

*Rhodiola rosea*

## Arctic Rose, Golden Root

### Related Species

*Rhodiola imbricate*, *Rhodiola sachalinensis*.

### Indications

An adaptogen used to help the body adapt to physical, mental, and environmental stresses; increase energy, stamina, strength, and mental capacity; improve athletic performance and sexual function; and balance mood for depressive and anxious states.

### Mechanism of Action

*Rhodiola* root contains phenylpropanoids and phenylethanol derivatives including salidroside (also known as rhodioloside and rhodosin), rosavin, rosin, rosarin, rhodiolin, and rosiridin. A range of antioxidant compounds have also been identified in *Rhodiola rosea* and related species, including flavonoids and phenolic acids such as *p*-tyrosol, gallic acid, caffeic acid, and chlorogenic acid; catechins; and proanthocyanidins. Salidroside is the most studied compound in *Rhodiola*, and along with *p*-tyrosol, rosin, rosavin, and rosarian, are thought to be critical for the plant's observed adaptogenic effects.<sup>1</sup>

Many of *Rhodiola*'s mood, stress, and cognition-enhancing effects are credited to effects on monoamines in the CNS. Animal investigation and molecular studies suggest *Rhodiola* to increase 5-hydroxytryptamine<sup>2,3</sup> and serotonin receptor expression and to act as  $\mu$ -opioid receptor<sup>4,5</sup> and  $\kappa$ -opiate receptor<sup>6</sup> agonists, promoting the release of  $\beta$ -endorphin and exerting an anxiolytic, antiarrhythmic, and hypotensive action.<sup>7</sup> Molecular studies demonstrate *R. rosea* roots to have potent antidepressant activity by inhibiting monoamine oxidase (MAO) A and may also find application in the control of senile dementia by their inhibition of MAO B.<sup>8</sup> *Rhodiola* may also reduce the stress-induced release of catecholamines,<sup>9</sup> possibly through the up-regulation of opiate pathways.<sup>10</sup>

Salidroside is credited with antioxidant and vascular protective properties and an ability to increase mitochondrial mass and up-regulate mitochondrial biogenesis factors.<sup>11</sup> Cell culture studies have shown salidroside to protect human cortical neurons from oxidative stress. It also protects against intracellular calcium increases invoked by various free radicals and optimizes  $\text{Ca}^{2+}$  homeostasis.<sup>12</sup>

## Evidence-Based Research

Research has suggested that *Rhodiola* is effective in asthenic conditions (decline in work performance, sleep difficulties, poor appetite, irritability, hypertension, headaches, and fatigue) developing subsequent to intense physical or intellectual strain.<sup>13</sup>

Much of the animal and human research has suggested *Rhodiola* to be helpful in situations of acute and chronic stress. Animal models of stress often use forced swimming to assess physical and biochemical parameters and the effects of pretreatment with medications. Several animal studies have compared pretreatment with *Rhodiola* salidroside to placebo on a forced swimming model of stress and reported that the serum improved some indices of free radical control and energy metabolism, increasing liver superoxide dismutase and glutathione peroxidase activity of antioxidant enzymes, stabilizing blood sugar, increasing liver glycogen and muscle glycogen reserves, and increasing the metabolism of fat. Human investigations have also shown *Rhodiola* to improve cardiovascular and respiratory efficiency in situations of extreme physical exertion.<sup>14</sup>

*Rhodiola* has shown positive effects on concentration, cognition, and mood. *Rhodiola rosea* may improve attention, cognitive function, and mental performance in fatigue and in chronic fatigue syndrome.<sup>15</sup> Single acute doses of *R. rosea* extract exerted significant antidepressant and anxiolytic effects in mice at doses of 10, 15 and 20 mg/kg.<sup>16</sup> Animal models of nicotine addiction show *Rhodiola* to increase and lessen the anxiety symptoms of nicotine withdrawal compared with control.<sup>17</sup>

A multicenter study investigated the effects of 200 mg of *Rhodiola* twice a day compared with placebo on stress symptoms and reported that improvements could be seen as early as 3 days, with continued improvements over each week of the study.<sup>18</sup> One randomized controlled trial on nursing students doing shift work showed 364 mg/day of *Rhodiola* to reduce fatigue compared with placebo.<sup>19</sup> A similar study showed *Rhodiola* to improve fatigue during night duty in young, healthy physicians compared with placebo.<sup>20</sup> A randomized, double-blind, placebo-controlled, parallel-group clinical study investigated the effect of a single dose of standardized *R. rosea* extract on capacity for mental work against a background of fatigue and stress, in a population of young healthy cadets aged 19–21 years. There was a significant antifatigue effect demonstrated by *Rhodiola* compared with placebo.<sup>21</sup>

A phase III randomized, double-blind, placebo-controlled study with parallel groups investigated the effects of *Rhodiola* in the treatment of stress-related fatigue. Participants received either 576 mg of *Rhodiola* extract per day or placebo and were evaluated with both symptoms questionnaires and with a.m. salivary cortisol testing on days 1 and 28 of the study. *Rhodiola* was shown to exert an antifatigue effect, with increased mental performance and ability to concentrate and decreased waking cortisol compared with placebo in patients with fatigue syndrome.<sup>22</sup> Researchers have proposed that *Rhodiola* could be an alternative medication to improve energy for thyroid cancer patients unable to use thyroid hormone medications.<sup>23</sup>

## Safety in Pregnancy and Breastfeeding

There are no published studies or investigations focusing on the use of *Rhodiola* in pregnancy or lactation at this time.

## General Safety

Toxicity studies dosing rats with 100, 250 or 500 mg/kg of *Rhodiola imbricata* have not revealed toxicity. There were no significant changes in the organ/body weight ratio or in the histological, hematological, and biochemical variables studied, except for an increase in plasma glucose and protein levels at both the higher doses, which were restored to normal after a 2-week withdrawal of treatment.<sup>24</sup> Toxicity investigations of *R. imbricata* has shown similar tolerability and safety profile.<sup>25</sup> Meta-analyses of clinical trials have not identified significant side effects, and *Rhodiola* is generally well tolerated.<sup>26</sup> Adverse events were mostly of mild intensity, and no serious adverse events were reported.

Salidroside has shown no genotoxicity under the conditions of the reverse mutation assay, chromosomal aberrations assay, and mouse micronucleus assay conditions.<sup>27</sup>

There is an anecdotal case of *Rhodiola* interacting with an antidepressant medication.<sup>28</sup> *Rhodiola* was found not to interfere with either warfarin or theophylline.<sup>29</sup>

## Dosage

*Rhodiola* is often dosed at 200–800 mg daily of an encapsulated root powder (standardized to 1%–2% rosavin). This herb is generally considered safe, even at doses up to 2 g/day; however, smaller doses are typical when *Rhodiola* is combined with other herbs in a formula or in a more concentrated extract.

## Traditional Uses

*Rhodiola rosea*, the Arctic rose, grows at high altitudes of the Northern Hemisphere. It has been used as a remedy for altitude sickness; to treat fatigue, both mental and physical; and to improve energy and stamina. The roots are used as mild nerve stimulants in cases of depression and lethargy. *Rhodiola* has also been used traditionally in traditional Chinese medicine, and it continues to be used for ischemic heart disease and angina pectoris in China. In the modern era, Arctic rose has become established as an adaptogenic herb—an agent capable of increasing resistance to a variety of chemical, biological, and physical stressors.

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