PHYTOCHEMISTRY, PHARMACOLOGY AND STANDARDIZATION OF RHODIOLA ROSEA ROOT EXTRACT

Out of more than 20 different plant species of the genus Rhodiola, only Rhodiola rosea (Crassulaceae), also known as Golden root, has undergone extensive clinical, pharmacological, and toxicological testing in humans and animals. A wide array of health benefits, specifically related to mental and physical performance, has been clinically demonstrated exclusively using standardized R. rosea root extract (Table 1).

Table 1. Phyto-medicinal Properties of Rhodiola rosea: An Overview

Mental performance: Anti-fatigue, anti-stress, and anti-depressant properties, increases the bioelectrical activity of the brain, reduces stress and depression, improves memory and brain energy (Saratikov 1974)

Physical performance: Reduces exhaustion and accelerates the recovery processes after training workloads (Saratikov and Krasnov 1987). Stimulates muscle ATP and Creatine phosphate synthesis, glycogen synthesis in muscles and liver (Saratikov 1974); muscle protein synthesis and anabolic activity (Adamchuk 1969; Revina 1969).

Cardiovascular health: Reduces and/or prevents stress-induced cardiac damage. Activates mu-opiate receptors in heart muscle, preventing reperfusion arrhythmias (Lishmanov et al. 1997a,b; Maslova et al. 1994; Maimeskulova et al. 1997).

Sexual performance: Substantially improves erectile dysfunction and/or premature ejaculation (of 1-20 years duration) in men, normalizes prostatic fluid, and increases 17-ketosteroids in urine (Gerasimova 1970).

Lipolytic activity: Activates the lipolytic (fat metabolism) processes and stimulates the release of lipids from adipose tissue (Dambueva 1968; Salnik 1970).

Anticancer effects: Substantially reduces liver toxicity elicited by anti-cancer pharmaceutical drugs, while it enhances their anti-carcinogenic effects on tumor cells and normal bone marrow cells. Reduces the incidence of chromosomal aberrations (antimutagenic), increases DNA repair in bone marrow cells after exposure to the mutagen (Salikhova 1997).

Endocrine effects: Enhances thyroid function without causing hyperthyroidism, enhances thymus gland function and protects or delays involution that occurs with aging. Improves adrenal glands reserve, without causing hypertrophy (Saratikov and Krasnov 1987).

Antioxidant properties: Reduces lipid peroxidation, protects the mucosa of animal small intestines subjected to acute x-ray irradiation (Bolshakova et al. 1997; Yakubovskii et al. 1997).

Safety: Rhodiola rosea extract is safe for human applications, possess very low level of toxicity. The LD50 (lethal dose at which 50% of animals die) was calculated to be appox. 3,360 mg/kg (Kurkin and Zapesochnaya 1986; Saratikov and Krasnov 1987). The equivalent dosage in a 70 kg man would be about 235 g (235,000 mg). Since the usual clinical doses are 200-600 mg/day, the lethal dose is 391 times greater than the higher clinical dose.

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Rhodiola rosea is the species that matters.

The pharmacological properties of plants belonging to the genus Rhodiola depend entirely upon which species is being analyzed and used (Kurkin and Zapesochnaya 1986). The vast majority of scientific evidence from all animal and human studies supporting Rhodiola's clinical effects are concentrated almost exclusively on R. rosea. Based on comprehensive review of the scientific and medical literature 95 percent of the human studies are focused specifically on R. rosea extracts. When extracts of other species of the genus Rhodiola were substituted, clinical benefits described in Table 1 diminished or disappeared altogether (Saratikov and Krasnov 1987).

Equally important, the toxicology on R. rosea is also the most complete. Its safety has been thoroughly investigated and confirmed. Standardized R. rosea extracts have been cleared for prolonged human use. They are safe and effective when taken according to instructions. Up to this point, they have shown no adverse side effects or undesirable interactions with conventional drugs.

Advances in standardizing Rhodiola rosea root extract

The standardization of R. rosea has been the subject of some scientific controversy, especially during the last decade.

Initially, in the 1970s it was generally accepted that the compound most responsible for its unique pharmacological properties was salidroside, also known as rhodioloside (Saratikov et al. 1967). Therefore, the first generation of R. rosea extracts/tinctures were standardized to a minimum 0.6 percent salidroside content, and this was the first form approved by the Russian Pharmacopoeia Committee.

However, by the late 1980s the Soviet mass-market demand for R. rosea root had dramatically increased and the wild-crafted raw material was being over-harvested and not naturally replenishing itself fast enough to be sustainable, a problem that is not unique for wild herb whose root or rhizome is the preferred article in commerce. This resulted in a dramatic, unexplained decline in the quality and effectiveness of "R. rosea" preparations, then in widespread use, undermining its credibility. The immediate investigation of this phenomenon revealed that the increased demand for raw material was being satisfied with supplies of R. crenulata, and other species of the genus Rhodiola. These alternative species also contained salidroside, yet the products in which they were used produced inferior results or no results at all.

Based on in depth comparative analysis, it was hypothesized that R. rosea might contain other compounds that contribute to the superior pharmacological activity of true R. rosea preparations over other preparations that mixed or substituted other Rhodiola species. The search was on for identification of new compounds unique to R. rosea extract that would help explain the significant differences in the results reported in various animal studies and clinical trials between preparations containing only R. rosea and those with either mixtures of various Rhodiola species with R. rosea, and or a merely containing those other species.

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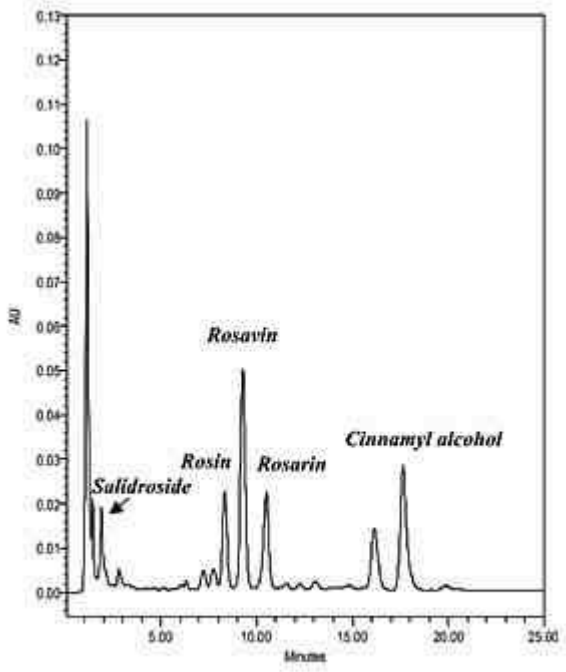
After more than a decade of intensive research by Zapesochnaya et al. (1983, 1984, 1985; Kurkin et al. 1985, 1986) presented convincing evidence that the chemical composition of R. rosea root is, in fact, significantly different from the other species of the genus Rhodiola. Finally, using a newly developed method, Dubichev et al. (1991) demonstrated that only R. rosea root contains the cinnamyl alcohol glycosides rosavin, rosin and rosarin (the rosavins). The typical HPLC fingerprint of true R. rosea and its common substitute R. crenulata are presented on Figure 1.



Typical HPLC chromatogram of *Rhodiola rosea* root extract.

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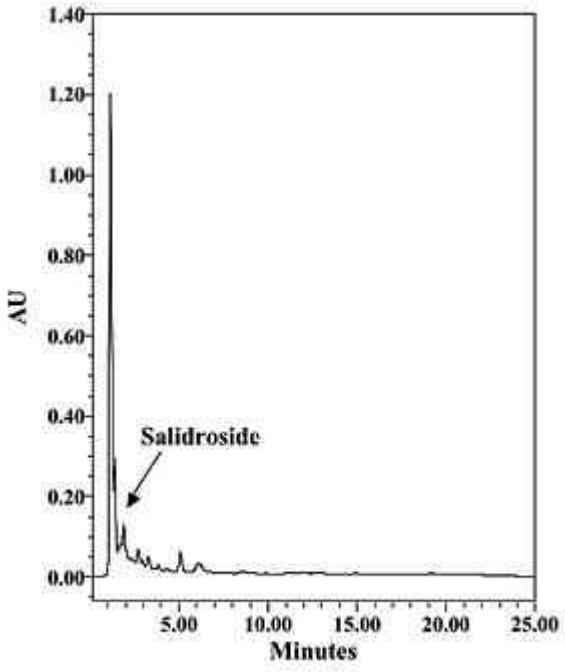

Figure 1B. HPLC chromatogram of *Rhodiola crenulata* root extract –common adulterant/substitute of *Rhodiola rosea*.

Table 2 summarizes the distribution of the rosavins and salidroside across the genus of Rhodiola, plus a variety of other plant species and microorganisms. While the presence of salidroside is pervasive among them all, only R. rosea contains the unique complex of compounds rosavins (Kurkin et al. 1986).

Table 2. The Distribution of Rosavins and Salidroside in Nature

Plants inside the genus of Rhodiola

Plant Species	Rosavins	Salidroside
R. rosea	YES	YES
R. alterna	NO	YES
R. brevipetiolata	NO	YES
R. coccinea	NO	YES
R. crenulata	NO	YES
R. ellipticum	NO	YES
R. fastigita,	NO	YES
R. gelida Schrenck	NO	YES

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(Table 2. The Distribution of Rosavins and Salidroside in Nature *Continued***)**

Plants inside the genus of Rhodiola R. heterodonta Boriss	NO	YES
R. kirilowii (Tibet) Regel	NO	YES
R. pinnatifida Boriss	NO	YES
R. quadfida Fish et Mey	NO	YES
R. sacra	NO	YES
R. sacchalinensis	NO	YES
R. wolongensis	NO	YES

Plants and organisms outside the genus Rhodiola

Plant Species	**Rosavins**	**Salidroside**
Salix trandra	NO	YES
Rhododendron caucasicum	NO	YES
Rhododendron ponticum	NO	YES
Vaccinium vitis-idaea	NO	YES
Vaccinium macrocarpon	NO	YES
Olea europea	NO	YES
Phillyrea latifolia	NO	YES
Buddleja officinalis	NO	YES
Ligustrum lucidum	NO	YES
Osmanthus fragrans	NO	YES
Yeast	NO	YES

KEY QUESTION: What identifiable constituents are unique to Rhodiola rosea compared to other species in the genus Rhodiola?

THE ANSWER: Rosavin, rosin and rosarin (collectively the rosavins).

It is clear that plant species in the genus Rhodiola phytochemically and therefore pharmacologically are very different.

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The Salidroside Syndrome

The presence of salidroside is not unique to the genus Rhodiola. It is commonly found in a wide variety of plants species outside of the genus Rhodiola (Saratikov et al. 1967; Kurkin 1985; Nekrasova et al. 1992; Wang et al. 1992a,b; Xu et al. 1998; Yoshikawa et al. 1995, 1996). The presence of both tyrosol and salidroside was found in white willow bark (Salix trandra, Vaccinium vitis-idaea, and in Rhododendron (Bridel and Beguin 1926; Thieme et al. 1969; Thieme and Winkler 1971).

The term "salidroside" is derived from the Latin name Salix, the botanical name of willow. Salidroside was isolated for the first time in 1926 from S. trandra by Bridel and Beguin (1926). Moreover, the concentration of salidroside and tyrosol in many of these other plants is even higher than implants in the genus Rhodiola. For example, particularly high levels of both salidroside and tyrosol are found in white willow bark (Salix alba) and olive leaf (Olea europae). Furthermore, tyrosol has been found in various microorganisms (Cremer et al. 1999) and phototrophic bacterium (Serdyuk et al. 1995).

In fact, a high salidroside product vaguely labeled "Rhodiola," with no mention of rosavins, probably means that it is not made from R. rosea root, and therefore lacks its clinically evaluated health promoting activity. For example, substitute products containing other species such as Rhodiola spp., or nonscientific terms such as "Tibetan" Rhodiola, "Himalayan" Rhodiola and/or so-called "African Rhodiola-like plant extract", should only have (possibly) salidroside content on their labels, since they cannot contain any rosavins, and should not claim to. These unproven substitutes are not equivalent to R. rosea root extract and cannot claim equal safety and efficacy, until independently proven by equivalent animal studies and clinical trials.

The Current Standard for Rhodiola rosea

The rosavins: salidroside ratio

Recent research clearly indicates that a whole extract of R. rosea must first; contain all the identifiable marker compounds and/or active constituents (the rosavins and salidroside) in ratios that reflect the phytochemistry of the natural plant, which is 3:1. It must also conform to the product specifications that have proven effective in repeated clinical trials. The ratio of rosavins to salidroside in the R.rosea root is approximately 3:1. Therefore, analysis of the ratio of the rosavins and salidroside in the extract is very powerful tool to evaluate the origin and purity of R.rosea extract. This is the new standard, which was adopted by the Russian Pharmacopoeia Committee (Kurkin and Zapesochnaya 1986; Dubichev et al. 1991; Bikov et al. 1999).

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CONCLUSION: As of the date of this publication, the only Rhodiola product that has been clinically tested and proven safe for humans is the R. rosea root extract standardized to a minimum of 3 percent rosavins.

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Consumer Guidance

Based on decades of research and consumer use, the following suggestions are recommended for American consumers interested in Rhodiola rosea products:

1. **Be sure that product contains Rhodiola rosea extract:** All informed consumers who expect to get health benefits demonstrated by available research on Rhodiola rosea should be certain that they are using R. rosea is in the products they purchase. Rhodiola rosea should be clearly stated in the ingredient listing in the Supplement Facts box on the product's label. If you are interested in any of these health benefits summarized in this review, you should also be certain that the R. rosea root extract standardized to 3% rosavins is in the product.

2. **Beware of substitutes:** Part of the problem with popularizing a relatively new phyto-medicinal product, such as standardized R. rosea root extract, is the confusion that arises when consumers are offered a variety of "Rhodiola" products, some much cheaper than others, without being given enough reliable information to judge for themselves which is the "real Rhodiola." Some of these "products" use other species of Rhodiola or non-standardized extracts and hope to "ride on the coattails" of the early consumer marketing efforts of ethical companies.

   Moreover, these adulterated products use misleading promotional materials or are even mislabeled to imply false equivalency with R. rosea extracts standardized for the minimum guaranteed potency of minimum 3 percent rosavins.

3. **Include Rhodiola rosea extract as part of your stress management program:** For best results, include taking R. rosea extract as part of a larger program for rebalancing and improving the health and well-being of your entire lifestyle. This comprehensive lifestyle program should include a healthy diet, regular exercise, stopping smoking or substance abuse, moderation with alcohol, steady weight management, taking time out for family and friends, improving communication and relationship skills, cultivating other interest besides work (travel, arts, education), and developing self-awareness and self-esteem.

Rhodiola rosea is a treasure of nature that deserves the protection of well-informed, satisfied users willing to defend their freedom of access to products of integrity that have proven themselves to be worthy of their loyal support.

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