

# Rhodiola SAP

Science-based nutraceutical for mental fatigue and stress\*

**Rhodiola SAP** provides a standardized dose of *Rhodiola rosea* (*R. rosea*) root extract, commonly used in herbal medicine as an adaptogen to help temporarily relieve symptoms associated with stress, such as mental fatigue and sensation of weakness.\* **Rhodiola SAP** can be used to enhance cognitive function, including mental focus and stamina.\* *R. rosea* extract contains a number of major bioactive compounds such as rosavin and salidroside, attributed to its adaptogenic effects; it is also a source of antioxidants such as *p*-tyrosol, gallic acid, caffeic acid, chlorogenic acid, and flavonoids.\* **Rhodiola SAP** can be used to alleviate depression, anxiety, life-stress symptoms, and mood disorders.\* In addition, **Rhodiola SAP** can be useful as an adjunctive support for improving the efficacy of cancer therapy.\*

## SUPPLEMENT FACTS

Serving Size: 2 Capsules	Amount Per Serving	Servings: 30 % Daily Value
Roseroot ( <i>Rhodiola rosea</i> ) root extract, 5% rosavins, 1.9% salidroside	400 mg	**
**Daily Value not established		NPN 80073937 - V0583-R1

**Other ingredients:** Vegetable magnesium stearate, microcrystalline cellulose and silicon dioxide in a capsule composed of vegetable hypromellose and purified water.

**This product is non-GMO and vegan friendly.**

**Contains no:** Gluten, soy, wheat, corn protein, eggs, dairy, yeast, citrus, preservatives, artificial flavor or color, starch, or sugar.

**Rhodiola SAP** contains 60 capsules per bottle.

## ADULT DOSAGE

Take 1-2 capsules daily or as directed by your healthcare practitioner. Not to be taken immediately before bedtime.

## INDICATIONS

**Rhodiola SAP** can:

- Help relieve stress-related symptoms, such as mental fatigue and sensation of weakness.\*
- Promote cognitive function, such as mental focus and stamina.\*
- Help alleviate anxiety, depression, and other mood disorders.\*
- Be used as an adjunct for enhancing the efficacy of cancer therapy.\*

## CAUTIONS AND WARNINGS

Do not use this product if you have bipolar disorder or bipolar spectrum disorder. Consult a healthcare practitioner if symptoms persist or worsen. Consult a healthcare practitioner prior to use if you are pregnant or breast-feeding. Consult a healthcare practitioner prior to use if you are taking antidepressant medication, hormone replacement therapy (HRT), or birth-control pills. Discontinue use if you experience irritability or insomnia. Do not use if seal is broken. Keep out of reach of children.

## PURITY, CLEANLINESS AND STABILITY

All ingredients listed for each **Rhodiola SAP** lot number have been tested by an ISO 17025-accredited third-party laboratory for identity, potency, and purity.

\* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Scientific Advisory Panel (SAP):  
adding nutraceutical research  
to achieve optimum health



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## INTRODUCTION

*Rhodiola rosea* (*R. rosea*)—also known as roseroot, golden root, and Arctic root—has a long-standing reputation of use in East-European and Asian traditional medicines for its valuable applications in nervous-system stimulation, including enhancement of work performance, improvement of depression and sleep disturbances, and management of fatigue, as well as high-altitude sickness. *Rhodiola* has also been widely used for its cardio- and hepatoprotective effects, as well as for its immunotropic, antiviral, anti-inflammatory, and antibacterial activities.

*R. rosea* contains an array of antioxidant compounds, including *p*-tyrosol, organic acids (gallic acid, caffeic acid, and chlorogenic acid), and flavonoids (catechins and proanthocyanidins).<sup>[1]</sup> The polyphenol content of *R. rosea* is approximately  $41.4 \pm 3.41\%$ , and the major bioactive compounds that are attributed to the medicinal properties of *R. rosea* are rosavin, salidroside (also called rhodioloside and rhododin), and *p*-tyrosol, including other key compounds such as rhodionoside, rhodioline, rosin, rosarin, and rosidin.<sup>[1]</sup>

## ADAPTOGENIC EFFECTS

Adaptogens are substances that enable the normalization of physiological responses to various stressors, enhance work performance, and increase the stress tolerance of the body.<sup>[1][2]</sup> *Rhodiola* is considered an adaptogen, due to its ability to enhance the resistance to stress and mitigate stress-induced impairments and disorders.<sup>[1][2]</sup> Substantial evidence from multiple randomized, controlled clinical trials demonstrates the adaptogenic effect of *R. rosea* root extract. In one double-blind, randomized, controlled clinical trial, a 70% ethanol water extract of *R. rosea* root orally administered in daily doses of 288–680 mg (1–4 tablets) for 2–6 weeks significantly improved mood, cognitive performance, attention, and fatigue in stress-related conditions.<sup>[3]</sup> The adaptogenic properties, cardiopulmonary protective effects, and central nervous system activities of *R. rosea* have been attributed primarily to its ability to influence levels and activity of biogenic monoamines—such as serotonin, dopamine, and norepinephrine—in the cerebral cortex, brain stem, and hypothalamus. In addition, *R. rosea* can prevent catecholamine release, cyclic AMP elevation in the myocardium, and the depletion of adrenal catecholamines induced by acute stress. *R. rosea*'s adaptogenic activity has also been linked to its ability in activating both central and peripheral opioid receptors.

## MENTAL HEALTH AND DEPRESSION

Several studies attest that *R. rosea* exerts neuroprotective effects through the suppression of oxidative stress, neuroinflammation, and excitotoxicity in brain tissues.<sup>[4]</sup> Activation of microglia is a major characteristic in the pathogenesis of Alzheimer's disease; activated microglia can generate inflammatory mediators, leading to neuroinflammation. In an animal study, *R. rosea* constituents (rosarin and salidroside) mitigated inflammatory mediators in activated microglia. Although limited, evidence-based data supports the effectiveness of *R. rosea* for depression in adults. Several studies in humans have demonstrated the multitargeted effects of *R. rosea* on various levels of regulatory responses to stress, indicating its beneficial effects on mood.<sup>[6]</sup> In one study, 57 individuals with mild to moderate depression were randomized to 12 weeks of standardized, 340 mg/d *R. rosea* extract or 50 mg/d of sertraline. Although less effective than sertraline in reducing depression-related symptoms, *R. rosea* extract resulted in lesser adverse events and was better-tolerated.<sup>[7]</sup> In another study, 80 mildly anxious participants were randomized into two different groups of either *R. rosea* standardized extract (400 mg/d) or placebo for 14 days. *R. rosea* demonstrated a significant reduction in self-reported anxiety, stress, anger, confusion, and depression, with profound improvements in total mood.<sup>[8]</sup>

In an open-label study of individuals with life-stress symptoms, a dose of 200 mg twice daily of *R. rosea* for 4 weeks was found to significantly improve the symptoms to a clinically relevant degree.<sup>[9]</sup>

## FATIGUE MANAGEMENT

A number of systematic reviews have determined that *R. rosea* standardized extracts alleviate stress-induced fatigue.<sup>[10][11][12]</sup> Daily doses (288–680 mg) of *R. rosea* were found to significantly reduce fatigue and improve attention in individuals with fatigue syndrome.<sup>[3]</sup> Even in healthy adults, randomized controlled trials have established the antifatigue effects of *R. rosea* standardized extracts during fatigue and under stressful conditions.<sup>[13][14][15]</sup>

## CANCER

Animal studies provide evidence to the anticarcinogenic effects of *R. rosea*. In animal tumour models, treatment using *R. rosea* extract, alone or in combination with the antitumour agent cyclophosphamide, improved the antitumour and antimetastatic efficacy, along with reduced drug-induced toxicity.<sup>[16][17]</sup> Also, preliminary clinical research in humans indicates the beneficial role of *R. rosea* in patients with bladder cancer.<sup>[18]</sup> However, more well-designed human studies are needed to confirm these observations.

## SAFETY

Studies show that *R. rosea* extracts are generally well-tolerated. Adverse events, if any, are mostly of mild intensity, with no serious adverse events reported.<sup>[9][10][11][12]</sup> *R. rosea* could potentially exert estrogenic effects in women.<sup>[19]</sup> The complex nature of interaction of components of *R. rosea* with estrogen receptors in different tissues remains to be clarified.<sup>[19]</sup> Hence, individuals undergoing hormone replacement therapy or using birth-control pills need to exert caution before consuming *R. rosea* extract.

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## INDICATION-SPECIFIC DOSAGE SUMMARY BASED ON HUMAN CLINICAL RESEARCH#

#Please note that these suggestions are guidelines based on clinical studies. Evidence for efficacy and safety has been assessed qualitatively (study quality in terms of study design, sample size, appropriate methods of analysis, use of appropriate placebo/control, bias, etc.) and has been rated using a 5-star ★ rating classification.

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Indication	Suggested Dosage	Supporting Evidence and study outcomes	Study design	Outcome Measures	Safety	Evidence quality rating
<b>WOMEN'S HEALTH</b>						
Menopause <sup>1</sup>	2 capsules/day	Noticeable relief from somatic, psychological, and urogenital issues*	Randomized, double-blind, placebo-controlled, parallel study (n=220; 12 weeks) Combination of 400 mg of <i>R. rosea</i> root and 13 mg of Black cohosh extracts/day	Kupperman Menopausal Index (KMI), Menopause Relief Score (MRS), and menopause Utian Quality of Life (UQOL) index	No adverse effects reported	★★★
<b>MENTAL HEALTH</b>						
Depression <sup>2, 3</sup>	1 capsule/day	Considerable reduction of depression and better tolerated compared to Sertraline <sup>2*</sup>	Randomized, double-blind, placebo-controlled, parallel-group, dose-escalation study (n=57; 12 weeks) 340 mg powdered <i>R. rosea</i> extract/day (standardized to a content of 3.07% rosavins and rhodioloside 1.95%)	Hamilton Depression Rating (HAM-D), Beck Depression Inventory (BDI), Clinical Global Impression Change (CGI/C)	No adverse effects reported	★★★
	2 capsules/day	Significant decrease in mild to moderate depression symptoms <sup>3*</sup>	Preliminary open-label study (n= 45; 6 weeks) Combination of 308 mg of <i>R. rosea</i> root and 30 mg of saffron stigma extracts/day	Hamilton Rating Scale for Depression scores (HDRS)	No adverse effects reported	★★
Anxiety <sup>4,5</sup>	2 capsules/day	Significant improvement in General Anxiety Disorder (GAD) symptoms*	Preliminary open-label study (n=10; 10 weeks) 340 mg/day of <i>R. rosea</i> root extract	Hamilton Anxiety Rating Scale (HARS), the Four-Dimensional Anxiety and Depression Scale, and the Clinical Global Impressions of Severity/Improvement Scale	No adverse effects reported	★★
	2 capsules/day	Significant reduction of anxiety-related symptoms*	Open-label, randomized, repeated measures study (n=81; 2 weeks) 400 mg of <i>R. rosea</i> root extract/day	BDI, HAM-D	No adverse effects reported	★★
<b>ADAPTOGENIC EFFECTS</b>						
Stress-related fatigue <sup>6,7,8</sup>	1 capsule/day	Significant mood, cognitive performance, attention, and fatigue improvement in stress-related conditions*	Randomized, double-blind, placebo-controlled, parallel-group study (n=60; 4 weeks) 2000 mg of <i>R. rosea</i> root extract/day {144 mg of proprietary <i>R. rosea</i> extract (drug extract ratio 4:1; extraction solvent 70% ethanol)}	Montgomery-Asberg depression rating scale (MADRS)	No adverse effects reported	★★★
	1 capsule/day	Relief from fatigue*	Double-blind cross-over, placebo-controlled study (n=56; 2 weeks) 170 mg of <i>R. rosea</i> extract /day	Total Fatigue Index (FI)	No adverse effects reported	★★★



	1 capsule/ day	Significant improvement in general well-being and physical fitness*	Randomized, double-blind, placebo-controlled, two parallel-group study (n=40; 20 days) 50 mg of <i>R. rosea</i> extract /day	Maze test, Tapping test, and mental fatigue test	No adverse effects reported	★★★★
Chronic fatigue <sup>9</sup>	1 capsule/ day	Significantly improved prolonged or chronic fatigue symptoms*	Uncontrolled, open-label, single-arm, multicenter study (n=100; 8 weeks) 400 mg of dry ethanolic <i>R. rosea</i> extract / day	Multidimensional Fatigue Inventory 20, Numeric Analogue Scales, Pittsburgh Sleep Quality Index (PSQI)	No adverse effects reported	★★
Burnout symptoms <sup>10</sup>	1 capsule/ day	Clear improvement from burnout symptoms*	Exploratory, open-label, multicenter, single-arm study (n= 118; 12 weeks) 400 mg of <i>R. rosea</i> extract/day Dry ethanolic (60% w/w) extract from <i>R. rosea</i> roots (1.5–5:1)	Maslach Burnout Inventory, Burnout Screening Scales I and II	No adverse effects reported	★★★

### EXERCISE AND SPORT SUPPORT

Endurance <sup>11</sup>	1 capsule/ day	Improved endurance exercise capacity, muscle strength, and speed of limb movement*	Randomized, double-blind crossover, placebo-controlled study (n=24; 4 weeks) 200 mg of <i>R. rosea</i> extract /day (3% rosavin and 1% salidroside)	Breath-by-breath ergospirometry system, Maximal isometric torque (Nm), ANOVA	No adverse effects reported	★★★
Anaerobic exercise performance <sup>12</sup>	3 capsules/ day	Enhanced anaerobic performance*	Randomized, single-blind, counterbalanced, placebo-controlled study (n=11; 3 days) 1500 mg of <i>R. rosea</i> root extract/day (3% rosavin and 1% salidroside) {Physically active female participants} (An additional 500 mg of <i>R. rosea</i> root extract before testing)	Wingate Anaerobic Tests (WAnTs)	No adverse effects reported	★★★★
Redox parameters in rowers <sup>13</sup>	1 capsule/ day	Significant increase in antioxidant levels*	Randomized, double-blind, placebo-controlled study (n=22; 4 weeks) 200 mg of <i>R. rosea</i> extract/day (Participants – Male Polish rowing team)	Total antioxidant capacity (TAC), Superoxide dismutase (SOD) activity, thiobarbituric-acid-reactive substances (TBARS)	No adverse effects reported	★★★

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