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File: ■ Rhodiola (*Rhodiola rosea*, Crassulaceae)
■ Alzheimer's Disease

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RE: Rhodiola Shows Potential for Protecting against Oxidative Stress and Neuroinflammation in Alzheimer's Disease

Nabavi SF, Braidy N, Orhan IE, Badiee A, Daglia M, Nabavi SM. *Rhodiola rosea* L. and Alzheimer's disease: from farm to pharmacy. *Phytother Res*. April 2016;30(4):532-539.

Alzheimer's disease (AD) is a common age-related debilitating neurodegenerative disorder that causes progressive cognitive decline, dementia, and eventual incapacity and death. The exact etiology and pathology are unknown, but evidence has shown that increases in oxidative stress are present with AD along with its standard pathology. Neuroinflammation also appears to play a role and several inflammatory molecules have been found with AD, including complement compounds, cytokines, macrophage colony-stimulating factor, transforming growth factor-α, C-reactive protein, S100β, and arachidonic acid. As such, antioxidants have been explored as a possible therapeutic strategy. Plants that are naturally high in antioxidants, such as flavonoids, have been shown to scavenge free radicals and have potent anti-inflammatory properties with minimal adverse effects. Rhodiola (*Rhodiola rosea*, Crassulaceae) root, an important traditional medicinal herb, is of increasing interest for its neuroprotective benefits. The goal of this review was to explore the beneficial effects of *R. rosea* in relation to AD.

The genus *Rhodiola* has over 200 species, with at least 20 that are used in different medical traditions. Rhodiola, an herbaceous flowering perennial, grows wild in high altitudes in northern Europe and North America. It has also been cultivated with some success in Russia, Sweden, Poland, Finland, and Germany.

Phytochemically, rhodiola is a storehouse of phenylpropanoid derivatives (notably rosavin, rosin, and rosarin), phenylethanoid derivatives (salidroside, tyrosol), flavonoids rhodiolin, rhodionin, rhodiosin), monoterpenes (rosiridol, rosiridin), and phenolic acids (chlorogenic, gallic, hydroxycinnamic), many with well-documented antioxidant effects. Salidroside, rhodiola's main constituent, is responsible for many of its reported activities, but many of its compounds are bioactive. Scientific reports of adverse effects are negligible, with toxicity levels believed to be about 235 g.

Traditionally, rhodiola has been used to treat diarrhea, headaches, hernias, and hysteria, as well as cognitive dysfunctions. It is an astringent and has been reported useful for mouth pain, kidney stones, swellings, and back disorders. Its roots have been used for

skin diseases, and it is said to benefit hair growth. It has vasoconstrictive and hemostatic effects on hemorrhoids. A known adaptogen, it is used to manage fatigue and stress.

A number of in vitro and in vivo studies have evaluated effects of rhodiola compounds on factors associated with AD, especially oxidative stress, neuroinflammation, neuronal excitotoxicity, and inhibition of p21-activated kinases (PAKs) and activation of 5' adenosine monophosphate-activated protein kinase (AMPK). Other neuroprotective effects have been observed.

Oligomeric proanthocyanidin from *R. rosea* (OPCRR), a type of phenolic, has been found in the roots of rhodiola and has potent antioxidant activity. Nitric oxide (NO) is a primary mediator of neuroinflammation. One study investigated the neuroprotective effect of rhodiola constituents on NO and found that the constituents rosarin and salidroside suppressed the generation of NO in activated microglia in a dose-dependent manner (no results were reported). It also found that oral administration of rhodiola significantly decreased (exact results not reported) other inflammatory factors and proinflammatory cytokine expression in the kidney and prefrontal cortex of the brain. The authors state that this suggests that rhodiola constituents can cross the blood-brain barrier to suppress inflammation in the central nervous system. Additional studies have found rhodiola to prevent neuronal toxicity.

The authors' search of ClinicalTrials.gov found only three clinical trials on the benefits of rhodiola – one evaluating fatigue in shift-working nurses, one comparing rhodiola and sertraline in major depression, and one comparing it with "ginseng" (species unstated) and with placebo in mild depression and stress. The authors conclude that rhodiola's demonstrated suppression of oxidative and inflammatory processes in neuronal tissue warrants future large-scale trials.

—Mariann Garner-Wizard