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A REVIEW ARTICLE ON *RHODIOLA ROSEA*: AN ADAPTOGEN HAVING MULTIPLE BENEFITS

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ABSTRACT: *Rhodiola rosea* is a plant that has become more popular due to its multiple benefits and less side effects. It has become more famous due to its adaptogenic properties. This herb has been used from a long time by Greeks (77 CE), Chinese, Russians, Monglians, Germans, and some parts of middle Asia for different purposes. In this review article, we have collected some detailed information about multiple uses of *Rhodiola rosea* with its mechanism of action, chemical constituents, side effects, contraindications, and related information based on their research, which is collected from different sources. The aim of this article is to provide some important information about the benefits of *Rhodiola rosea* and its possible uses in the management of various diseases on the basis of the clinical research conducted by different experts and researchers.

INTRODUCTION: *Rhodiola rosea* (*R. rosea*) is a botanical adaptogen with putative anti-stress and antidepressant properties. Evidence-based data supporting the effectiveness of *R. rosea* for depression in adults is limited, and therefore a comprehensive review of available animal and human studies suggesting a putative antidepressant action is warranted¹. It is commonly known as 'golden root,' 'arctic root,' 'roseroot,' 'king's crown' and 'aaron's rod' around various parts of the world, *Rhodiola rosea* (*R. rosea*) belongs to *Rhodiola* genus of the *Crassulaceae* plant family. This herb usually appears at high altitudes in the Arctic area and across Eastern Europe and Asia, particularly in the Northern latitudes.

For many centuries, this unique herb has held a prominent place in traditional medicine systems across Asia, Europe, and Russia. It was in 77 CE when the Greek physician Dioscorides first recorded the medicinal usage of *rodiazia*, which was later renamed as *Rhodiola rosea* by Linnaeus². Due to its purported adaptogenic properties, it has been studied for its performance-enhancing capabilities in healthy populations and its therapeutic properties in a number of clinical populations³. More recently, *R. rosea* has received attention from the scientific community for its potential therapeutic capacity as an adaptogen.

Adaptogen is the most common natural herbal products, which are non-toxic in normal doses, produce a non-specific response, and have a normalizing physiologic influence⁴. *R. rosea* has been referred to as an ergogenic aid, *i.e.*, an herb used to enhance physical and mental performance. Common indications pertaining to the adaptogenic and ergogenic capacity of *R. rosea* include performance enhancement, fatigue reduction, and



alleviation of depression symptoms. Existing reviews suggest a benefit in physical and mental performance attributable to *Rhodiola rosea* however such reviews fail to critically appraise included literature^{5,6}.



FIG. 1: RHODIOLA ROSEA PLANT⁶¹

History: In 1961, G. V. Krylov, a Russian botanist and taxonomist in the Department of Botany at the Novosibirsk Branch of the Russian Academy of Sciences, led an expedition to the cedar taiga in the Altai Mountains of southern Siberia where he located and identified the "golden root" as *Rhodiola*

*rosea*⁷. Traditional folk medicine used *R. rosea* to increase physical endurance, work productivity, longevity, and resistance to high altitude sickness and to treat fatigue, depression, anemia, impotence, gastrointestinal ailments, infections, and nervous system disorders. In mountain villages of Siberia, a bouquet of roots is still given to couples prior to marriage to enhance fertility and assure the birth of healthy children⁸. In Middle Asia, *R. rosea* tea was the most effective treatment for cold and flu during severe Asian winters. Mongolian doctors prescribed it for tuberculosis and cancer⁹. In 1755 *R. rosea* was included in the first Swedish pharmacopeia. Vikings used the herb to enhance their physical strength and endurance¹⁰. German researchers described the benefits of *R. rosea* for pain, headache, scurvy, hemorrhoids, as a stimulant, and as an anti-inflammatory^{11,12}.

Chemical Composition: About 140 chemical compounds are in the subterranean portions of *R. rosea*¹³.

Rhodiola roots contain phenols, rosavin, rosin, rosarin, organic acids, terpenoids, phenolic acids, and their derivatives, flavonoids, anthraquinones, alkaloids, tyrosol and salidroside^{14,15}.

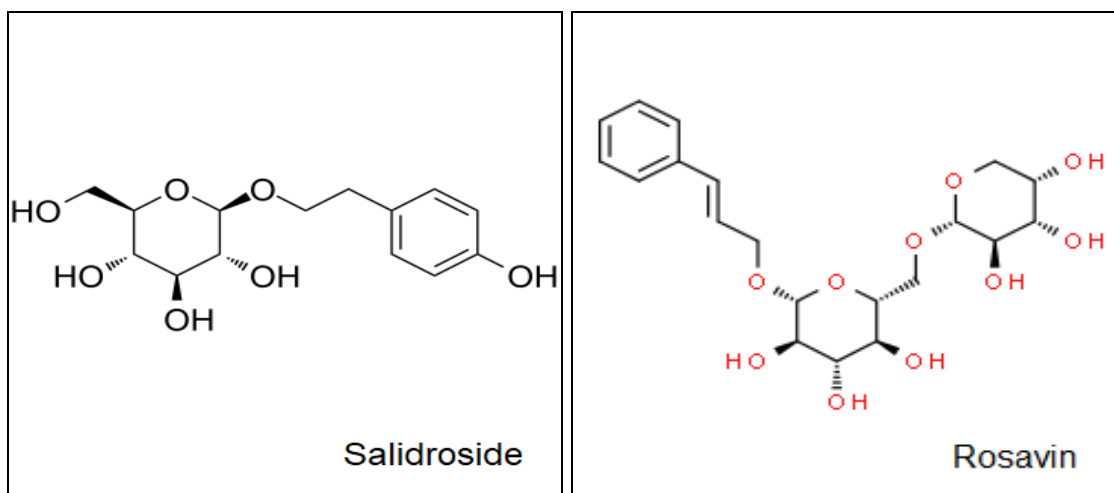


FIG. 2: STRUCTURES OF SALIDROSIDE AND ROSAVIN

The chemical composition of the essential oil from *R. rosea* root growing in different countries varies. For example, rosavin, rosarin, and rosin at their highest concentration according to many tests can be found only in *R. rosea* of Russian origin; the main component of the essential oil from *Rhodiola* growing in Bulgaria are geraniol and myrtenol; in

China, the main components are geraniol and 1-octanol; and in India, the main component is phenethyl alcohol. Cinnamyl alcohol was discovered only in the sample from Bulgaria. Although rosavin, rosarin, rosin, and salidroside (and sometimes p-tyrosol, rhodioniside, rhodiolin, and rosiridin) are among suspected active

ingredients of *R. rosea*, these compounds are mostly polyphenols. There are no peer-reviewed studies demonstrating that these chemicals have any physiological effect in humans that could prevent or reduce the risk of disease¹⁶. Salidroside (Rhodioloside) is a glucoside of tyrosol found in the plant *Rhodiola rosea*¹⁷. Salidroside may be more active than rosavin,^{18, 19} even though many commercially marketed *Rhodiola rosea* extracts are standardized for rosavin content rather than salidroside.

Although, these phytochemicals are typically mentioned as specific to *Rhodiola rosea* extract's, *rosea* and other *Rhodiola* species contain many other constituent polyphenols, including proanthocyanidins, quercetin, gallic acid, chlorogenic acid and kaempferol²⁰.

Clinical Research: A randomized, double-blind clinical trial (Darbinyan V *et al.* 2007) compared two different doses of a standardized extract from *Rhodiola rosea* L. (SHR-5) to placebo for 6 weeks in 89 mild to moderately depressed patients. The *Rhodiola* group showed improvement in overall depression and symptoms such as insomnia, emotional stability, and also self-esteem for the higher dose group. Indeed, important positive outcomes were mood stabilization and energy restoration²¹. Another study (Lishmanov IuB *et al.* 1987) found that when *Rhodiola rosea* L. administered to rats, injections of the plant extract prevented stress-induced elevations of beta-endorphins, adrenocorticotrophic hormone, cortisol, insulin, thyroxin and triiodothyronine²². Some publications on clinical efficacy have demonstrated that *Rhodiola* extracts are helpful for learning and memory, especially concentration and that they are extremely helpful for patients with mild-to-moderate depression. A double-blinded RCT pilot study examined the effect of a repeated low dose of *R. rosea* on foreign students' mental and physical well-being during their examination period²³.

Subjects were randomized into 2 groups to receive either 100 mg *R. rosea* once per day or identical placebo for 20 days. Hand-eye coordination (maze test), motoric speed (tapping test), mental work capacity (correction of text test), fatigue and well-being (self-evaluation questionnaire), heart rate, and physical work capacity (bicycle ergometer test)

were assessed. Significant improvements were observed in hand-eye coordination ($p < 0.01$), mental fatigue, and general-well being ($p < 0.01$) in favor of *R. rosea*. Students on placebo had a significantly higher heart rate ($p < 0.05$). Drop-outs and adverse events were not reported by authors²⁴.

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. 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 strain²⁵.

Single acute doses of *R. rosea* extract exerted significant antidepressant and anxiolytic effects in mice at doses of 10, 15, and 20 mg/kg²⁶. Animal models of nicotine addiction show *Rhodiola* to increase and lessen the anxiety symptoms of nicotine withdrawal compared with control²⁷.

Mechanism of Action: 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^{28, 29}, and serotonin receptor expression and to act as μ -opioid receptor^{30, 31} and κ -opiate receptor³² agonists, promoting the release of β -endorphin and exerting an anxiolytic, antiarrhythmic and hypotensive action³³. Chen *et al.* previously demonstrated that *Rhodiola rosea* extract is able to improve the level of 5-HT in the hippocampus in an animal model³⁴. *Rhodiola rosea* to rats for 10 days modulated biogenic monoamines in the cerebral cortex, brain stem, and hypothalamus. In the cerebral cortex and brain stem, levels of norepinephrine and dopamine decreased, while the amount of serotonin increased substantially. In the hypothalamus, the results were reversed with a 3-fold increase in the amount of norepinephrine and dopamine and a trend toward reduced serotonin levels. It is believed these changes in monoamine levels are a result of *Rhodiola rosea* inhibiting the activity of the enzymes responsible for monoamine degradation, monoamine oxidase, and catechol-O-methyl-

transferase. It is also believed *Rhodiola rosea* facilitates the transport of neurotransmitters within the brain³⁵. It has been reported that *Rhodiola rosea*, a traditional Tibetan medicine plant in China, can treat acute mountain sickness through inhibiting HIF-1 degradation pathway³⁶.

Benefits of *Rhodiola Rosea*:

1. Stress Reduction: *Rhodiola* has long been known as an adaptogen, a natural substance that increases your body's resistance to stress in non-specific ways. One study investigated the effects of *rhodiola* extract in 101 people with life- and work-Related stress. Participants were given 400 mg per day for four weeks³⁷. It found significant improvements in symptoms of stress, such as fatigue, exhaustion, and anxiety, after just three days. These improvements continued throughout the study. In the test of swimming "to the limit," *Rhodiola rosea* administration increased the swimming time of rats 135-159 percent. The working capacity of the rats consistently improved throughout the supplementation period³⁸.

2. Can Fight Fatigue: Due to its adaptogenic properties, *rhodiola* is thought to help alleviate fatigue. One four-week study in 60 people with stress-related fatigue looked at its effects on the quality of life and symptoms of fatigue, depression, and attention. Participants received either 576 mg of *Rhodiola* or a placebo pill daily. It found that *Rhodiola* had a positive effect on fatigue levels and attention, compared to the placebo³⁹.

In one study (Abidov *et al.* 2003) the effects of oral treatment with an ethanolic extract (ethanol 40%) from *Rhodiola rosea* (50 mg/kg) and *Rhodiola crenulata* (50 mg/kg) roots on the duration of exhaustive swimming and ATP content in mitochondria of skeletal muscles in rats were investigated. Treatment with *Rhodiola rosea* extracts significantly (by 24.6%) prolonged the duration of exhaustive swimming in comparison with control rats and rats treated with *Rhodiola crenulata*⁴⁰.

3. Antidepressant: *Rhodiola rosea* has also been suggested to have antidepressant properties by balancing the neurotransmitters in your brain^{41, 42, 43}. Clinical assessment of *R. rosea* L. rhizome extracts in humans with various depressive

syndromes is based upon results from two randomized, double-blind, placebo-controlled trials of 146 subjects with major depressive disorder and seven open-label studies totaling 714 individuals with stress-induced mild depression (diagnosed as an asthenic syndrome or psychoneurosis). Overall, the results of these studies suggest a possible antidepressant action for *R. rosea* extract in adult humans⁴⁴. The methanol and water extracts exhibited respectively inhibitions of 92.5% and 84.3% on MAO-A and 81.8% and 88.9% on MAO B, at a concentration of 100 µg/ml. The most active compound (Rosiridin) presented an inhibition of over 80% on MAO B at a concentration of 10(-5) M (pIC50=5.38±0.05). The present investigation demonstrates that *Rhodiola rosea* L. roots have potent anti-depressant activity by inhibiting MAO-A and may also find application in the control of senile dementia by their inhibition of MAO B⁴⁵.

4. Cardioprotective: Cardioprotective effects of *R. rosea* include: prevention of stress-induced cardiac damage^{46, 47, 48} decreased myocardial catecholamines and cyclic adenosine monophosphate (cAMP) levels; and reduced adrenal catecholamine release^{46, 47}.

5. Anti-aging: *Rhodiola rosea* extract SHR-5 was shown to increase the mean and maximum lifespan of the fruit fly up to 24% and 31%, respectively⁴⁹. Nevertheless, mechanisms for the anti-aging effects of *Rhodiola rosea* extracts are still largely unknown. *Rhodiola rosea* extracts can extend lifespan at different caloric levels.

The effect of *R. rosea* extracts on lifespan was independent of caloric restriction-related signaling pathways, including SIR2 proteins, insulin, and insulin-like growth factor signaling and the TOR in fruit flies⁵⁰.

6. Anti-anxiety: One study found evidence to suggest that *Rhodiola rosea* may reduce symptoms of generalized anxiety disorder. Ten people were included in this study, and they took 340 mg of *Rhodiola rosea* extract for 10 weeks. A significant improvement in GAD symptoms was found with *R. rosea*. Individuals treated with *R. rosea* showed significant decreases in mean Hamilton Anxiety Rating Scale (HARS) scores at endpoint (t = 3.27, p = 0.01)⁵¹.

7. Neuroprotective: One study suggests that *Rhodiola* may help in the prevention of Alzheimer's disease and other neurodegenerative diseases and suppresses neuroinflammation. The study reported that *R. rosea* has potent neuroprotective effects through the suppression of oxidative stress, neuroinflammation, and excitotoxicity in brain tissues and antagonism of oncogenic p21-activated kinase. Accumulation of amyloid-beta protein in the brain cells is the hallmark of Alzheimer's disease. It causes oxidative stress and damages brain cells. Salidroside inhibits such activity by amyloid-beta by elevating antioxidant defenses. Apart from Alzheimer's disease, *R. rosea* extracts may aid in the prevention of Parkinson's disease. Salidroside protects the dopaminergic neurons by improving antioxidant defenses hence may have antiparkinson activity⁵². The present study supports the hypothesis that salidroside may act as an effective neuroprotective agent through modulation of the ROS-NO related mitochondrial pathway *in-vitro* and *in-vivo*⁵³.

8. Antioxidant and Anticarcinogenic: Animal studies have shown that *R. rosea* decreases toxicity from cyclophosphamide, rubomycin, and adriamycin (anti-cancer drugs), while it enhances their anticarcinogenic effects^{54, 55}. One study conducted by Majewska A, Hoser G, et al., shows possible anticancer activity of *Rhodiola rosea*. Promyelocytic leukemic cells of a type known as HL-60 cells were exposed to standard extracts of *Rhodiola* for 6 to 72 h, and the survival of the cells was tested with automatic equipment.

The result of the current testing for cell survival or apoptosis and necrosis was that *Rhodiola* decreased the survival of the HL-60 leukemic cells. The lowest concentrations of the herb reduced cell survival after 12 h of incubation. The highest concentrations of *Rhodiola* (225 and 450 µg/ml) reduced cell survival to almost zero after 48 and 72 h of incubation. This study shows that *Rhodiola* acts against the division of HL-60 leukemic cells, with apoptosis and reduced survival of the cells. Hence it shows *Rhodiola rosea*'s anticancer roles and its future possible in modern cancer treatment⁵⁶.

Safety and Side Effects: *Rhodiola rosea* has a very low level of toxicity. In rat toxicity studies

(Kurkin and Zapesochnaya 1985) the LD₅₀ (lethal dose at which 50% of animals die) was calculated to be 28.6 mL/kg, approximately 3360 mg/kg⁵⁷. The equivalent dosage in a 70-kg man would be about 235 g or 235000 mg. Because the usual clinical doses are 200 to 600 mg/d, there is a huge margin of safety (Udintsev and Schakov 1991)⁵⁸. Some side effects usually occur when you are on a higher dosage, and when you take it with caffeine. Most common effects with *Rhodiola rosea* are drowsiness, trouble to sleep and gastrointestinal problems, headache and dizziness, anxiety and agitation, nauseous, restlessness, insomnia, hyper-salivation⁵⁹. There is not enough clinical research data about its safety during pregnancy and during breastfeeding.

Contraindications: *Rhodiola rosea* should not be prescribed to patients with manic behavior disorders. If you have bipolar disorder, for example, *Rhodiola* can be dangerous because it can cause mania. *Rhodiola* should not be prescribed to patients with antidepressant sensitivity, either. *Rhodiola rosea* can cause drowsiness for patients on benzodiazepines, SSRI, and SNRI anti-depressants.

It is not recommended for patients on SSRI medications or MAOI medication because it can cause serotonin syndrome. *Rhodiola* can increase the symptoms of autoimmune disorders because it stimulates the immune system conditions such as rheumatoid arthritis, inflammatory bowel disorders (Crohn's disease/ulcerative colitis), and neurological disorders such as multiple sclerosis⁵⁹. *Rhodiola* may affect platelet aggregation in higher doses. *Rhodiola* may interfere with birth control pills. *Rhodiola* may interfere with diabetic or thyroid medication⁶⁰. Therefore it is advised to consult a physician before taking *Rhodiola rosea*.

CONCLUSION: This review article gives some possible important uses of *Rhodiola rosea* in the management of different diseases/psychological conditions with some additional information. *Rhodiola rosea* has shown its multi-benefits in many research works carried out by different researchers worldwide. Primary benefits of *Rhodiola rosea* include antidepressant, anti-anxiety, anti-fatigue, stress reduction, increase in work capacities, and elevated performance in our daily life, antioxidant, and anti-aging properties.

Rhodiola rosea also found to have cardioprotective, anticancer, and neuroprotective properties in different researches. *Rhodiola rosea* usually does not show side effects at clinical doses, although some precautions should be taken before using it.

Consumers using antianxiety, antibiotic, or anti-depressant medications, birth control pills, or diabetic and thyroid drugs should consult with the prescribing physician. Nowadays, *Rhodiola rosea* is becoming a promising herbal drug in the world for a safe and effective way in the treatment of depression, anxiety, fatigue, and stress.

This plant shows its positive capability for the treatment of Alzheimer's disease, Parkinson's disease, and cancer. *Rhodiola rosea* extract is currently available in the market by different manufacturers, and it is more popular nowadays. However, more research on this herb is required.

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