

## **Eleuthero**

*Eleutherococcus senticosus*

Plant family: Araliaceae (Ginseng Family)

Eleuthero, although a distant relative of Asian ginseng (*Panax ginseng*), is not a ginseng.

Other common names: Previously referred to as Siberian ginseng

Parts used: The root and aerial parts are used in medicine, with the root being much more researched.

### Overview and Author's Commentary

Eleuthero 1:1 extract is the most well-known, well-researched, and well-suited adaptogen in the world. True Russian eleuthero 1:1 root as well as leaf extract are the predominant herbs in my adaptogenic formulations. They make up about 20 percent by volume. Eleuthero is well suited for the young and for all energetic types. It blends well with other herbs, and because it grows abundantly and quickly throughout areas of Russia and Northern China it can be produced in large quantities for the masses.

Although it was first introduced into the United States during the late 1970s as "Siberian ginseng," in May of 2002 the United States congressional amendment to the Federal Food, Drug, and Cosmetic Act stated that the name ginseng could only be used with the genus *Panax*. This creates great confusion, even many years later.

Therapeutic dosing range:

1:1 extract (Russian): 4 to 10 ml daily

### Safety Profile

Eleuthero is well tolerated, free of side effects, and can be taken for long periods of time.

Eleuthero extract was recently found not to disrupt drug metabolism pathways, demonstrating its safety even when coadministered with drugs. A recent rat study found no negative interaction between eleuthero and warfarin.<sup>1</sup>

### Habitat and Cultivation

Eleuthero is a thorny creeping plant that grows to about two to three meters in height. Its geographic area coincides with ginseng, but these two plants never grow together; it is as if they were purposely avoiding each other. This species grows widely though northern and eastern Russia (Far East of Siberia), and various relatives are spread throughout Northern China, Korea, and Japan.

### Key Constituents

The root contains glycosides, referred to as eleutherosides; sugars, volatile oils, lignans, phenols,  $\beta$ -sitosterol, chlorogenic acid, carophylline, isofraxidine, syringaresinole, cesamine, caffeic acid, coniferol aldehydein, starch, and minerals. No alkaloids are detected. Glycosides are the major compounds of interest and provide the primary therapeutic activity of eleuthero as well as ginseng. The major glycosides have been identified and given the term eleutherosides (A, B, B<sub>1</sub>, C, D, E, F, and G). Eleutherosides are steroidal glycosides: Eleutheroside A is identical to daucosterol; eleutheroside B<sub>4</sub> is identical to sesamin; eleutheroside B<sub>1</sub> is isofraxidin which is more accurately known as isofraxidin-7-O -b -L -glucoside, or

syringaresinol; eleutheroside E is (–)-syringaresinol-4,4'-O-β-D diglucoside, also identical to acanthoside D; and eleutheroside E1 is (–)-syringaresinol-O-β-D monoglucoside. Secondary compounds include, phenolic compounds, chlorogenic acid being the most abundant. Also present is betulinic and caffeic acid, vitamin E and β-carotene, sitosterol and daucosterin, as well as a number of lignans, such as sesamin and syringin, all of which contribute to Eleuthero's redox-antioxidative and anti-cancer effect(s). In the stem bark and fruits rutoside (quercetin-3-rhamnoglucoside) is also present. Eleuthero not only synthesizes lignans such as syringin, syringaresinol and sesamin, but also makes lignan precursors such as hydroxycinnamic acid-caffeic acid and other intermediate compounds of lignan synthesis such as coniferylaldehyde. These precursor compounds have been shown to have significant anti-cancer activity. (M. Davydov, A.D. Krikorian, *Eleutherococcus senticosus* (Rupr. & Maxim.) Maxim. (Araliaceae) as an adaptogen: a closer look. J Ethnopharmacol. 2000 Oct;72(3):345-93.)

Eleutheroside B is the most important compound found in eleuthero, and eleutheroside E is the second most important. In Russia both these markers are tested on each batch of eleuthero extract for quality assessment. Triterpene saponins include eleutheroside I, K, L, and M. Minerals include calcium, phosphorus, potassium, magnesium, sodium, aluminium, barium, iron, strontium, boron, copper, zinc, manganese, and chromium.<sup>2</sup> The roots are collected for extraction during the month of October when active constituents of the roots are highest.<sup>3</sup>

Eleuthero leaf contains a multitude of eleutherosides, including A, B, C, D, E, F, and G; glucosides; fatty acids; and flavonoids, including anthocyanins (redox-antioxidative).

The constituents in eleuthero that have been most studied are the eleutherosides.<sup>4</sup> Seven primary eleutherosides have been identified, with most of

the research focusing on eleutherosides B and, to a lesser extent, E.<sup>5</sup> It is important to note that much eleuthero commercially available outside of Russia is from China, where it is known as Ciwuja and is acknowledged to be less potent than the eleuthero grown in Siberia. Eleuthero of Russian origin contains larger amounts of several bioactive compounds, including the eleutherosides, especially eleutheroside B, B<sub>1</sub>, and E, which play significant roles in the adaptogenic, antistress, and anabolic actions of eleuthero. A number of studies made at the Molecular Biology Institute of Chemical Physics of the Russian Academy of Sciences, under the guidance of I. N. Todorov, clearly demonstrated that eleutheroside B is the major compound in eleuthero and is responsible for its antistress, adaptogenic, and anabolic effects, although B<sub>1</sub> and E are also important. Eleutheroside B is highest in the Russian plant and is completely absent in the eleuthero grown in China, which supplies most of the eleuthero sold in the United States—and which is why chemical standardization of plant extracts is needed.<sup>6</sup>

### Traditional Use

The use of eleuthero root, referred to as Ciwuja in traditional Chinese medicine, dates back 2,000 years; it was used to prevent respiratory tract infections, colds, and the flu. It was also believed to provide energy and vitality. In Russia, eleuthero was originally used by the people in the Taiga region of Siberia to increase performance and quality of life and to decrease infections. The use of eleuthero as a popular remedy in Russia did not begin until the late 1950s; in 1964 it was approved by the Ministry of Health in Russia as an adaptogen.<sup>7</sup>

Eleuthero leaf was traditionally used as a poultice, a compress, and as an anti-inflammatory remedy.<sup>8</sup>

## Modern Research

Eleuthero is the most widely studied adaptogenic herb and is often referred to as the “king” adaptogen. There are more published scientific studies (more than 3,000) on eleuthero than on any other herb in the world.

Eleuthero protects the body and enhances its various systems against the ill effects of any type of stress, including that resulting from work load, heat, cold, excessive exercise, hypokinesia, and radiation. Eleuthero demonstrates favorable effects on various human functions as well, including visual acuity, color differentiation, hearing, fatigability, and thinking association with motor activity. More so than any other adaptogenic agent it displays a normalizing effect regardless of the physiological abnormalities (e.g., normalization of blood pressure in patients with both elevated or lowered blood pressure and normalization of blood sugar levels in hyper- or hypoglycemia).<sup>9</sup> Eleuthero decreases adrenal hypertrophy, a common manifestation of prolonged stress response, and spares the loss of vitamin C from the adrenal glands. Its wide range of therapeutic actions, lack of side effects and toxicity, and overall normalizing action justify its reputation as the king adaptogen.

Eleuthero grows much faster than *Panax ginseng* and can be more easily cultivated while retaining active compounds, as long as it is grown in its native areas, particularly in Russia. It is without any adverse effects, whereas ginseng in some people can produce a few adverse effects. Modern research proved that eleuthero increased stamina and endurance in Soviet Olympic athletes and Russian cosmonauts, explorers, divers, sailors, factory workers, pilots, train operators, and miners. Eleuthero extract, because of its enhanced ergogenic activity (Ergogenic is an adjective derived from the Greek word ‘ergo’ for work and ‘gen’, meaning ‘production of’), was incorporated into their athlete-training

protocols by Soviet-era coaches. (Same reference as above) Research also demonstrated that eleuthero prevented and treated infectious diseases such as the flu and prevented stress-related illness and fatigue, diabetes, heart disease, cancer, and chemical toxicity. After the Chernobyl nuclear accident, many Russian and Ukrainian citizens were given eleuthero to counteract the effects of radiation. Eleuthero has been shown to protect humans and animals from radiation and chemotherapy; it has been studied and used in oncology as an immune-modulating compound to improve cancer patient survival and recovery as well as to inhibit metastasis and cancer reoccurrence.<sup>10</sup>

Many studies show the role of eleuthero as an important tool in cancer treatment, as an antitoxin and antioxidant, as a radiation/chemotherapy-protective and immune restorative/enhancing agent, and to further inhibit cancer growth. I use eleuthero and other adaptogens in every one of my cancer protocols. Israel Brekhman has said this about eleuthero: “Eleutherococcus is not a panacea, but a necessary agent for virtually all patients.”

Eleuthero's actions:

- Nonspecific antistress effects
- Adaptogenic<sup>11</sup>
- Ergogenic

Anabolic/anticatabolic

- Antitoxic<sup>12</sup>
- Radioprotective<sup>13</sup>
- Chemoprotective<sup>14</sup>
- Immunoprotective<sup>15</sup>
- Immunoregulatory<sup>16</sup>
- Antiviral<sup>17</sup>

- Gonadotrophic<sup>18</sup>
- Insulintrophic/antidiabetic<sup>19</sup>
- Neuroprotective

D. Lee, J. Park, J. Yoon, M.Y. Kim, H. Y. Choi, H. Kim. Neuroprotective effects of Eleutherococcus senticosus bark on transient global cerebral ischemia in rats. *J Ethnopharmacol.* 2012 Jan 6;139(1):6-11. Epub 2011 May 27.

Eleuthero is believed to support adrenal gland function when the body is challenged by stress. It enhances physical capability and stamina and stimulates mental work ability (quality of work).<sup>20</sup> The leaf extract is more effective in mental and physical stimulation, while the root extract is more effective at sustaining performance over a long period of time. The leaf is also more effective for balancing blood insulin and glucose levels than the root. Using the leaf and root extract together appears to be more effective than either one used alone.<sup>21</sup>

Eleuthero, the king of adaptogens:

- Antifatigue; enhances mental acuity and physical endurance, work, and exercise capacity without the letdown that comes with stimulants such as caffeine products<sup>22</sup>
- Increases noradrenalin and serotonin and quicker recovery from acute stress<sup>23</sup>
- Improves oxygen uptake by exercising muscles, enabling longer workouts and quicker recovery time for performance athletes<sup>24</sup>
- Anabolic effect; stimulates protein synthesis in the pancreas, liver, and adrenal cortex<sup>25</sup>
- Improves learning and memory<sup>26</sup>
- Protects against environmental pollutants and radiation<sup>27</sup>
- Normalizes body temperature, thus treating hypothermia<sup>28</sup>
- Regulates blood-sugar levels (leaf extract is more effective than the root)<sup>29</sup>

- Protects the liver and enhances its ability to break down and eliminate drugs from the body<sup>30</sup>
- Increases the body's ability to resist infection; prevents colds and flu and shortens recovery time<sup>31</sup>
- Antiviral<sup>32</sup>
- Supports optimum endocrine function<sup>33</sup>
- Immunoprotective<sup>34</sup>
- Anticancer<sup>35</sup>
- Inhibits metastasis of cancer<sup>36</sup>
- Decreases the side effects of toxic therapies like chemotherapy and radiation<sup>37</sup>
- Strong antioxidant against free radicals and antilipid peroxidative activities<sup>38</sup>
- Improves visual acuity and color perception<sup>39</sup>
- Antialcoholic<sup>40</sup>
- Protects against bone loss induced by steroid hormones<sup>41</sup>
- Antitoxin<sup>42</sup>
- Improves circadian biorhythms

There are a great many clinical studies on the capacity of eleuthero to modulate various systems of the body, inhibiting the process of diseases such as those of the upper respiratory tract (in particular influenza), atherosclerosis, hypertension, arrhythmia, rheumatic heart disease, nephritis, and diabetes. Among the multiple effects of Eleutherococcus fluid extract 1:1, the predominant accumulation of eleutheroside B is critical to its adaptogenic actions. Eleutheroside B has demonstrated normalizing actions throughout the endocrine system, including the pituitary, adrenals, and pancreas.<sup>43</sup>

A stress reaction is based on the activation of an organism's energy supply by means of catabolic processes. The key trigger of these processes is the stress-induced hyperproduction and hypersecretion of adrenal cortical glucocorticoid



hormones. The most striking biological property of eleuthero is its ability to prevent or alleviate the general adaptation syndrome, which is well known to be an overall nonspecific defense reaction of the body to any sufficiently strong exogenous or endogenous factor. The defense reaction is generally designed briefly as stress.

There are over 100 publications available on the antistress action of eleuthero, which was first discovered by O.I. Kiriliov and further researched by Israel Brekhman and Igor Vasilevich Dardymov. These scientists discovered that the administration of a 1:1 fluid extract of eleuthero root to animals under stress as a result of many hours of immobilization led to a significant alleviation of the initial stress stage alarm. In these studies it was found that there was no adrenal hypertrophy; less weight loss of the thymus, spleen, thyroid gland, liver, and kidneys; less urinary 17-ketosteroid excretion; and less loss of ascorbic acid (vitamin C) from the adrenal glands. When individual eleutherosides were tested, eleutheroside B<sub>1</sub> prevented some stress manifestations, while eleutheroside E spared glycogen stores in the liver and muscle and in creatine phosphate, thus preserving energy.<sup>44</sup>

Eleuthero has the ability to decrease the level of the alarm reaction, delaying the onset of adrenal exhaustion (the third phase of Hans Selye's general adaptation syndrome). Eleuthero allows a more economical and efficient release of corticosteroids and adrenaline. Endocrine effects of eleuthero can be inferred from an increase in the weight of the adrenal cortex, while the simultaneous decrease in the content of cholesterol and ascorbic acid indicates an increased formation of corticosteroids.<sup>45</sup>

When it comes to stress, eleuthero enhances the ability to energize and mobilize the protective mechanisms. It increases the mobilization of energy and working tissue during stress and decreases the response back to normal levels following its usage, thus decreasing the long-term damaging effects of stress. It is

well suited for anyone who is stressed out, run down, “burning the candle at both ends,” traveling and not getting enough sleep, working long hours, pushing mentally and/or physically, and undergoing surgery or cytotoxic cancer treatments. Eleuthero is highly effective in improving our adaptive capability to respond to adverse conditions. It can help with temperature extremes, immobilization, recovery from injury, recovery from drug intoxication, cancer therapies, X-rays, the effects of high-dose hormone therapies (insulin, epinephrine, steroids), and jet lag. It has a preventive effect against biological pathogens and improves both mental and physical work capacity. Eleuthero can be used in any circumstance where there is a need to normalize any physiological, biochemical, or immunological defect.<sup>46</sup>

Eleuthero extract increases the ability of humans to withstand many adverse physical conditions (i.e., heat, noise, motion, work-load increase, exercise, and decompression) and improves mental alertness and work output, especially under stressful conditions. A variety of stress-related illnesses have been studied, including angina, hypertension, hypotension, acute pyelonephritis (kidney inflammation), various types of neuroses, acute craniocerebral trauma, rheumatic heart disease, chronic bronchitis, and cancer.<sup>47</sup> In all such cases, the anabolic effects of eleuthero extract contribute to an enhanced immune system response.<sup>48</sup> Eleuthero extract increases general immunogenesis and in particular interferon production and is thus antiviral.<sup>49</sup>

Eleuthero has both an overall tonic effect and an immune-enhancing antiviral effect that contributes to its reputation as a disease-preventative herb. A double-blind, placebo-controlled, randomized phase 3 pilot study of an adaptogenic formula consisting of extracts of *Rhodiola rosea*, *Schisandra chinensis*, and *Eleutherococcus senticosus* was carried out on two parallel groups of patients suffering from acute nonspecific pneumonia. The adaptogenic formula produced a

significant effect on the recovery of patients by decreasing the duration of the acute phase of the illness, by increasing mental performance of patients in the rehabilitation period, and by improving their quality of life.<sup>50</sup>

Though eleuthero has no direct cytotoxic effect on cancer cells, it has been clinically proven to demonstrate a host of other beneficial effects with regard to cancer. These include:

- Increasing the body's immune response against cancer
- Improving the overall health of the patient, reducing fatigue, and enhancing the health of all the vital organs
- Serving as a general antitoxic/antioxidant
- Retarding the development of cancer and cancer metastases
- Increasing tolerability of radiation treatment and preventing radiation sickness; protecting and enhancing the effectiveness of radiation
- Increasing the tolerability and effectiveness of chemotherapy and biological therapy; improving immune system recovery; protecting vital organs and enhancing the general condition in terms of appetite, sleep, energy level, etc.<sup>51</sup>

In a double-blind clinical trial for stress-induced hypertension it was found that eleuthero is able to reduce cardiovascular responses to stress in healthy young volunteers, while the placebo was ineffective.<sup>52</sup> Eleuthero modulates lipids and reduces cholesterol<sup>53</sup> and improves patients with ischemic heart disease.<sup>54</sup> Repeated prophylactic administration of plant adaptogen preparations based on extracts from rhodiola, eleuthero, leuzea, and ginseng produced a pronounced antiarrhythmic effect on the model of adrenal arrhythmia in animals.<sup>55</sup> Administration of eleuthero to albino rats (eighteen to twenty months old) for thirty days activated the anticoagulating system and protected the animals from thrombosis with an intravenous administration of tissue thromboplastin (a plasma

protein aiding blood coagulation) . The effect of the adaptogen was more obvious after a sixty-day treatment.<sup>56</sup>

Eleuthero extract (leaf and root) can substantially lower blood sugar levels in humans and animal adrenaline and dietary hyperglycemia <sup>57</sup>

Oral administration of Eleuthero powder offered significantly neuroprotection, by reduced hippocampal neuronal death by up to 53.1%, respectively, compared with a vehicle-treated group. Eleuthero mechanism included antiinflammatory and protection from ischemia. <sup>58</sup>

Numerous studies have demonstrated that memory deficits induced by sleep deprivation in experimental animals can be used as a model of behavioral alterations. Eleutheroside E, a principal component of Eleutherococcus senticosus, improves behavior in sleep deprivation stress model. <sup>59</sup>

Extracts of Eleuthero have shown to neuroprotective effects, as well as an ability to regenerate neurites and the reconstruct synapses in rat cultured cortical neurons damaged by amyloid  $\beta$ . Eleutheroside B is the most regenerative active constituent in Eleuthero. <sup>60</sup>

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