Eleuthero may possibly increase the effect of insulin and diabetic drugs. Diabetics taking eleuthero and antidiabetic medication should be closely monitored.



The information contained on this sheet has been excerpted from *The ABC Clinical Guide to Herbs* © 2003 by the American Botanical Council (ABC). ABC is an independent member-based educational organization focusing on the medicinal use of herbs. For more detailed information about this herb please consult the healthcare provider who gave you this sheet. To order *The ABC Clinical Guide to Herbs* or become a member of ABC, visit their website at www.herbalgram.org.

Eleuthero

Eleutherococcus senticosus (Rupr. & Maxim.) Maxim.
(syn. *Acanthopanax senticosus* [Rupr. & Maxim.] Harms)

[Fam. *Araliaceae*]

OVERVIEW

Eleuthero root has been widely known in the U.S. as “Siberian ginseng.” It was first marketed in the U.S. in the late 1970s (Foster, 1991), and since become one of the top-selling herbal dietary supplements in the natural foods class of trade (Brevoort, 1998; Tyler, 1998). It has been used in Traditional Chinese Medicine (TCM) for over 2,000 years and is listed in the *Shen Nong Ben Cao Jing*, China’s oldest pharmacopoeia, as well as in the pharmacopoeia of Li Shih-Zhen of the Ming dynasty (Halstead and Hood, 1984). However, it was modern Russian researchers who popularized this herb in the West (Foster and Chongxi, 1992; Kenner and Requena, 1996). From the 1940s through the 1960s, Soviet scientists conducted extensive clinical research on eleuthero in their search for a more abundant and economical alternative to Asian ginseng (*Panax ginseng*). “Adaptogen” has traditionally been defined as a substance useful for both sick and healthy individuals, which

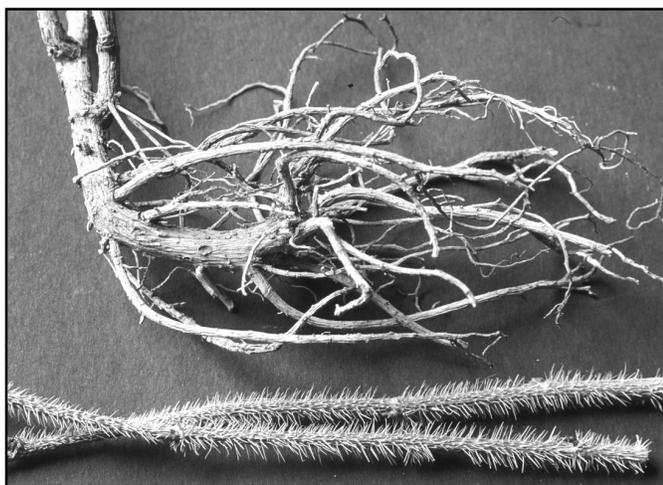


Photo © 2003 stevenfoster.com

improves dysfunction without side effects (Brekman, 1980; Davydov and Krikorian, 2000; Farnsworth, *et al.*, 1985). In the case of eleuthero, “adaptogen” is defined as a substance that is innocuous and relatively free of side effects, has nonspecific actions, increases resistance to a wide range of environmental or other physical stressors, and may have a normalizing action in the body, irrespective of a diseased state (Brekman, 1980). Russian Olympic athletes, explorers, divers, sailors, and miners have used eleuthero as a preventive agent against stress-related illnesses (Brekman, 1980; Fulder, 1980). Eleuthero is official in Russia, China, France, and Germany (see “Regulatory Status” below). Scientific comparisons of eleuthero to the more familiar Asian ginseng (“true ginseng”) underscored that they differ considerably chemically and pharmacologically, and cannot be considered interchangeable. Accordingly, the herb industry has

recommended that the common name “Siberian ginseng” be replaced with the more preferred common name “eleuthero” (Foster, 1992; McGuffin, 2001). Federal regulations now require that, “the common or usual name of ingredients of dietary supplements that are botanicals...shall be consistent with the names standardized in *Herbs of Commerce*, 1992 edition” (US FDA, 1999). This nomenclature has been accepted by the U.S. Food and Drug Administration.

DESCRIPTION

Eleuthero preparations consist of the dried roots and/or rhizomes of *Eleutherococcus senticosus* (Rupr. & Maxim.) Maxim. (syn. *Acanthopanax senticosus* [Rupr. & Maxim.] Harms [Fam. *Araliaceae*]). The dried root contains no less than 4% water-soluble extractive (BHP, 1996), and no less than 6% water- and ethanol-soluble extractive (DAB, 1999).

PRIMARY USES

Immunology

- Decrease in severity, duration, or frequency of attacks of herpes simplex type II infections (Williams, 1995)
- Decrease in the occurrence of influenza complications (Shadrin *et al.*, 1986)

Fatigue

- Tonic for invigoration and fortification in treatment of: fatigue, debility (Bradley, 1992; Blumenthal *et al.*, 1998), declining work capacity and concentration, convalescence (Blumenthal *et al.*, 1998); chronic fatigue syndrome and supportive therapy during radiation or chemotherapy (Brown, 2000)
- Functional asthenia (Bruneton, 1999)

Memory Disturbance

- Improvements in selective memory (Winther *et al.*, 1997)

OTHER POTENTIAL USES

- Decrease in total cholesterol, LDL cholesterol, and triglyceride levels (Szolomicki *et al.*, 2000); atherosclerosis (Golikov, 1963)
- Insomnia and other conditions characterized by anxiety-like behavior in modern Chinese medicinal use (as a single-herb remedy) (Chang, 1986). This is consistent with eleuthero’s observed sedative activity, primarily in animal studies (Newall *et al.*, 1996)
- Chronic inflammatory conditions (Bradley, 1992)

Vision, perception

- Increased color perception level and functional stability level, enhanced spectral and contrast sensitivity and range of signal light visibility and increased speed of color discrimination (Sosuova, 1986)

DOSAGE

Internal

Crude Preparations

POWDERED ROOT: 2–3 g daily (Bradley, 1992), 1–4 g daily (MediHerb, 1994).

DECOCTION: 9–27 g (PPRC, 1997).

INFUSION: 150 ml of boiling water is poured over 2–3 g and steeped for 5–10 minutes (Blumenthal *et al.*, 1998).

FLUID EXTRACT: 1:1 (*g/ml*), 33% ethanol, 2–4 ml, 1–3 times daily (Pizzorno and Murray, 1999; Werbach and Murray, 2000), 1:2 (*g/ml*): 2–8 ml per day (MediHerb, 1994), 2–3 g daily powdered or cut root aqueous alcoholic extract (Blumenthal *et al.*, 1998).

TINCTURE: 1:5 (*g/ml*), 10–20 ml, 1–3 times daily (Pizzorno and Murray, 1999).

NATIVE EXTRACT: 20:1 (*w/w*), 300–450 mg, 3 times daily; tablets containing 150 mg native extract, 2–3 tablets, twice daily (PPRC, 1997).

Standardized Preparations

DRY EXTRACT: (>1% eleutheroside E), 100–200 mg, 3 times daily (Werbach and Murray, 2000).

NOTE: In healthy individuals, maintenance doses should be based on the lower end of the dosage range. For treatment of illness and high-stress situations, the upper end of the dosage range should be considered (MediHerb, 1994).

DURATION OF ADMINISTRATION

Some sources recommend a course of one month (Bradley, 1992) to three months (Blumenthal *et al.*, 1998) followed by a two month break (Bradley, 1992). A repeat course is feasible (Blumenthal *et al.*, 1998). While the issue has not been studied specifically, it is a general practice to temporarily halt herb consumption after a reasonable period when it is not considered essential for maintaining vital functions. This provides an opportunity to reassess the case and either stop its use completely, continue at a lower dose, or re-institute its use as before. Such a recommendation is not a limitation, but advice on its reasonable use, as opposed to assuming regular, ongoing consumption is necessary or appropriate.

CHEMISTRY

Eleuthero contains ca. 0.6–0.9% eleutherosides A-G in an approximate ratio of 8:30:10:12:4:2:1. Eleutheroside A is the sterol daucosterol; eleutheroside B is the phenylpropanoid syringin; eleutheroside C is the sugar methyl α -D-galactoside. Eleutheroside D is the lignan (-)-syringaresinol di-O- β -D-glucoside, and its diastereoisomer is eleutheroside E (Bradley, 1992; Farnsworth *et al.*, 1985). Eleuthero also contains immunostimulant polysaccharides (Fang *et al.*, 1985; Huang, 1999). An extensive review of the chemistry of eleuthero with 29 chemical structures has been published (Tang and Eisenbrand, 1992).

PHARMACOLOGICAL ACTIONS

Human

Increases lymphocyte count (Blumenthal *et al.*, 1998); adaptogen; tonic (BHP, 1996); anti-stress activity (Wagner *et al.*, 1994); immunomodulatory effect on the cellular immune system (Bohn *et al.*, 1987); tranquilizes central nervous system; reduces heart palpitations and headaches due to high-altitude hypoxia syndrome (Huang, 1999); increases phagocytic activity of neutro-

cytes (Szolomicki *et al.*, 2000); increases the absolute numbers of immunocompetent cells, particularly T-cells, predominantly of the helper/inducer type, but also on cytotoxic and natural killer cells (Bohn *et al.*, 1987); in TCM theory, reinforces and tonifies vital energy known as “qi,” invigorates the function of the “spleen” and “kidney,” and tranquilizes (Chang and But, 1986; PPRC, 1997).

Animal

Enhances endurance (Blumenthal *et al.* 1998); chemical-, biological-, and radioactive-protective (Collisson, 1991; Minkova and Pantev, 1987; Yonezawa *et al.*, 1989); antioxidant, antihypertensive, hypo/hyperglycemic activity (Farnsworth *et al.*, 1985; Hikino *et al.*, 1986; Medon *et al.*, 1981); sedative (Medon *et al.*, 1984); stress reduction (Takasugi *et al.*, 1985). Eleuthero's isolated glucosides protect against myocardial infarction and can lower blood sugar levels in normal and hyperglycemia-induced mice (Hikino *et al.*, 1986; Tang and Eisenbrand, 1992).

In vitro

Mutual potentiation of antiproliferative effects on leukemia cells when applied in combination with conventional antimetabolite drugs (Hacker and Medon, 1984); slight gamma radiation protection (Ben-Hur and Fulder, 1981); inhibition of hexobarbital metabolism in mice (Medon *et al.*, 1984).

MECHANISM OF ACTION

Most studies on eleuthero were conducted to investigate its adaptogenic effects. The chemical compounds and pharmacological actions of eleuthero support the theory that the primary benefit of an adaptogen is its protective and inhibitory action against free radicals (Davydov and Krikorian, 2000). The exact mechanisms of action of eleuthero and/or the significance of its constituents are not yet fully understood (MediHerb, 1993), despite numerous pharmacological investigations in human and animal models. According to the literature, eleuthero acts via the following mechanisms:

- Increases immune system function by enhancement of T-cell activation (Wagner, 1985). Active principles responsible for its immunomodulation activities are not yet known (Wagner, *et al.*, 1994).
- Intensifies regeneration, *in vivo*, of subcellular structures and accelerates recovery during experimental myocardial infarction; may be related to the transformation of lipids into glycogen (Afanas'eva and Lebkova, 1987).
- May support and enhance adrenal function and the optimal functioning of the hypothalamic-pituitary-adrenal cortex axis (Baranov, 1982; Brekhman and Dardymov, 1969; Filaretov *et al.*, 1988; Kirilov, 1964). Greater energy and better reaction to stress are associated with optimal adrenal function.
- Maximizes the utilization of oxygen by working muscles, which prolongs the aerobic state (Asano *et al.*, 1986).
- Increases endurance and reduces activation of the adrenal cortex in response to stress (alarm phase reaction) and also has significant prophylactic effects on stress reactions (Brekman and Kirillov, 1969; Czygan, 1984).
- *In vitro*, ethanolic fluid extract increases phagocytosis of *Candida albicans* by granulocytes and monocytes from healthy donors by 30–40% (Wildfeuer and Mayerhofer, 1994).

- *In vitro*, binds to progestin, mineralocorticoid, glucocorticoid receptors, and estrogen receptors, which could explain the observed glucocorticoid-like activity of the extract (Pearce *et al.*, 1982).
- Increases cAMP levels (Wagner *et al.*, 1994).

CONTRAINDICATIONS

The Commission E contraindicates eleuthero for patients with high blood pressure (Blumenthal *et al.*, 1998). This is based on a Russian study on patients with rheumatic lesions of the heart that recommended that eleuthero not be given to persons with blood pressure higher than 180/90 mm Hg (Mikunis *et al.*, 1966; Farnsworth *et al.*, 1985). However, there is no other literature available to support the contraindication of eleuthero in otherwise normal hypertensive patients. Based on Russian clinical experience, eleuthero should not be used during the acute phase of infections, though it is used to treat dysentery in combination with antibiotic use (MediHerb, 1994).

PREGNANCY AND LACTATION: No known restrictions (Brown, 2000; McGuffin *et al.*, 1997). An absence of teratogenicity with administration of eleuthero has been demonstrated in animals (Farnsworth *et al.*, 1985).

ADVERSE EFFECTS

No side effects have been documented for eleuthero in healthy individuals (Farnsworth *et al.*, 1985; Blumenthal *et al.*, 1998). In rare cases, mild, transient diarrhea has been reported. In rare cases, sleep disturbances have been reported (Hänsel, 1991; Brown, 2000). In patients with rheumatic heart disease, side effects such as pericardial pain, headaches, and elevated blood pressure have been reported (Werbach and Murray, 2000). Reports of neonatal/maternal androgenization (“hairy baby” syndrome) have been attributed to maternal ingestion of products labeled as “Siberian ginseng” (Koren *et al.*, 1990), though subsequent investigations determined the implicated product did not contain eleuthero but was adulterated with Chinese silk vine (*Periploca sepium*) (Awang, 1991; Awang, 1996b).

DRUG INTERACTIONS

There are few well-documented reports of interactions with eleuthero. Mutual potentiation of beneficial effects when eleuthero is administered with the radioprotector drug adeturone has been reported (Minkova and Pantev, 1987). Eleuthero potentiates effects of antibiotics monomycin and kanamycin in treatment of *Shigella* dysentery and *Proteus* enterocolitis (Brinker, 2001).

One case of unexplained elevated digoxin levels has been reported (McRae, 1996). It is unclear whether some unknown component of eleuthero was converted to digoxin *in vivo*, interfered with digoxin elimination, caused a false serum assay result, or was a result of a possible substituted herbal material, since the identity of the raw material was not confirmed and may have been another case of adulteration with Chinese silk vine (Awang, 1996a; 1996b). Possible interactions with prescription drugs warrants caution regarding the concomitant use of eleuthero and antipsychotic drugs, barbiturates, and sedatives (Medon, 1984); however, there are no actual reports to support this speculation. Eleuthero may produce an enhanced effect on insulin and antidiabetic therapy, at least theoretically (Brinker, 2001); diabetics should monitor blood glucose levels closely due to the potential hypoglycemic action.

AMERICAN HERBAL PRODUCTS ASSOCIATION (AHPA) SAFETY RATING

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

REGULATORY STATUS

CANADA: Drug Identification Number (DIN) assigned (Health Canada, 2001).

CHINA: One eleuthero-containing multi-ingredient product has schedule OTC status with a Drug Identification Number (DIN) assigned (Health Canada, 2001).

EUROPEAN UNION: Dried root official in the *European Pharmacopoeia*, 3rd ed. Supplement 2000 (Ph.Eur., 2000).

FRANCE: Traditional Herbal Medicine (THM) for specific indication (Bradley, 1992; Bruneton, 1999). Added to *French Pharmacopoeia* in 1996 (Bruneton, 1999; Ph.Fr., 1996).

GERMANY: Approved non-prescription drug of the German Commission E (Blumenthal *et al.*, 1998). Official in the *German Pharmacopoeia* (DAB, 1999).

RUSSIAN FEDERATION: Official in the *State Pharmacopoeia of the Union of Soviet Socialist Republics* since 1962 (Foster, 1991; Fulder, 1980; Schulz and Hänsel, 1996; USSR, 1990).

SWEDEN: As of January 2001, no eleuthero products are listed in the Medical Products Agency (MPA) “Authorised Natural Remedies” (MPA, 2001).

SWITZERLAND: No licensed herbal medicines containing eleuthero. No monograph in the *Swiss Pharmacopoeia*.

U.K.: Not included on the *General Sale List*, and no product licenses granted (Bradley, 1992; Newall *et al.*, 1996).

U.S.: Dietary supplement (USC, 1994).

CLINICAL REVIEW

Nine studies are outlined in the following table, “Clinical Studies on Eleuthero,” conducted on 1,984 participants. All but one of these studies (Dowling *et al.*, 1996) demonstrate positive effects for immune response, stress, fatigue, and cardiovascular health. The table includes four double-blind, placebo-controlled (DB, PC) studies investigating the effects of eleuthero on concentration, selective memory, cognitive function, and well-being (Winther *et al.*, 1997); ergogenic parameters in athletes (Dowling *et al.*, 1996); immune protection against herpes simplex type II infection (Williams, 1995); and immunomodulatory measurements (e.g., T-cells) in healthy volunteers (Bohn *et al.*, 1987). A single-blind, placebo-controlled (SB, PC) study evaluated eleuthero’s effects on work capacity, stamina, and fatigue in male athletes (Asano *et al.*, 1986). Clinical studies on eleuthero extracts have been extensively conducted in the former Soviet Union since the early 1960s. More than 2,100 normal and stressed human subjects were orally administered eleuthero root fluid extract, 33% ethanol. The studies examined the adaptogenic response of humans to adverse conditions such as heat, noise, motion, workload increase, and exercise. These studies also measured a significant improvement in auditory disturbances, increased mental alertness, work output, and quality of work under stress (Farnsworth *et al.*, 1985).

BRANDED PRODUCTS

Elagen: Eladon Ltd. / 63 High Street / Bangor, Gwynedd / LL57 1NR / U.K. / Tel: +44-01-24-83-7005-9 / www.elagen.com. Hydro-alcoholic dried extract (10:1) of *Eleutherococcus senticosus* root extract standardized root at 0.4% eleutheroside B and 0.4% eleutheroside E in 375 mg tablets. This product is now called Eleugetic®.

Eleukokk®: Pharma-Inter-Med / Am Born 19 / 22765 Hamburg / Germany. 10 g of test preparation consisted of 1.96 g eleuthero root ethanolic fluid extract 1:1 (0.20% (w/v) eleutheroside B, 1.30 g sorbitol water 70% (w/v), and 6.74 g dessert wine. This product is no longer available.

Maxim-L®: Omega Nutripharm. No manufacturer information available. Eleuthero root fluid extract with 30–34% ethanol (eleutherosides B and E present).

Medexport: Moscow, Russia. No manufacturer information available. Eleuthero root fluid extract Ph. USSR: 42-358-72, 335 ethanol. Each ml of fluid extract contains 75 mg of soluble extractive of *Eleutherococcus senticosus*, including 0.53 mg of syringin (eleutheroside B) and 0.12 mg of syringaresinol di-glucoside (eleutheroside D).

Taigutan® Eleuthero root fluid extract: Dr. Mewes Heilmittel GmbH / PF 1325 / 56194 Höhr-Grenzhausen / Germany / Tel: +49-02-62-49-4529-0 / Fax: +49-02-62-49-4529-1 / www.paesel.lorei.de. A 1:1 (w/v) extract in 35% (v/v) ethanol. Unable to confirm manufacturer.

REFERENCES

- Afana's'eva T, Lebkova N. Effect of *Eleutherococcus* on the subcellular structures of the heart in experimental myocardial infarct. [in Russian]. *Biull Eksp Biol Med* 1987;103(2):212–5.
- Asano K Takahashi T, Miyashita M, et al. Effect of *Eleutherococcus senticosus* extract on human physical working capacity. *Planta Med* 1986;3:175–7.
- Awang D. Maternal use of ginseng and neonatal androgenization. *JAMA* 1991;266(3):363.
- Awang D. Eleuthero. *CPJ* Oct 1996b;52–4.
- Awang D. Siberian ginseng toxicity may be case of mistaken identity. *Canadian Med Assoc J* 1996a;155(9):1237.
- Baranov A. Medicinal uses of ginseng and related plants in the Soviet Union: recent trends in the Soviet literature. *J Ethnopharm* 1982;6:339–53.
- Ben-Hur E, Fulder S. Effect of *Panax ginseng* saponins and *Eleutherococcus senticosus* on survival of cultured mammalian cells after ionizing radiation. *Am J Chin Med* 1981;9(1):48–56.
- Berdyshev V. Effect of the long-term intake of *Eleutherococcus* on the adaptation of sailors in the tropics. [in Russian]. *Voen Med Zh* 1981;(5):57–8.
- BHP. See: *British Herbal Pharmacopoeia*.
- Blumenthal M, Busse WR, Goldberg A, Gruenwald J, Hall T, Riggins CW, Rister RS (eds.), Klein S, Rister RS (trans.). *The Complete German Commission E Monographs—Therapeutic Guide to Herbal Medicines*. Austin, TX: American Botanical Council; Boston: Integrative Medicine Communication; 1998;124–5.
- Bohn B, Nebe C, Birr C. Flow-cytometric studies with *Eleutherococcus senticosus* extract as an immunomodulatory agent. *Arzneimforschung* 1987;37(10):1193–6.
- Bradley P (ed.). *British Herbal Compendium*, Vol. 1. Bournemouth, UK: British Herbal Medicine Association; 1992;89–91.
- Brekhman II, Dardymov I. New substances of plant origin which increase nonspecific resistance. *Annu Rev Pharmacol* 1969;4:419–30.
- Brekhman II, Kirillov O. Effect of *Eleutherococcus* on alarm-phase of stress. *Life Sci* 1969;8(3):113–21.
- Brekhman II. *Man and Biologically Active Substances, The Effect of Drugs, Diet and Pollution on Health*. Oxford: Pergamon Press Ltd; 1980.
- Brevoort P. The booming U.S. botanical market: a new overview. *HerbalGram* 1998;44:33–48.
- Brinker F. *Herb Contraindications and Drug Interactions*, 3rd ed. Sandy, OR: Eclectic Medical Publications; 2001;86–87.
- British Herbal Pharmacopoeia* (BHP). Exeter, UK: British Herbal Medicine Association; 1996;74–5.
- Brown D. *Herbal Prescriptions for Health & Healing*. Rocklin, CA: Prima Publishing; 2000;69–77.
- Bruneton J. *Pharmacognosy, Phytochemistry, Medicinal Plants*, 2nd ed. Paris, France: Lavoisier Publishing; 1999;709–10.
- Chang H, But P. *Pharmacology and Applications of Chinese Materia Medica*. Singapore: World Scientific; 1986;725–35.
- Collisson R. Siberian ginseng (*Eleutherococcus senticosus*). *Br J Phytother* 1991;2(2):61–71.
- Czygan F (ed.). *Biogene Arzneistoffe*. Wiesbaden, Germany; 1984;212–6, 220–2.
- DAB. See: *Deutsches Arzneibuch*.
- Davydor M, Krikorian AD. *Eleutherococcus senticosus* (Rupr. & Maxim.) Maxim. (Araliaceae) as an adaptogen: a closer look. *J Ethnopharmacol* 2000;72(3):345–393.
- Deutsches Arzneibuch Ergänzungslieferung*. Stuttgart, Germany: Deutscher Apotheker Verlag; 1999.
- Dowling E, Redondo DR, Branch JD et al. Effect of *Eleutherococcus senticosus* on sub-maximal and maximal exercise performance. *Med Sci Sports Exerc* 1996;28(4):482–9.
- European Pharmacopoeia* (Ph.Eur. 3 Supplement 2000). Strasbourg, France: Council of Europe; 2000;762.
- Fang J, Proksch A, Wagner H. Immunologically active polysaccharides of *Eleutherococcus senticosus*. *Phytochem* 1985;24(11):2619–22.
- Farnsworth N, Kinghorn A, Soejarto D, Waller D. Siberian Ginseng (*Eleutherococcus senticosus*): Current status as an adaptogen. In: Wagner H, Hikino H, Farnsworth NR (eds.). *Economic and Medicinal Plant Research*, Vol. I. London, UK: Academic Press; 1985;155–215, 217–284.
- Filaretov A, Bogdanova T, Podvigina T, Bogdanov A. Role of pituitary-adrenocortical system in body adaptation abilities. *Exp Clin Endocrinol* 1988;92(2):129–136.
- Foster S (ed.). *Herbs of Commerce*. Austin, TX: American Herbal Products Assn.; 1992.
- Foster S. *Siberian Ginseng—Eleutherococcus senticosus*. *Botanical Booklet Series No. 302*. Austin, TX: American Botanical Council; 1991.
- Foster S, Chongxi Y. *Herbal Emissaries: Bringing Chinese Herbs to the West*. Rochester, VT: Healing Arts Press; 1992;73–9.
- Fulder S. The drug that builds Russians. *New Scientist* 1980;576–9.
- Golikov P. Influence of aqueous extracts of roots, stems and leaves of *Eleutherococcus senticosus* and *Panax ginseng* on the mental abilities of working humans. [in Russian]. *Mater K Izuch Zhen-shenya i Drug Lek Dal'nego Vostoka* 1963;5:233–5.
- Hacker B, Medon P. Cytotoxic effects of *Eleutherococcus senticosus* aqueous extracts in combination with N6-(delta 2-isopentenyl)-adenosine and 1-beta-D-arabinofuranosylcytosine against L1210 leukemia cells. *J Pharm Sci* 1984;73(2):270–2.
- Halstead BW, Hood LL. *Eleutherococcus senticosus* (Siberian Ginseng): An Introduction to the Concept of Adaptogenic Medicine. Taiwan, R.O.C.: Oriental Healing Arts Institute; 1984.
- Hänsel R. *Phytopharmaka*, 2nd ed. Berlin, Germany: Springer Verlag; 1991;272–5.
- Health Canada. Product Information: Enzymatic Therapy Vitamin B-12 Capsules with Non-Medicinal Liquid Liver Extract and Siberian Ginseng. In: *Drug Product Database (DPD)*. Ottawa, Ontario: Health Canada Therapeutic Products Programme; 2001.
- Hikino H, Takahashi M, Otake K, Konno C. Isolation and hypoglycemic activity of eleutherosans A, B, C, D, E, F, and G: glycans of *Eleutherococcus senticosus* roots. *J Nat Prod* 1986;49(2):293–7.
- Huang K. *The Pharmacology of Chinese Herbs*, 2nd ed. Boca Raton, FL: CRC Press; 1999;46–8.
- Kaloeva Z. Effect of the glycosides of *Eleutherococcus senticosus* on the hemodynamic indices of children with hypotensive states. [in Russian]. *Farmakol Toksikol* 1986;49(5):73.
- Kaptrchuck T. The Organs of the Body: The Harmonious Landscape. In: *The Web That Has No Weaver: Understanding Chinese Medicine*. Chicago, IL: Congdon & Weed, Inc.; 1983;50–76.
- Kenner D, Requena Y. *Botanical Medicine: A European Professional Perspective*. Brookline, MA: Paradigm Publications; 1996;132–3.
- Kirilov O. The effect of fluid extract of *Eleutherococcus* root on the pituitary-adrenocortical system. [in Russian]. *Sib Otd Acad Nauk S.S.S.R.* 1964;23:3–5.
- Kolomivsky L. Control over adaptive reactions of cardiologic patients using small doses of *Eleutherococcus* extract. In: *New Data on Eleutherococcus: Proceedings of the Second International Symposium on Eleutherococcus*. Moscow, Russia: Academy of Sciences of the USSR Far East Science Center; 1986;265–71.
- Koren G, Randor S, Martin S, et al. Maternal ginseng use associated with neonatal androgenization. *JAMA*. 1990;264:86.
- Leung A, Foster S. *Encyclopedia of Common Natural Ingredients Used in Food, Drugs, and Cosmetics*, 2nd ed. New York, NY: John Wiley & Sons, Inc; 1996;225–7.
- McGuffin M, Hobbs C, Upton R, Goldberg A (eds.). *American Herbal Product Association's Botanical Safety Handbook*. Boca Raton: CRC Press; 1997;45.
- McGuffin M, Kartesz J, Leung A, Tucker A (eds.). *Herbs of Commerce*, 2nd ed. Silver Spring, MD: American Herbal Products Assn; 2001.

- McRae S. Elevated serum digoxin levels in a patient taking digoxin and Siberian ginseng. *Canadian Med Assoc J* 1996;155(3):293–5.
- Medical Products Agency (MPA). Naturläkemedel: Authorised Natural Remedies (as of January 24, 2001). Uppsala, Sweden: Medical Products Agency; 2001.
- MediHerb. *Eleutherococcus* — a herbal adaptogen, Part 1. *MediHerb Professional Newsletter*. 1993 Nov;Number 36.
- MediHerb. *Eleutherococcus* — a herbal adaptogen, Part 2. *MediHerb Professional Newsletter*. 1994 Jan;Number 37.
- Medon P, Thompson EB, Farnsworth NR. Hypoglycaemic effect and toxicity of *Eleutherococcus senticosus* following acute and chronic administration in mice. *Zhongguo Yao Li Xue Bao* 1981;2(4):281–5.
- Medon P, Ferguson P, Watson C. Effects of *Eleutherococcus senticosus* extracts on hexobarbital metabolism *in vivo* and *in vitro*. *J Ethnopharmacol* 1984;10(2):235–41.
- Minkova M, Pantev T. Effect of *Eleutherococcus* extract on the radioprotective action of adeturone. *Acta Physiol Pharmacol Bulg* 1987;13(4):66–70.
- Mikunis R, Serkova V, Shirkova T. The effect of *Eleutherococcus* on some biomedical parameters of the blood in the combined treatment of patients with rheumatic lesions of the heart. *Lek Sredstva Dal'nego Vostoka* 1966; 7:227–30.
- MPA. See: Medical Products Agency.
- Newall C, Anderson L, Phillipson J. *Herbal Medicines: A Guide for Health-care Professionals*. London, UK: The Pharmaceutical Press; 1996;141–4.
- Novozhilov G, Sil'chenko K. Mechanism of adaptogenic effect of *Eleutherococcus* on the human body during thermal stress. [in Russian]. *Fiziol Cheloveka* 1985;11(2):303–6.
- Pearce P, Zois I, Wynne K, Funder J. *Panax ginseng* and *Eleutherococcus senticosus* extracts — *in vitro* studies on binding to steroid receptors. *Endocrinol Jpn* 1982;29(5):567.
- Ph.Eur. See: *European Pharmacopoeia*.
- Ph.Fr. See: *Pharmacopée Française*.
- Pharmacopée Française*. (Ph.Fr.). Paris, France: Adrapparm; 1996.
- Pharmacopoeia of the People's Republic of China* (PPRC English Edition, 1997). Beijing, China: Chemical Industry Press; 1997;132–3, 272, 380–1.
- Pizzorno JE, Murray MT, editors. *Textbook of Natural Medicine*, Volume 1, 2nd ed. New York: Churchill Livingstone; 1999;713–7.
- PPRC. See: *Pharmacopoeia of the People's Republic of China*.
- Schulz V, Hänsel R. *Rationelle Phytotherapie*, 3rd ed. Berlin, Germany: Springer Verlag, 1996;305–306.
- Shadrin A *et al.* Estimation of prophylactic and immunostimulating effects of *Eleutherococcus* and *Schisandra chinensis* preparations. In: *New Data on Eleutherococcus: Proceedings of the Second International Symposium on Eleutherococcus*. Moscow, Russia: Academy of Sciences of the USSR Far East Science Center.; 1986;289–93.
- Sosnova T. The effect of *Eleutherococcus spinosus* on the color discrimination function of the optic analyzer in persons with normal trichromatic vision. [in Russian]. *Vestn Oftalmol* 1969;82(5):59–61.
- Sosuova T. *Eleutherococcus* as a means to raise colour perception of locomotive engineers. In: *New Data on Eleutherococcus: Proceedings of the Second International Symposium on Eleutherococcus*. Moscow, Russia: Academy of Sciences of the USSR Far East Science Center; 1986;258–64.
- State Pharmacopoeia of the Union of Soviet Socialist Republics*, 11th ed., Vols. 1 & 2 (USSR XI). Moscow, Russia: Medicina; 1990
- Szolomicki S, Samochowiec L, Wójcicki J, Drodzdzik M. The influence of active components of *Eleutherococcus senticosus* on cellular defense and physical fitness in man. *Phytother Res* 2000;14:30–5.
- Takasugi N, Moriguchi T, Fuwa T, *et al.* Effect of *Eleutherococcus senticosus* and its components on rectal temperature, body and grip tones, motor coordination, and exploratory and spontaneous movements in mice under acute stress. *Shoyakugaku Zasshi* 1985;39(3):232–7.
- Tang W, Eisenbrand G. *Chinese Drugs of Plant Origin: Chemistry, Pharmacology, and Use in Traditional and Modern Medicine*. New York, NY: Springer Verlag; 1992.
- Tseitlin G, Saltanov A. Some parameters of antistress activity of *Eleutherococcus* extract in patients with Hodgkin's disease after splenectomy. [in Russian]. *Pediatriia* 1981;(5):25–7.
- Tyler VE. Importance of European phytomedicinals in the American market: an overview. In: Lawson LD, Bauer R (eds.). *Phytomedicines of Europe: Chemistry and Biological Activity*. Washington, DC: American Chemical Society; 1998;2–12.
- United States Congress (USC). Public Law 103-417: *Dietary Supplement Health and Education Act of 1994*. Washington, DC: 103rd Congress of the United States; 1994.
- United States Food and Drug Administration (US FDA). 21 CFR (Code of Federal Regulation, Title 21, Volume 2, Parts 100–169), Revised as of April 1, 1999. Washington, DC: Office of the Federal Register National Archives and Records Administration. 1999; 15–19.
- US FDA. See: United States Food and Drug Administration.
- USC. See: United States Congress.
- USSR. See: *State Pharmacopoeia of the Union of Soviet Socialist Republics*.
- Vereschchagin I. Treatment of dysentery in children with a combination of monomycin and *Eleutherococcus*. [in Russian]. *Antibiotiki* 1978;23(7):633–6.
- Wagner H, Nörr H, Winterhoff H. Plant adaptogens. *Phytomedicine* 1994;1:63–76.
- Wagner H. Immunostimulants from medicinal plants. In: Chang H, Yeung W, Tso W, Koo A (eds.). *Advances in Chinese Medicinal Material Research*. Singapore: World Scientific; 1985.
- Werbach M, Murray M. *Botanical Influences on Illness: A Sourcebook of Clinical Research*, 2nd ed. Tarzana, CA: Third Line Press; 1994; 2000.
- Wildfeuer A, Mayerhofer D. The effects of plant preparations on cellular functions in body defense. [in German]. *Arzneimittelforschung* 1994;44(1), Nr. 3:361–6.
- Williams M. Immuno-protection against *Herpes simplex* type II infection by *Eleutherococcus* root extract. *Int J Altern Comp Med* 1995;13:9–12.
- Winther K *et al.* Russian root (Siberian Ginseng) improves cognitive functions in middle-aged people, whereas *Ginkgo biloba* seems effective only in the elderly. (XVI World Congress of Neurology, Buenos Aires). *J Neurologic Sci* 1997;150:S90.
- Yonezawa M, Katch N, Takeda A. Radiation protection by Shigoka extract on split dose irradiation in mice. *J Radiation Res* 1989;30(3):247–54.
- Zaikova M, Verba A, Snegireva M. *Eleutherococcus* in ophthalmology. [in Russian]. *Vestn Oftalmol* 1968;81(3):70–4.

Clinical Studies on Eleuthero (*Eleutherococcus senticosus* [Rupr & Maxim.] Maxim.)

Immunology

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Szolomicki et al., 2000	Immunology	R, Cm n=50 healthy male volunteers	30 days	25 drops eleuthero 3x/day vs. 40 drops echinacea 3x/day	Taigutan® Eleuthero root fluid-ex- tract 1:1 (w/v) vs. Echinacin® echinacea herb fresh juice preparation	In cellular defense mechanism assays, the phagocytic activity of neutrocytes in the eleuthero group rose significantly, and the number of neutrocytes actively participating in phagocytosis increased. Authors conclude that eleuthero extractives affect cellular defense, physical fitness, and lipid metabolism.
Williams, 1995	Immune protection against herpes simplex type II infection	DB, R, PC (2 parallel groups) n=93 volunteers of the Herpes Association	6 months	375 mg 4x/day	Elagen® eleuthero standardized extract (eleuthero- sides B and E)	Effects on frequency, duration, and severity of recurrent episodes of herpes simplex type II infections were observed. Statistically significant results ($p = 0.0002$ to 0.0007) in the eleuthero group where 75% reported improvements in severity, duration, or frequency of attacks vs. 34% in the placebo group.
Shadrin et al., 1986	Immunology	PC n=1,376 students	Fall of 1981 during influen- za epidemic	2 ml extract diluted into a sweetened tea/day	Eleuthero root fluid extract	Occurrence of typical influenza complications (pneumonia, bronchitis, maxillary sinusitis, otitis) in eleuthero group were lower (1.5 cases per 100 persons) vs. control group (3.2 cases per 100), a statistically significant difference ($p < 0.05$).
Bohn et al., 1987	Immunology	DB, PC n=36 healthy volunteers	1 month (followed by a 6-month observation period)	10 ml fluid- extract dilut- ed in wine and sorbitol water 3x/day vs. dry wine with same ethanol content	Eleukokk® fluidextract (0.2% eleutheroside B w/v) vs. dry wine	Eleuthero improved non-specific immune reactivities as determined by quantitative flow-cytometry. Significant increase in the absolute numbers of immunocompetent cells, particularly T-cells, predominantly of the helper/inducer type, but also on cytotoxic and natural killer cells. A general enhancement of the activation state of T-lymphocytes was also observed.

Adaptogenic

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Dowling et al., 1996	Adaptogen, stress, fatigue during submaximal and maximal aerobic exercise	DB, R, PC (2 parallel groups) n=20 male & female athletes (mean age 37 years)	2 months	3.4 ml/day, (6-week treatment, 2-week withdrawal)	Maxim-L® eleuthero fluidextract, 30–34% ethanol (eleuthero- sides B and E present)	No significant differences were observed between test and control groups in heart rate, oxygen consumption, expired-minute volume, respiratory exchange ratio, perceived exertion, and serum lactate. The authors concluded that ergogenic claims cannot be supported based on their results.
Kolomisvsky, 1986	Adaptive response to stress in cardiac patients, which activates protective forces to maintain homeostasis.	Cm n=147 cardiologic patients in 3 groups Group 1: n=42 (ages 23–72); Group 2: n=39 (ages 28–67); Group 3: n=66 (ages 23–56)	7–10 days	Group 1: Received con- ventional therapy (not defined). Group 2: 30 drops/day extract on empty stomach. Group 3: 15–35 drops/day	Eleuthero root fluid- extract (brand not stated) vs. usual treatment (not defined)	Group 1: Adaptive reaction background in non-eleuthero group did not improve. Group 2: Eleuthero extract showed an anti-stress effect and helped to normalize adaptive reactions. Group 3: When used to control adaptive reactions with activation therapy, eleuthero helped patients recover from stress state, resulting in significant increase in normal adaptive reactions.
Asano et al., 1986	Adaptogen, stress, fatigue	SB, PC, CO n=6 healthy male athletes (mean age 21.5 years)	8 days	2 ml extract or placebo 2x/day (morning and evening) 0.5 hours before meal	Medexport (eleuthero root fluid extract) or placebo	Significant increase in all parameters tested for eleuthero treatment period including maximal oxygen uptake ($p < 0.01$), oxygen pulse ($p < 0.025$), total work ($p < 0.005$), and exhaustion time. Athletes in the eleuthero group showed a 23.3% ($p < 0.005$) increase in total exercise duration and stamina compared to 7.5% in placebo group. Increase in total work appeared to be attributable to improvement of bodily oxygen metabolism reflected in the increase in maximal oxygen uptake and maximal oxygen pulse.

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

Clinical Studies on Eleuthero (*Eleutherococcus senticosus* [Rupr & Maxim.] Maxim.) (cont.)

Other

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Winther et al., 1997	Neurology, psychiatry	DB, PC, R, C (4-armed) n=24 healthy volunteers	9 months (3 months eleuthero, 3 months ginkgo, 3 months placebo)	62.5 mg eleuthero root 2x/day or 28.2 mg <i>Ginkgo biloba</i> flavone glycosides 2x/day or placebo	Eleuthero root vs. ginkgo leaf extract (containing 28.2 mg ginkgo flavone glycosides and 7.2 mg ter-pene lactones) vs. placebo	At end of each 3-month dose period, concentration, selective memory, cognitive function, and well-being were measured. Significant improvements in selective memory of eleuthero group vs. placebo group (p<0.02) were demonstrated. No change in concentration was discovered in any group. Significant effects from eleuthero were also noted in feelings of well-being and levels of activity.
Sosuova, 1986	Ophthalmology	PC n=232 healthy locomotive engineers (ages 24–45 years)	100 days	2 ml with 30 ml water, 1x/day (40 days treatment, 60 days no treatment)	Eleuthero root fluidextract (brand not stated)	Eleuthero increased color perception level, induced a one-and-a-half to two-fold increase in functional stability level, 30–50% rise in spectral and contrast sensitivity, 2.5–4.5% rise in range of signal light visibility and 10–15% increase in speed of color discrimination. The effects remained at this level throughout administration and 2–2.5 months after end of treatment period. The placebo group did not experience these changes in perception.

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