

## *Rhodiola rosea* – Rhodiola

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Family: Crassulaceae

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Part Used: Root

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### General Information

*Rhodiola rosea* (*Sedum roseum*) is found in Arctic regions including Alaska, north-eastern Siberia and northern parts of Europe. The botanical name alludes to the rose-like odour of the rootstock when freshly cut. The use of Rhodiola in the orthodox medicine of the former USSR goes back to a number of pharmacological and clinical investigations in the early 1960s. Rhodiola preparations became incorporated into the official medicine by 1969 and are described in the last official USSR Pharmacopoeia and the current Russian Pharmacopoeia. Other common names include golden root, rose root, Arctic root and Russian Rhodiola.

### Traditional Uses

The root of Rhodiola has been used in the traditional medicine of many countries including Russia, Scandinavia and Middle Asia. Rhodiola was regarded as a tonic and stimulant and used to increase physical endurance, attention span, memory and work productivity and resistance to high altitude sickness. Other uses included to treat fatigue, depression, anaemia, impotence, infections (including colds and influenza), cancer, nervous system disorders and headache; for longevity and to enhance fertility.<sup>1-3</sup> *Rhodiola rosea* root was used as a food, for example in Siberia, Greenland and Alaska, but not in Norway perhaps because of the sharper taste of plant from that location. The root has been used to flavour beer in Norway, and a decoction of the root was used as a hair wash, to promote hair growth, prevent hair loss, and for treatment of dandruff.<sup>4</sup>

### Scientific Studies

#### Constituents

Phenylpropanoids such as rosavin, rosarin and rosin are typical components of *Rhodiola rosea* root. Other constituents include salidroside (a hydroxyphenethyl (tyrosol) glucoside) and the monoterpene rosiridin. Salidroside is present in a variety of species, including

some outside the Rhodiola genus. The term rosavins is used collectively for rosavin, rosin and rosarin. Because of the occurrence of salidroside in other species, Rhodiola extracts are best standardised for both rosavins and salidroside. The naturally occurring ratio of rosavins to salidroside in the authentic root is approximately 3:1. Other species containing salidroside but not rosavins have been substituted for *R. rosea*. Analysis of commercial samples of Rhodiola available in the United States in 2000 found that although all of the samples contained *R. rosea* extracts, the amounts of phenylpropanoid constituents were lower than in the reference plant material, suggesting admixture with other species. The daily dose of phenylpropanoid constituents varied widely from 0.78 to 6.87 mg, based on the manufacturers recommended tablet dosage.<sup>1,2</sup> Russian experience in the 1980s found that products manufactured with Rhodiola root not containing rosavins were therapeutically inferior.<sup>5</sup>

Other constituents of Rhodiola root include flavonoids, tannins and an essential oil. (In comparison with some other medicinal roots, Rhodiola root contains a low content of essential oil.) In terms of the characteristic rose fragrance of the root, several compounds with a rose odour and other floral notes have been identified from specimens grown in Norway. Geraniol was found to be the main rose-like odour compound, which is one of the most abundant monoterpene alcohols in the essential oil from roses.<sup>6</sup>

### Pharmacodynamics

#### Adaptogenic & Tonic Activity

Following extensive pharmacological investigations of a range of plants, Russian scientists proposed Rhodiola as an adaptogenic herb in 1968. Results established that administration of *Rhodiola rosea*, *Panax ginseng*, *Eleutherococcus senticosus* and *Raponticum carthamoides* contributed to a more sparing use of carbohydrates and to an enhanced resynthesis of glycogen and high-energy phosphorus compounds. This action was demonstrated unequivocally when under physical strain. Results also indicated an anabolic action which was demonstrated only in the presence of an appropriate test setting, and contrary to steroid anabolic agents, was not accompanied by

virilisation. The adaptogenic activity became apparent when the resistance of the organism was diminished or the organism was placed under stress.<sup>7</sup>

Subsequent research supported these initial findings. Rhodiola improved physical work capacity<sup>8</sup> and prevented the reduction of adrenal catecholamines during stress *in vivo*.<sup>9</sup> Rhodiola (dry root, providing 0.12 mg/kg of salidroside by gavage) and a small amount of ascorbic acid assisted adaptation and improved nonspecific immunity in rats exposed to radiation.<sup>10</sup> Repeated doses of the Rhodiola glycosides increased the restoration of protein, RNA and free amino acids in the muscles of rats after exhausting exercise. Administration of Rhodiola resulted in weight gain in young rats and piglets.<sup>11</sup>

Compared to control treatment, administration of *Rhodiola rosea* extract increased leu-enkephalin (endogenous opioid peptide) concentration in blood plasma, suprarenal glands and myocardium of rats exposed to stress. Activation of myocardial protein and RNA synthesis, decreased catabolic hormone (somatostatin, glucagon) levels and higher resistance to stress were also demonstrated.<sup>12</sup> Rhodiola normalised the induced suppression of erythropoiesis caused by sleep deprivation in mice.<sup>13</sup>

### Effect on CNS

A single dose of Rhodiola liquid extract (0.1 mL of 1:1) improved learning and retention after 24 hours in rats exposed to a maze method. Improvement of long-term memory was established in memory tests after 10 days of treatment. A favourable effect was demonstrated on the training process using the staircase method with positive reinforcement. However, there was no substantial effect on learning and memory in the other methods used.<sup>14,15</sup>

Rhodiola tincture improved CNS function and motor activity in adult rats, but decreased motor activity in young animals.<sup>16</sup> Injection of Rhodiola extract caused a synergistic effect with pentobarbital in depressing the CNS response in mice.<sup>17</sup> Rhodiola extract demonstrated a protective effect against neurotoxicity induced by beta-amyloid proteins in cultured rat hippocampal neurons.<sup>18</sup>

### Cardiovascular Activity

Rhodiola prevented the reperfusion-induced decrease in contraction amplitude of isolated perfused rat heart, and prevented reduction of coronary flow and development of contracture in the postischaemic period. An antiarrhythmic effect has also demonstrated *in vivo* (oral route). The activity may be partially due to an increase in the level of endogenous opioid peptides.<sup>19-21</sup> Rhodiola prevented stress-induced cardiac damage in rats.<sup>9</sup> Administration of Rhodiola to rats prevented the decrease in cardiac contractility which occurs immediately after acute cooling.<sup>22</sup>

Rhodiola extract had an antioxidant effect in rats exposed to high levels of dietary fat. Plasma cholesterol was also lowered and excretion of cholesterol was stimulated.<sup>23</sup>

### Other Activity

Rhodiola extracts demonstrated antimutagenic activity in mice exposed to cyclophosphamide, by reducing the development of chromosomal aberrations and increasing the efficiency of DNA repair mechanisms.<sup>24</sup> A decrease in tumour size and tumour frequency was observed in the spontaneous liver carcinogenesis model,<sup>25</sup> and tumour growth and metastasis was reduced in mice and rats with Pliss lymphosarcoma, the solid form of Ehrlich adenocarcinoma<sup>26</sup> and Lewis lung carcinoma<sup>27</sup> after oral administration of Rhodiola. In the Ehrlich ascites tumour and Lewis lung carcinoma models, Rhodiola enhanced the antitumour and antimetastatic activity of cyclophosphamide while reducing its toxicity and maintaining normal bone marrow cells.<sup>27</sup> In addition to exhibiting an antimetastatic effect in Ehrlich adenocarcinoma, Rhodiola reduced the toxicity of the antimetastatic drug adriamycin when administered concurrently.<sup>28</sup> In other oncological models Rhodiola inhibited the growth and metastasis of a number of transplantable tumours and increased the efficacy of cytostatic therapy.<sup>26</sup> Rhodiola stimulated reparative regeneration in a model of liver damage and demonstrated a hepatoprotective effect in toxic hepatitis.<sup>26,29</sup> An oestrogenic activity was produced in sexually mature female mice by injection of an isolated fraction of Rhodiola (probably mainly salidroside).<sup>2</sup>

### Toxicology

The toxicity of Rhodiola root is regarded as very low. The LD<sub>50</sub> values for Rhodiola and a number of other adaptogens including *Panax ginseng* and *Eleutherococcus senticosus* were measured between 10 and 30 g/kg (route undefined, but likely to be oral).<sup>7</sup>

### Clinical Studies

In a randomised, double-blind, placebo-controlled, crossover trial, the effect of a standardised Rhodiola extract on mental performance was assessed in healthy doctors under a moderate level of fatigue and stress (on night duty). The placebo and test preparations were taken for 14 days (the extract containing 4.5 mg/day salidroside – which was considered a low dose) with a 2-week wash out between the two treatments. Two groups were assessed, one receiving Rhodiola first the other receiving placebo first. The effect was measured using 5 tests involving complex perceptive and cognitive functions (such as associative thinking, short-term memory, calculation and ability to concentration, and speed of audiovisual perception) which were calculated as a total fatigue index. In the group that received Rhodiola first, administration of Rhodiola produced a significant improvement in the total

fatigue index ( $p < 0.01$ ). Efficacy was not demonstrated in the second group (who received Rhodiola last) but they had been on night duty for a considerably longer time.<sup>3</sup>

Standardised Rhodiola extract produced significant improvement ( $p < 0.01$ ) in physical fitness, mental fatigue and neuromotoric tests (maze test, measuring accuracy versus speed) compared to placebo in students during an examination period in a pilot trial of randomised, double-blind design. General well-being (self-assessed) was also significantly better in the Rhodiola group ( $p < 0.05$ ), but no significant difference was observed in the correction of texts or neuromuscular tapping tests. The average exam marks from the examination immediately after the end of the study were higher in the Rhodiola group.<sup>30</sup> Although not defined in the publication and assuming the usual standardisation of this extract,<sup>2</sup> Rhodiola extract containing 3 mg/day rosavins and 0.8 mg/day salidroside prescribed for 20 days was the likely dosage. The dosage was described as low dose and probably suboptimal by the authors.<sup>30</sup>

A significant antifatigue effect, measured as improved mental work quantity and quality per unit time, was demonstrated after acute (single dose) administration of standardised Rhodiola extract in young cadets under stress. In this randomised, double-blind trial, two doses of Rhodiola (extract containing 9 mg/day salidroside (standard dose) and the higher dose of 13.5 mg/day salidroside) were tested against a placebo group and an untreated control group. Both Rhodiola groups demonstrated a significantly higher antifatigue effect compared to the placebo group ( $p < 0.001$ ). There was no significant difference between the two dosage groups, although a trend in favour of the lower dose group was suggested. The untreated controls were not significantly different from the placebo group. The authors regard the optimum dose, based on well-established use in Russian medicine together with the results of clinical trials, to be within the range of 0.5 to 3 times the lowest dose in this study (ie standardised extract providing 4.5–27 mg/day of salidroside).<sup>31</sup>

A formula containing standardised extracts of Rhodiola, *Eleutherococcus senticosus* and *Schisandra chinensis* improved physical work capacity in healthy but sedentary men (aged 20–31 years) evaluated over 7 days. Their heart rate variability and inotropic functions improved. A variable dosage regime was used, and provided 12–24 mg/day of salidroside.<sup>2</sup> In a placebo-controlled trial, this formula also assisted students and engineers maintain high mental performance under extreme stress (24 hours of continuous work). It reduced fatigue, prolonged working time and assisted cosmonauts to endure changes in their environment (the atmosphere in the spaceship).<sup>32</sup>

Other clinical studies, many of them Russian and Swedish with minimal detail are outlined below. Trials were

uncontrolled except where indicated as controlled (§) and unknown (†), and trials administering single dose are not listed. Rhodiola was administered in several of these trials (marked by #) as a 1:1 tincture manufactured according to the Russian Pharmacopoeia, and equivalent to standardised extract ranging from 150 to 750 mg/day. Based on the date of these trials and the fact that the first generation of extracts were standardised to a minimum of 0.6%, 0.9–4.5 mg/day of salidroside was administered. (Later extracts were also standardised for rosavins.)<sup>5</sup>

Rhodiola:

- increased physical and mental efficiency;†<sup>7</sup>
- relieved symptoms of asthenia due to psychiatric and physical causes, including fatigue, decline in work capacity, sleeplessness, poor appetite, irritability, headache;#<sup>2,5</sup>
- improved the amount and quality of intellectual work and prevented loss of work capacity due to fatigue in healthy students, doctors, scientists with a history of poor endurance and tiredness at work;#<sup>5</sup>
- increased physical work capacity, coordination, general wellbeing and decreased mental fatigue and situational anxiety in a study involving 60 foreign students at a Russian high school;§<sup>2</sup>
- improved mental activity in 25 to 35-year-old students, and decreased the quality of intellectual work in students (14 to 16 years old);†<sup>16</sup>
- improved symptoms of depression in 64% of patients with depression and neurasthenia; improved intellectual workload by the fourth day of treatment;#<sup>5</sup>
- improved energy levels, day-time sleepiness and mood in a majority of patients with depression;#<sup>5</sup>
- improved sleep in 67% of patients with chronic sleep-related problems;#<sup>5</sup>
- improved anxiety and mood in patients with depressive disorders who were medicated with tricyclic antidepressants, but intensified symptoms in patients with hysteric-depressive and depressive-phobic symptoms;§<sup>33</sup>
- provided some benefit in schizophrenic patients whose anticholinergic medications had failed to relieve Parkinson's disease induced by antipsychotic medications;<sup>2</sup>
- improved sexual function in men with erectile dysfunction and/or premature ejaculation;<sup>2</sup>
- produced normal menstruation in over 60% of women with amenorrhoea (oral Rhodiola or salidroside by injection);<sup>2</sup>
- reduced the frequency of recurrence of superficial cancer of the bladder, improved the characteristics of the urothelial tissue integration and improved T-cell immunity in patients who had undergone removal of the primary tumour;<sup>34</sup>
- sped up the recovery of patients with acute infections of the mouth (as adjunctive treatment);§<sup>32</sup>
- did not influence nausea-induced stress hormone release or prevent motion sickness;§<sup>35</sup>

- did not improve blood oxygenation, but demonstrated the potential to decrease oxidative stress in simulated altitude-induced hypoxia.<sup>§36</sup>

## Clinical Summary

### Actions

Adaptogen, tonic, antitumour, hepatoprotective, hepatotrophorestorative.

### Therapeutic Indications

- Fatigue, mental and/or physical exhaustion.
- To improve mental performance, concentration and memory, especially when under stress.
- To enhance physical performance and endurance.
- May assist sexual function in men.
- Adjuvant treatment of cancer.

### Dosage & Administration

The usual adult dosage of a 2:1 liquid extract is 20 to 40 mL per week. Extracts providing quantified levels of rosavins and salidroside are recommended, ideally containing not less than 3 mg/mL of rosavins and 1 mg/mL of salidroside.

### Suggested Combinations

Rhodiola combines well with other adaptogens and tonics (in appropriate dosages\*): *Panax ginseng*, *Eleutherococcus senticosus*, *Withania somnifera*, *Astragalus membranaceus*, shatavari (*Asparagus racemosus*) and damiana (*Turnera diffusa*). It also would combine well with cat's claw (*Uncaria tomentosa*) and pau d'arco (*Tabebuia avellanedae*) for the adjuvant treatment of cancer, and with hepatoprotective and hepatotrophorestorative herbs (*Schisandra chinensis*, St Mary's thistle (*Silybum marianum*)).

\* With regard to *Panax ginseng*: overstimulation may occur in susceptible patients at high doses.

### Adverse Reactions

Very few side effects have been reported. A small clinical study found an increase in symptoms in a subgroup of depressed patients with hysteric and phobic symptoms.

### Contraindications & Cautions

Caution is advised in depressed patients with hysteric and phobic symptoms, such as might occur with bipolar disorder. As with all strong adaptogenic and tonic herbs, concurrent use with stimulants such as caffeine is best avoided.

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