

*Eleutherococcus senticosus*/  
*Acanthopanax senticosus*

## Siberian Ginseng, Eleuthero

### Indications

Fatigue, poor stamina, and stress intolerance. Used for nervous and mood disorders such as depression, mental fatigue, and poor concentration and is a traditional remedy to improve immune function in both chronic and acute infections.

### Mechanism of Action

Much of medicinal actions of *Eleutherococcus* are credited to the eleutherosides, a group of liposoluble phenylpropanoid and lignin glycosides found in the roots and stems, including syringin (eleutheroside B) and syringaresinol (eleutheroside E),<sup>1</sup> schisandrin, and sesamin.<sup>2</sup> Species related to *E. senticosus* have also been found to contain some of the same eleutherosides.<sup>3</sup>

Eleutherosides are largely credited with the antifatigue effects of *Eleutherococcus*<sup>4</sup>; for example, syringin has an insulintropic effect;<sup>5</sup> enhances the secretion of  $\beta$ -endorphin from adrenal medulla; and stimulates peripheral opioid receptors, resulting in a decrease of plasma glucose in insulin-dependent diabetic rats.<sup>6</sup> Eleutherosides have also been shown to exert antifatigue effects in a forced swimming test, lowering plasma triglycerides, lactate dehydrogenase, and blood urea nitrogen compared to controls. The lowering of lactate dehydrogenase and blood urea nitrogen suggests a decrease in muscle damage from intense physical exertion.<sup>7</sup> Eleuthero improves stamina by enabling skeletal muscle to better use lipids and spare glycogen, thereby reducing lactic acid buildup and increasing oxygen saturation and blood glucose and free fatty acid availability in situations of heavy exertion, improving lipid utilization and boosting cardiovascular metabolism.<sup>8,9</sup>

Other active compounds include triterpenoid saponins called acanthopanaxosides<sup>10</sup> including sessilaside, tauroside, ciwujianosides, and chiisanoside and a sesquiterpenoid saponin called oplopanone B.<sup>11</sup> Ciwujianosides are mast cell stabilizers, reducing histamine release provoked by immunoglobulins. One study reported the antihistamine effects to be approximately 6800 times stronger than that of disodium cromoglycate at a similar dosage.<sup>12</sup>

*Eleutherococcus* also contains coumarins such as isofraxidin,<sup>13,14</sup> and flavones.<sup>15</sup> The coumarin isofraxidin, found in *Eleutherococcus* and other plants, is credited with antioxidant, anti-inflammatory, and immune-modulating activities. Isofraxidin inhibits cyclooxygenase expression in the lungs that regulates the production of prostaglandins<sup>16</sup> and inhibits nuclear factor- $\kappa$ B (NF- $\kappa$ B) pathways,<sup>17</sup> offering tissue-protective effects.

In addition, *Eleutherococcus* contains immune polysaccharides, a group of water-soluble, acidic, branched-chain heteroglycans compounds with high molecular weights, which show significant immune-

stimulatory activities as demonstrated by granulocyte and carbon clearance tests and are noted to protect against pathogens and toxins.<sup>18</sup> One mouse investigation showed the polysaccharide fraction to suppress tuberculosis from propagating the lungs.<sup>19</sup> Another animal study showed the polysaccharides to inhibit tumor growth.<sup>20</sup>

The many neuroprotective and antidepressant abilities of *Eleutherococcus* are based on its antioxidant mechanisms, providing protection from numerous cytokines and inflammatory mediators.

*Eleutherococcus* protects neurons from corticosterone-induced cytotoxicity and protects against lowering of natural killer cell activity seen with physical stress. Different concentrations of Eleuthero (50, 100, 200, and 400 µg/mL) significantly increase cell viability in animals and cell cultures, decreasing lactate dehydrogenase release, suppressing apoptosis of cells, attenuating intracellular Ca(2+) overloading, and up-regulating brain-derived neurotrophic factor mRNA level and cAMP response element-binding protein expression compared equal to that of a corticosterone-treated control group.<sup>21</sup> Animal studies suggest that Eleuthero has antidepressant effects at doses of 1000 and 2000 mg/kg/day, via significant elevation in serotonin, norepinephrine, and dopamine levels in the brain.<sup>22,23</sup>

## Evidence-Based Research

*Eleutherococcus* has fairly extensive molecular, animal, and human research demonstrating antistress, antiulcer, anticancer, antioxidant,<sup>24</sup> anti-inflammatory,<sup>25</sup> neuroprotective,<sup>26,27</sup> hepatoprotective, and cardioprotective<sup>28,29</sup> activities.

*Eleutherococcus* improves basic immune status and has immune-modulating effects, up- or down-regulating various cytokines as appropriate to the situation.<sup>30</sup> A human placebo-controlled study evaluated the effects of 10 mL of *Eleutherococcus* tincture 3 times a day for 4 weeks on immune parameters in healthy subjects. *Eleutherococcus* was shown to significantly increase the number of immune-competent cells, particularly T helper lymphocytes, as well as cytotoxic and natural killer cells.<sup>31</sup> *Eleutherococcus* may impact the immune system by helping to protect the body from immunosuppressive and toxic compounds. For example, animal studies show *Eleutherococcus* restores macrophage and B and T lymphocyte levels when suppressed due to cadmium toxicity<sup>32</sup>; enhances survival after parathion exposure;<sup>33</sup> and protects animals from endotoxic shock, reducing production of inflammatory mediators and NF-κB activation and preventing the infiltration of inflammatory cells into the heart, liver, and lung.<sup>34</sup>

*Eleutherococcus* has demonstrated supportive effects on mood and fatigue. The “central fatigue hypotheses” proposes that depression, lethargy, and poor stress tolerance correspond to declining neurotransmitter levels in the central nervous system. *Eleutherococcus* can mitigate the decline of serotonin and other neurotransmitters and support the levels to recover after physical stress and heavy exertion, as well as psychic stress.<sup>35</sup> A single dose of *Eleutherococcus* to rats is shown to elevate noradrenaline and dopamine and their metabolites in the brain acutely.<sup>36</sup> *Eleutherococcus* has been shown to restore the behavioral changes and hippocampal monoamines in sleep-deprived mice to normal levels.<sup>37</sup> *Eleutherococcus* has demonstrated numerous neuroprotective properties via anti-inflammatory effects and prevents neuritic atrophy and synaptic loss, which may contribute to concentration- and memory-enhancing effects of the plant.<sup>38</sup>

*Eleutherococcus* has also demonstrated effects on improving stamina in exhausted patients and vitality in cancer patients,<sup>39</sup> as well as increase exercise tolerance in trained athletes. Animal studies have shown eleutherosides to significantly alleviate both physical and mental fatigue in forced swimming tests,<sup>40</sup> lowering the corticosterone spike compared with control animals.<sup>41</sup> *Eleutherococcus* improves

endurance in healthy athletes compared to placebo in a small crossover study at a dose of 800 mg/day for 8 weeks.<sup>42</sup> Another study showed *Eleutherococcus* to improve exercise performance in middle-aged healthy volunteers.<sup>43</sup> *Eleutherococcus* may increase rather than decrease hormonal indices of stress in athletes, a finding consistent with animal research and suggesting there to be a threshold of stress where *Eleutherococcus* increases cortisol responses; and when this threshold is exceeded, *Eleutherococcus* decreases the stress response. One clinical trial on fit endurance athletes showed *Eleutherococcus* to decrease the testosterone-to-cortisol ratio (increase cortisol), but in a nonsignificant trend.<sup>44</sup>

## Safety in Pregnancy and Breastfeeding

There are no published studies focusing on teratogenicity of the use of *Eleutherococcus* during pregnancy and lactation. One rat study demonstrated Eleuthero to protect embryos from the toxic and teratogenic effects of ethanol in pregnant rats.<sup>45</sup>

## General Safety

Human trials have not shown adverse events or significant side effects with the use of 300 mg/day for several months' time.<sup>46,47</sup>

## Dosage

This herb is generally considered safe at doses up to 800 mg/day (standardized to >1% eleutheroside content), depending on the strength of the extract and whether it is being used alone or in combination with other herbs.

## Traditional Uses

Many *Eleutherococcus coccus* (aka *Acanthopanax*) species grow in Siberia, China, Korea, Japan, and the Philippines; however, *E. senticosus* is the most well-known and studied species. The plant is known as “Siberian ginseng” in North America, Shigoka in Japan, and Ciwujia in China where it has been widely used to invigorate qi/chi, meaning general energy and vitality. It should be noted that *Eleutherococcus* is not a true ginseng, but that it does share some similarities as an adaptogen and immune tonic with members of the *Araliaceae* such as *Panax ginseng* (aka Chinese or Korean ginseng).

Traditional uses for *Eleutherococcus* are numerous and include an emphasis for fatigue, poor stamina, and stress intolerance and also nervous and mood disorders such as depression, mental fatigue, and poor concentration. *Eleutherococcus* is considered a traditional remedy to treat chronic and acute infections and improve immune function and to protect against toxins including hepatotoxins, neurotoxins, and cerebral vascular inflammation. *Eleutherococcus* has been used to improve cardiovascular inflammation and treat ischemic disorders, hypertension, and hepatitis.

Due to its multitude of tonifying and protective actions, *Eleutherococcus* is considered one of the most important “adaptogenic” herbs for supporting immunity and improving resistance to stress and fatigue.<sup>48</sup> Adaptogens are traditionally used to support health and prevent disease in both sick and healthy individuals through nonspecific effects, which neutralize various environmental and physical stressors while remaining relatively safe and free of side effects.

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