

Plant Monograph - Rhodiola Rosea

by Liz Bartlett

General Overview

Rhodiola rosea is a beautiful plant with lovely scented yellow blossoms and a root and rhizome with a scent of rose. It is considered by many in the herbal industry as one of the newer 'fad' herbs, not backed by traditional use or valid clinical research. In



actuality, Rhodiola rosea is a very ancient herb first recorded medicinally as Rodia Riza in 77 AD in *De Materia Medica* by the Greek physician, Dioscorides. Linnaeus gave it the name Rhodiola rosea due to the rose-like fragrance of the fresh cut rootstock. (Darbinyan et al, 2000). In their 2002 monograph of Rhodiola rosea, Brown, Gerbarg, and Ramazanov reviewed the literature and found that between 1725 and 1960, there were many references to medicinal use of Rhodiola in the scientific literature of Sweden, Norway, France, Germany, the Soviet Union, and Iceland (Brown et al, 2002).

Rhodiola was in the official medicine of the former USSR by 1969 and is described in the last official USSR Pharmacopoeia and the current Russian Pharmacopoeia (Darbinyan et al, 2000). There is significant clinical and pharmacological research backing the efficacy of Rhodiola rosea yet much of this research has been done in Russia and is found in Russian and Scandinavian medical journals (Brown and Gerbarg, 2004). Although much of this research is unavailable for review, the available research supports the use of Rhodiola as an adaptogen, a stimulant, and for other medicinal uses (Brekhman et al, 1968). Only in the last few years has some of this research been translated into English and available for review. New clinical research has been conducted as well, allowing a wider review of Rhodiola rosea.

Rhodiola has many medicinal applications as will be discussed in the following monograph. As indicated, one of these applications is as an adaptogen. Rhodiola rosea is considered one of the 'original' adaptogens (Brekhman et al, 1968). In the appendix of this monograph there is an extended discussion of adaptogens, including a general overview, history, and a discussion of Selye's General Adaptation Syndrome and the more modern concept of allostasis.



Botanical Nomenclature

Rhodiola Rosea (Crassulaceae family) (Darbinyan et al, 2000). Other names include Sedum roseum (Morgan and Bone, 2005). Common names include Arctic root (Sanctis et al, 2004), Russian Rhodiola (Morgan and Bone, 2005), golden root (Sanctis et al, 2004) (Petkov et al, 1986), roseroot (Brown et al, 2002) and Hong Jing Tian (Memorial Sloan-Kettering Cancer Center, 2005).

In their translation of German literature, specifically the *Illustrierte Flora von Mitteleuropa* by G. Hegi, Brown et al found that Rhodiola belongs to the plant family Crassulaceae, the subfamily of Sedoidae, genus Rhodiola. Brown et al found some

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lack of clarity on the taxonomical status of the genus *Rhodiola*. Pre World War II some taxonomists put different species of *Rhodiola* into an independent genus. Then *Rhodiola* was reclassified as a subgenus of the larger genus *Sedum*, which included approximately 10 species. In 1963 Hegi identified more than 50 species of *Rhodiola* and thus once again classified them as a separate genus, specifically the genus of *Rhodiola*. Even today there is some difference of opinion on which species should be included in the genus *Rhodiola*. *Rhodiola rosea* is, however, classified as part of the genus *Rhodiola*. (Brown et al, 2002)

Definition (Composition of Drug)

Rhodiola rosea, a deciduous (PIW, 2006) perennial, herbaceous plant (Petkov et al, 1986) is found predominantly in dry, sandy ground (Darbinyan et al, 2000) at high altitude, Arctic and Alpine regions (Darbinyan et al, 2000) of the world, including in northeastern parts of Europe, eastern Siberia, and Alaska (Morgan and Bone, 2005). The plant is distributed in mountains of the Pyrenees, the Alps, the Vosges, the Sudety, and the Carpathians; in Western Siberia – Altai, Sayan; in Eastern Siberia – Yakutia; in the Far East – Sakhalin, Kamchatka. In Bulgaria, it is found at a height above 2,000 meters above sea level in the Rila, Pirin, Rhodopes and the Balkan Range. (Petkov et al, 1986).



The natural habitat of *Rhodiola rosea* is in the crevices of mountain rocks and on sea cliffs (PIW, 2006). The plant grows 12-30 inches (70 cm) tall and produces yellow flowers clustered in scutiform inflorescences (Petkov et al, 1986). The flowers are dioecious (male and female plants must be grown if seed is required), scented, and pollinated by bees and flies (PIW, 2006). *Rhodiola* has a thick rhizome (Brown et al, 2002). The rhizome is fragrant when cut, with a rose-like odor, thus the reference to



roses in the botanical name (Petkov et al, 1986). The plant part used in commerce and in medicine appears to be the rootstock (Darbinyan, 2000) and rhizome (Majewska, 2006). In Russia, roots and rhizomes are standardized for the content of rosavine (qualitative) and salidroside (qualitative and quantitative) (Majewska, 2006). In some of the literature studied, the terms root and rhizome are used interchangeably.

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Identification

Various species of *Rhodiola* naturally display a circumpolar distribution in mountainous regions in the higher latitudes and elevations of the Northern Hemisphere (Brown et al, 2002). There are more than 50 species of *Rhodiola*. There is some controversy around which new species should be included in the genus *Rhodiola*, and this controversy has resulted in some public confusion around which species are most beneficial for health. The public is sometimes offered *Rhodiola* products without identifying the species, which can be misleading at the very least. Most of the clinical research has been on the *Rhodiola rosea* species specifically. The pharmacological and medicinal properties of *Rhodiola* are species-dependent. It is therefore important that the public not be misled and that the appropriate *Rhodiola*, that is, *Rhodiola rosea*, be used to support the benefits as described. (Brown et al, 2002)



Rhodiola rosea has been the most studied of the *Rhodiola* genus. In their review of Russian and other literature, Brown et al found that approximately 51% of all animal studies and 94% of all human studies have been done on *Rhodiola rosea* specifically. *Rhodiola rosea* is the only species of the genus that has passed extensive toxicological studies and determined to be safe

for animals and humans in reasonable doses. (Brown et al, 2002)

One of the main defining markers or characteristics of *Rhodiola rosea* is that there are three cinnamyl alcohol-vicianosides – rosavin, rosin, and rosarin – that are *unique to the rosea species* of *Rhodiola*. The collective term for these three is rosavins. (Abidov et al, 2003).

The *Rhodiola rosea* extracts used in most of the human clinical trials were standardized to at least 3% rosavins and 0.8-1 % salidroside (these constituents occur naturally in the root of the plant at a ratio of 3:1). (Brown et al, 2002) (Morgan and Bone, 2005). In Russia, roots and rhizomes are standardized for the content of rosavine



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(3% of dry mass in underground stems) and salidroside (1% of dry mass) (Majewska et al, 2006).

The fresh cut rootstock (Darbinyan et al, 2000) of *Rhodiola rosea* has a characteristic fragrance, resembling attar of roses (Petkov et al, 1986). It appears that the rootstock (Darbinyan et al, 2000) of the plant is best harvested in the autumn (Petkov et al, 1986), during the late blooming period (Abidov et al, 2003) (PIW, 2006). This information is based on when the plant was harvested during several studies. Since so many of the earlier studies are in Russian, this information is not verified.

Traditional Use

Besides being used as far back as 77 C.E., as recorded by Dioscorides in Greece in 77 C.E., *Rhodiola* has been used for hundreds of years as the traditional medicine of Russia, Scandinavia, and other countries (Darbinyan et al, 2000). Darbinyan et al mention that since the 1700s, medicinal uses of *Rhodiola* were cited in the literature in Sweden, Norway, France, Germany, the Soviet Union, and Iceland. References include the French, Swedish and Russian pharmacopeias as well as the *Materia Medica* of Linnaei of 1749 (Darbinyan et al, 2000).

In their review of Russian literature, Brown et al found that *Rhodiola* was considered a tonic and stimulant, used to increase physical endurance, memory, attention span, work productivity and resistance to high altitude sickness (Brown et al, 2002). It was also used to treat various other conditions, including fatigue, depression, anemia, impotence, many infections, including colds and flu, cancer, nervous system disorders and headache, to promote longevity and fertility (Morgan and Bone, 2005) and treat gastrointestinal ailments and nervous system disorders (Brown et al, 2002).



Interestingly, in some mountain villages in Siberia, a bouquet of roots is still given to couples before their nuptials to assure many healthy children. Mongolian doctors prescribed *Rhodiola* for tuberculosis and cancer. (Brown et al, 2002) *Rhodiola* is still used by the aborigines of Siberia to prevent fatigue and general 'disinclination' to work (Wagner et al, 1994). The special "golden roots" of *Rhodiola* and methods of preparation were kept somewhat secret and within the confines of the family treasured secrets. Siberians so treasured *Rhodiola* that they would carry it in secret down ancient trails to trade for other coveted goods, including wines, fruits, garlic and honey. Even the Chinese emperors coveted *Rhodiola* and would send expeditions to Siberia to return with the herb for medicinal use. (Brown et al, 2002).

Linnaeus wrote of the root as astringent and for treatment of hernia, leucorrhoea, hysteria, and headache. The Vikings used *Rhodiola* to enhance

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their physical strength and endurance. The Germans also used Rhodiola for pain relief, headache, scurvy, hemorrhoids, and as a stimulant and anti-inflammatory. (Brown et al, 2002) (Darbinyan et al, 2000). In England, Rhodiola was known as lignum rhodium in apothecary shops, in France, Rhodiola was used as a brain tonic in the early 19th century, and in Tibetan medicine since 300 A.D., Rhodiola was used to treat lung diseases, particularly lung-heat disorders (Darbinyan et al, 2000).

The root of Rhodiola rosea was used as food in some locations, i.e. Alaska, Siberia, and Greenland (Morgan and Bone, 2005). The young succulent leaves and shoots are eaten raw or cooked like spinach, with a slightly bitter taste (PIW, 2006) (Darbinyan et al, 2000). Even the stems are cooked and eaten like asparagus. The root was eaten raw or cooked and was fermented before being eaten by the North American Indians. (PIW, 2006). The root has even been used to flavor beer in Norway. A decoction of the root was used as a shampoo, to promote hair growth, prevent hair loss, and for treatment of dandruff. (Morgan and Bone, 2005)

It's been largely unknown to the Western hemisphere. Reasons for this include the language barrier and the sacred, secretive nature surrounding the herb in general (Brown and Gerbarg, 2004)

Taste/Odor/Energetics – Sweet, slightly bitter, cool, neutral (Winston, 2003) (Winston, 2005), astringent (Brown et al, 2002)

Summary of Physiological Actions – Adaptogenic (Brekhman et al, 1968) (Boon-Niermeijer et al, 2000), antitumor (Majewska et al, 2006), psychostimulant (Shevtsov et al, 2003) (Spasov et al, 2000) (Panossian et al, 2005), memory enhancer (Petkov et al, 1986) (Hillhouse et al, 2004), anti-fatigue (Darbinyan et al, 2000) (Abidov et al, 2003) (De Bock et al, 2004) (Spasov et al, 2000), thyroid function enhancement (based on review of Russian literature by Brown et al, 2002), cardioprotective (based on review of Russian literature by Brown et al, 2002) antioxidant (Battistelli et al, 2005) (Sanctis et al, 2004), anti-carcinogenic (Majewska et al, 2006), female and male reproductive tonic (based on review of Russian literature by Brown et al, 2002), physical performance and endurance enhancement (Spasov et al, 2000) (De Bock et al, 2004)

Specific Indications

Fatigue, mental and/or physical exhaustion (Darbinyan et al, 2000) (Abidov et al, 2003) (De Bock et al, 2004); to improve mental performance, concentration and memory, especially when stressed (Shevtsov et al, 2003) (Spasov et al, 2000) (Panossian et al, 2005) (Brekhman et al, 1968) (Petkov et al, 1986) (Hillhouse et al, 2004), to enhance physical performance and endurance (De Bock et al, 2004); may assist sexual function in men (based on review of Russian literature by Brown et al, 2002); adjuvant treatment of cancer (Majewska et al, 2006) (based on review of Russian literature by (Morgan and Bone, 2005) (Brown et al, 2002); excess constitutions with hypertension, liver fire rising headaches (red face, ears, and eyes, sharp pain behind the eyes, and excessive anger), yang insomnia, anxiety and ADHD (based on clinical experience Winston, 2003); cardiovascular tonic (based on review of Russian literature by Brown et al, 2002)

Key Plant Constituents

The main chemical compounds in *Rhodiola rosea* include:

- Cinnamic glycosides (Rohloff, 2002) including rosavin, rosin, rosarin (specific to *Rhodiola rosea*) (Brown et al, 2002);
- Phenylethanol derivatives: salidroside (rhodioloside), tyrosol;
- Flavanoids: rodiolin, rodionin, rodiosin, acetylrodalgin, tricin (Brown et al, 2002); catechins (Battistelli, 2005);
- Phenolic acids: chlorogenic and hydroxycinnamic, gallic acids. (Brown et al, 2002)
- Tannins (Rohloff, 2002)
- Monoterpenes: rosiridol, rosaridin;
- Triterpenes: daucosterol, beta-sitosterol; (Brown et al, 2002)

As indicated previously, an interesting feature of *Rhodiola rosea* is the rose-like scent of the root and rhizome (Darbinyan et al, 2000). In an attempt to find a potential source of large-scale production of the essential oils and flavor essences from the rhizomes of *Rhodiola rosea*, Rohloff characterized the composition of the essential oils of *Rhodiola* (Rohloff, 2002). The terpenes and volatile oils from the rhizomes of *Rhodiola rosea* were isolated and found to contain 0.05% essential oil with the following main chemical classes:

- Monoterpene hydrocarbons (25.40%), monoterpene alcohols (23.61%) and straight chain aliphatic alcohols (37.54%).
- The most abundant volatiles detected in the essential oil were *n*-Decanol, geraniol and 1,4-*p*-menthadien-7-ol.
 - Geraniol was found to be the most important rose-like odor compound besides geranyl formate, feranyl acetate, benzyl alcohol and phenylethyl alcohol.
- A total of 86 compounds were identified.
- Floral notes such as linalool and its oxides, nonanal, decanal, nerol and cinnamyl alcohol highlight the flowery scent of the *Rhodiola* rhizomes.

(Rohloff, 2002)

The stimulating and adaptogenic properties of *Rhodiola* are attributed to *p*-tyrosol, salidroside, rhodioniside, rodiolin, rosin, rosavin, rosarin and rosaridin. *p*-Tyrosol has been shown to absorb readily and dependent of dose after an oral dose. (Alternative Medicine Review, 2002) The salidroside, cinammoyl-glycosides (rosin, rosavin and rosarin), and *p*-tyrosol are thought to be responsible for the high therapeutic action (Battistelli, 2005).

The following Figures 1-5 show the different chemical structures of the main constituents in *Rhodiola rosea*, including rosavin, rosin, rosarin, tyrosol and salidroside (Brown et al, 2002).

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Figure 1: Rosavin

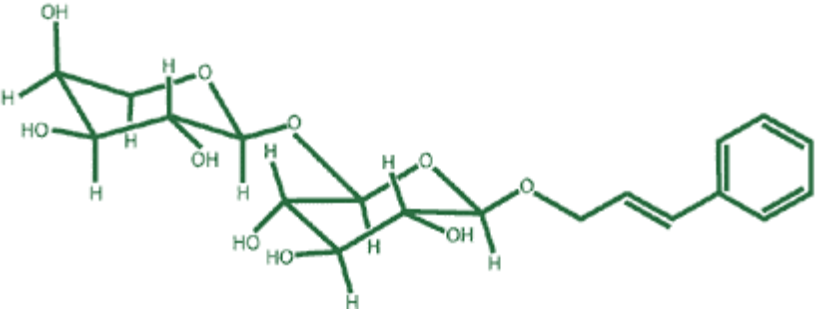


Figure 2: Rosin

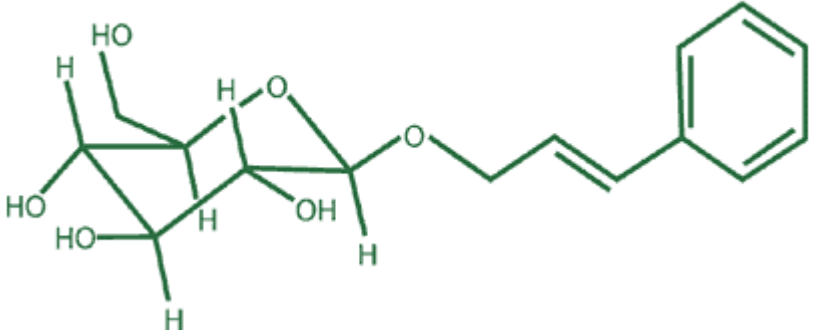


Figure 3: Rosarin

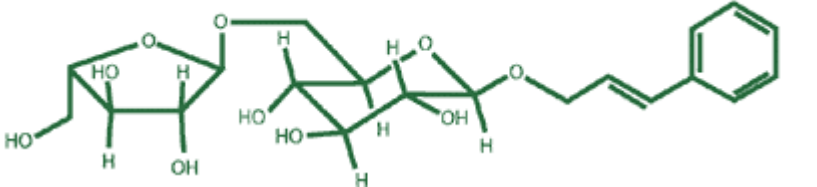


Figure 4: Tyrosol

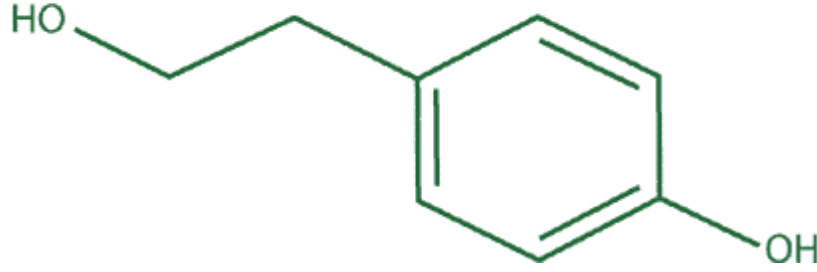
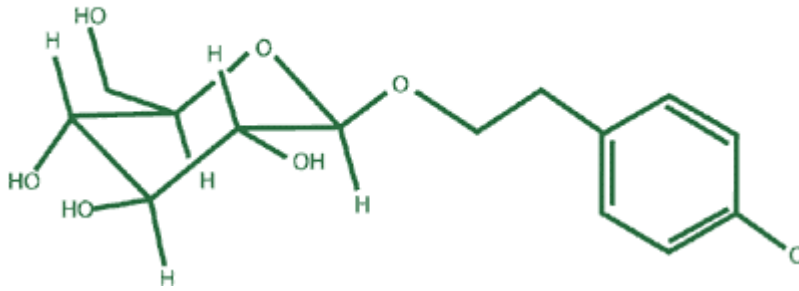


Figure 5: Salidroside



Pharmacology

Effect on the Central Nervous System

- *Rhodiola rosea* extract, in a single dose of 0.10 ml per rat, was found to improve learning and retention after 24 hours. Significant improvement of long-term memory was also established in memory tests after a 1-day treatment period with the same dose of extract. Using the 'staircase' method with positive food reinforcement, at a dose of 0.10 ml per rat, *Rhodiola* extract had a positive effect on the training process. However, with the other methods used in the study, *Rhodiola* had no substantial effect on learning and memory. (Petkov et al, 1986) The authors postulate that the differences in the effects due to the different training methods used could be due to the different neurochemical mechanisms underlying the different training methods. The role of the cholinergic transmitter system in the learning and memory formation process was discussed. (Petkov et al, 1986).
- *Rhodiola* extract was shown to cause moderate inhibition of acetylcholine esterase (AChE) when tested at 10g/L. Other plants, like *Salvia lavandulaefolia* (Spanish Sage), also cause AChE inhibition and improve memory. The enzymatic action was performed in a flat-bottom plate and inhibition observed. This AChE inhibition may explain the physiological reasons for the reported mental and memory-enhancing properties of *Rhodiola rosea*. *Rhodiola* appears to contain a multitude of different AChE inhibitors. The authors suggested that *Rhodiola rosea* should be further examined for its effectiveness at treating memory impairments like that seen in Alzheimer's disease. (Hillhouse et al, 2004)

Effects on Physical Work Capacity

- Treatment with *Rhodiola rosea* extract significantly prolonged (by 24.6%) the duration of exhaustive swimming in comparison with control rats and rats treated with a different species of *Rhodiola*, *Rhodiola crenulata*. *Rhodiola crenulata* does not contain the rosavins, which is the biggest difference between the two species. *Rhodiola rosea* activated the synthesis or resynthesis of ATP in the mitochondria and stimulated the repair of the energy processes after intense exercise. ATP content in the muscle mitochondria of rats was studied before and after the exhaustive swimming test. *Rhodiola crenulata* did not produce these effects, leading the authors to conclude that the rosavins present in *Rhodiola*

rosea may have produced these effects, or other bioactive compounds present. (Abidov et al, 2003)

Antioxidant and Anti-carcinogenic Effects

- In a study investigating the effect of a *Rhodiola rosea* aqueous extract in an *in vitro* model of oxidative stress, human erythrocytes were exposed to hydrochlorous acid (HOCl) after receiving increasing doses of *Rhodiola rosea* extract, which were added to the RBC suspensions at the same time as the HOCl. *Rhodiola rosea* was able to significantly protect, in a dose dependent manner, human erythrocytes from GSH (glutathione) depletion, glyceraldehyde-3-phosphate dehydrogenase inactivation and hemolysis induced by the oxidant. It was concluded from the study that *Rhodiola rosea* aqueous extract was able to protect human erythrocytes against some of the damages induced *in vitro* by HOCl suggesting important antioxidant activity. (Sanctis et al, 2004)
- In an investigation of the biological action (survival, cell cycle, apoptosis) of the antimetabolic activity of *Rhodiola rosea* (2 year old rhizomes grown in a lab, where the HPLC analysis showed the presence of rosavin and cinnamyl alcohol, but no salidroside was found – this apparently is present in roots more than 5 years old) on promyelotic leukemia cells (of the HL-60 line), it was found that the *Rhodiola rosea* extract led to inhibition of cell division of HL-60 cells, which is preceded by an increase in the cells at the prophase stage. This led to induction of apoptosis and necrosis in the HL-60 cells and to a marked reduction of their survival. No chromosome aberrations or micronuclei were observed after treatment with the *Rhodiola*, which suggests its mild effect. Based on the combination of *Rhodiola*'s cytostatic and antiproliferative effect, the authors note that there is increased hope for its use in anticancer therapy. (Majewska, 2006)
- In a study investigating the effect of *Rhodiola* root aqueous extract on *in vitro* human erythrocytes exposed to hypochlorous acid (HOCl)-oxidative stress, *Rhodiola rosea* provided significant protection. In the face of the oxidative stress of HOCl, damages to the erythrocytes occur including membrane protein and lipid changes, changing the shape of the erythrocyte and determining lysis eventually. With the *Rhodiola* extract, there was a positive dose-dependent antioxidant effect, with high doses severely altering the cell shape, while lower doses offered a more protective effect. (Battistelli, 2005)

Endocrine and Reproductive Effects

- In their review of a Russian study on the effect of *Rhodiola rosea* on ovarian functional activity, Brown et al described that an extract of *Rhodiola rosea* was administered by injection to sexually mature female mice over a period of 4 weeks. Menses were prolonged from 1.3 days in the control group to 2.8 days in the *Rhodiola* extract treated group. The number of estrus days was increased from 29% to 56%. In most of the *Rhodiola* treated animals, there was an increase seen in the number of growing follicles, oocyte volumes, and the accumulation of RNA in oocyte cytoplasm, the proliferation of the uterine lining and the preparation of uterine mucosa for fertilization. As there were no changes noted in the *Rhodiola* treated sexually immature female white mice, it appears

that the 'estrogenic' effects of *Rhodiola rosea* 'depend on a specific hormonal milieu'. (Brown et al, 2002)

Adaptogenic, Anti-Stress, and Neuroendocrine Effects

Please note that in the addendum section found at the end of this monograph is a discussion of adaptogens, including definition and terminology, history, and discussion of the stress response and how adaptogens in general are useful in supporting health. What immediately follow are studies showing the adaptogenic, anti-stress, and neuroendocrine effects of *Rhodiola rosea*.

- *Rhodiola rosea* and *Acanthopanax senticosus* were found to exert a protective action to embryos of freshwater snails (*Lymnaea stagnalis*) exposed to a variety of environmental stressors. Plant extracts of each plant were applied for 20 hours to 3-day old larvae of the pond snail. The embryos were then exposed to a high and toxic dose of different environmental stressors, including a physical stress condition (heat shock: 43 degrees C for 4 minutes), an oxidative stress condition (superoxide radicals induced by menadione) and heavy metal-induced stress (copper or cadmium). Both plants exerted a strong protective action against lethal heat shock and protected against the negative effect of the superoxide radicals. A small but significant protection was seen against the intoxication with the copper or cadmium. The authors of the research concluded that phyto-adaptogens are universal enhancers of non-specific resistance against different kinds of stress conditions. (Boon-Niermeijer et al, 2000)
- Repeated doses of glucosides isolated from *Rhodiola rosea* increased significantly the restoration of protein, RNA, and free amino acids in the muscles of rats after exhaustive exercise ((Panossian et al, 1999)
- Repeated application of *Rhodiola rosea* and *Eleutherococcus* glycosides resulted in weight gain in rats and piglets, without an increase in testicular weight (Panossian et al, 1999).
- In a reference to a Russian study by Azizov et al on the effect of adaptogens on the work capacity of experimental animals, Kelly reiterates that *Rhodiola* increased the swimming time of rats 135-159% in a physical endurance test . (Kelly, 2001)
- In a review of Russian literature, Brown et al found that when rats were treated with *Rhodiola* and put through a four hour period of non-specific stress, there was no observation of the expected increase in beta-endorphins, in fact, there was even a substantial decrease noted. This led these Russian scientists to conclude that the expected upregulation of the H-P-A axis was either decreased or prevented by *Rhodiola* (Brown et al, 2002) (Alternative Medicine Review, 2002).
- In their review of Russian literature, Brown et al found that neuroendocrine animal studies showed that *Rhodiola rosea* enhanced thyroid function without causing hyperthyroidism, similar to other adaptogens. The thyroid function was enhanced and protected from involution that happens with age (Brown et al, 2002).

Clinical Trials

As indicated previously, there have been a multitude of clinical trials done on *Rhodiola rosea*, mostly in Russia. However, in more recent years, more clinical trials have been done and translated where appropriate. Herein are some of those clinical trials so summarized.

Effects on the Central Nervous System

- In a randomized placebo-controlled, double blind, cross-over study, healthy physicians (ages 24-35) were given a low dose of a standardized extract of *Rhodiola rosea* (SHR-5) while under stressful conditions (lack of sleep during night duty). The dose of SHR-5 was 170 mg (containing 4.5 mg salidroside). *Rhodiola* was tested for its anti-fatigue effects. Results showed that total fatigue index was significantly improved after two weeks of taking the *Rhodiola* preparation. Regular night duty work is known to be stressful. The authors note some methodological difficulties in measuring such a subjective and complex notion as fatigue however. The Fatigue Index was used to make the test more relevant and included evaluation of aural and visual short-term memory and ability for mental attention. Five tests were used which focused on the determination of speed of visual and aural perception, attention capacity and short-term memory. (Darbinyan et al, 2000)
- In a double-blind, randomized and placebo-controlled study of male, Indian medical students (ages 17-19) studying for final exams in Russia, *Rhodiola rosea* resulted in significant improvements in physical fitness tests, psychomotoric tests, mental fatigue tests, and in general well-being. Investigated was a repeated low-dose regimen of an extract of *Rhodiola rosea* radix, SHR-5, at a total of 100 mg/day for 20 days. (Spasov et al, 2000)
- In a randomized, double-blind, placebo-controlled, parallel-group study, *Rhodiola rosea* was found to significantly improve performance in healthy, trained, young



men under conditions of stress and fatigue. 161 male cadets of the Military Institute of the Russian Federation Ministry of Defense in their education and training, ages 19-21 years, were randomly assigned to one of four groups: (1) 41 men received 2 capsules of *Rhodiola* (2) 20 men received 3

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capsules of Rhodiola (3) 40 men received 2 placebo capsules, and (4) 20 men received no capsules (untreated control group). Each capsule of Rhodiola contained 185 mg of dry extract SHR-5, standardized to 4.5 mg of salidroside. The objective was to evaluate the antistress and stimulant effects of single doses of Rhodiola and to compare the efficacy of two different doses in this study group. All subjects were on a 24-hour shift and were given a series of baseline medical exams, self-assessment questionnaires, and mental performance tests beginning at 5:00 pm. The capsules of either Rhodiola or placebo were given at 4:00 am after the cadets were awake all night. At 5:00 am the tests and exams were repeated. Rhodiola treatment significantly improved the antifatigue index, which measured the amount of work per unit of time and the quality of work. There appeared to be greater efficacy in the lower-dose group (370 mg versus 555 mg) in the psychometric test. Results of the individual tests showed that Rhodiola improved quality of work more than quantity. This is in line with the recognition of *Rhodiola rosea* as an adaptogen. (Shevtsov et al, 2003)

Effects on Physical Work Capacity

- In a double-blind placebo-controlled randomized study, acute *Rhodiola rosea* intake was found to improve endurance capacity in healthy young volunteers. 12 men and 12 women, physically active students, participated in this two-phase study, separated by a 5 day wash-out period. Phase I investigated the effects of acute Rhodiola intake on endurance exercise performance, muscle strength, reaction time, speed of limb movement, and capacity for sustained attention. Dose of Rhodiola during phase I was 200 mg containing 1% salidroside and 3% rosavin versus 350 mg starch in the placebo. Phase II investigated the effects of Rhodiola intake for 4 weeks using the same doses as in Phase I following by evaluation of the above mentioned tests. According to the authors, significant results were only found for endurance capacity. The test for endurance capacity was an incremental exercise test to volitional exhaustion on a bicycle ergometer. In phase I, time to exhaustion was 24 seconds longer in comparison to placebo; peak oxygen uptake and peak carbon dioxide output were 5% higher after acute Rhodiola intake. Also pulmonary ventilation was higher in the Rhodiola users in Phase I. In Phase II, Rhodiola did not alter any of the variables measured.

The supplement used in the study contained a high amount of rosavin and salidroside, the two constituents considered to be the 'active' compounds of the plant. The authors note that these active compounds are presumed to be responsible for stimulating endorphin secretion, providing a possible physiological mechanism for enhancing performance. The ability to do exhaustive exercise depends partially on each



person's ability to handle pain and discomfort. It has been shown previously and repeatedly that the endogenous opioid system (i.e. endorphins) is involved in the modulation of pain tolerance. It was not clear from this study whether the rosavin and salidroside content in the Rhodiola extract really can stimulate endorphin action during exercise. Results also showed that contrary to other CNS stimulants like caffeine and amphetamines whose temporary effect fades over time, Rhodiola after 4 weeks intake at 200 mg/day continued to have positive effects (ergogenic effects). Rhodiola intake at 200 mg was shown to improve endurance exercise capacity in young healthy volunteers. (De Bock et al, 2004)

Endocrine and Reproductive Effects

- In their review of Russian literature and a study of ovarian function and Rhodiola rosea, Brown et al write that forty women suffering from amenorrhea were given either 100 mg Rhodiola rosea extract twice a day for two weeks, or 1 ml rhodosin (extract of Rhodiola) intramuscularly for 10 days. The cycle was repeated in some of the women 2-3 times. Menses were restored in 25 women, and 11 became pregnant. (Brown et al, 2002)
- In another Russian study review, Brown et al reiterate that 26 out of 35 men with erectile dysfunction and/or premature ejaculation, after intake of Rhodiola rosea at 150-200 mg/day for 3 months, showed significant improved sexual function and normalization of prostatic fluid (Brown et al, 2002)

Cardioprotective Effects

- In Brown et al's review of joint Swedish and Russian double-blind, randomized placebo-controlled studies, 10 healthy but sedentary men (ages 20-31) were evaluated in a series of complex 1-7 day trials comparing the effects of an adaptogen formula that included 3 mg rhodioloside from Rhodiola rosea root extract, 50 mg; 3 mg total of different glycosides from Eleutherococcus root extract, 100 mg; and 4 mg of different constituents of Schisandra fruit extract, 150 mg. Results showed that the mean increase in work capacity was 28% with the adaptogens. The subjects were able to perform in the lower level of trained athletes without any exercise training. The strength of their heart muscle contractility and heart rate variability functions improved. The hearts showed increased reserves under greater intensity levels of stress. Although the formula contained other herbs in addition to Rhodiola, these findings are consistent with other research conducted only on Rhodiola (Brown et al, 2002).

Anti-carcinogenic Effects

- Rhodiola root extract (minimum 0.9% salidroside and 3% rosavin) improved parameters of leukocyte integrins and T-cell immunity in a small study of 12 patients with superficial bladder carcinoma. There was less frequency of relapse noted. (Brown et al, 2002)

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Preparation and Dosage

Doses range from 100-600 mg/day of extract standardized to 3% rosavins and 0.8%-1% salidroside (Darbinyan et al, 2000) (Spasov et al, 2000) (Shevtsov et al, 2003) (De Bock et al, 2004). In their review of Rhodiola, Morgan and Bone note that 150–600 mg/day of extract corresponds to 6-12 grams of original root, ideally standardized to 2% rosavins (6-12 mg/day) and 3% salidroside (9-18 mg/day) (Morgan and Bone, 2005).

As an adaptogen and/or to improve endurance capacity over time, administration should proceed for several weeks prior to a period of expected increased physiological, chemical or biological strain and continued through the duration of the event or activity (De Bock et al, 2004). Acute intake of doses as low as 200 mg/day can improve endurance exercise capacity (De Bock et al, 2004).

Lower doses (i.e. 370 mg versus 555 mg in one study) showed greater efficacy (Shevtsov et al, 2003). In double-blind placebo-controlled studies, doses were in the lower ranges of 100 – 200 mg per day of standardized extract (Darbinyan et al, 2000) (Spasov et al, 2000) (De Bock et al, 2004).



As noted in their book and monograph on Rhodiola, Brown et al observe that in their respective clinical practices many people would not be able to tolerate a single dose of 555 mg or even 370 mg of standardized extract without experiencing some anxiety,



agitation, insomnia, or nausea. In their opinion, most people need to start at a lower dose of 100 mg of standardized extract and increase to a maximum of 400 mg (200 mg 30 minutes before breakfast and 200 mg 30 minutes before lunch) over one to two weeks. Due to the stimulant nature of Rhodiola rosea, those more sensitive to the stimulating effects may be able to only tolerate 50 mg to 100 mg as a total daily dose. On the other hand, individuals

with certain conditions (i.e. treatment resistant depression and certain neurological disorders) may require 600 mg a day or more. (Shevtsov et al, 2003) (Brown et al, 2002) (Brown and Gerbarg, 2004).

Safety Issues

- **Toxicology** – In their review of Russian literature on the chemical composition and pharmacological characteristics of Rhodiola rosea, Brown et al found that in rat toxicity studies, the LD₅₀ (the lethal dose at which 50% of animals die) was 28.6 ml/kg, which is approximately 3,360 mg/kg. An equivalent dose in a 70 kg man would be approximately 235 grams or 235,000 mg. (Brown et al, 2002). As the recommended clinical doses range from about 100-600 mg/day (Spasov et al, 2000) (Shevtsov et al, 2003) (Darbinyan et al, 2000) (corresponding to approximately 6-12 grams of original root) (Morgan and Bone, 2005), this herb is considered safe.

- **Contra-indications and cautions** – In their review of Rhodiola, Morgan and Bone cite a small clinical study whereby depressed patients with hysteric and phobic symptoms showed an increase in symptoms after intake of Rhodiola. The citation did not include a reference and the study could not be found to verify this information, however it's worth mentioning as a general caution (Morgan and Bone, 2005); Similarly, Brown et al cite that Rhodiola is contraindicated in excited states, again without a specific reference. However, Brekhman et al in their landmark review of adaptogens found that certain adaptogens like Rhodiola and Eleutherococcus have a stimulating action (Brekhman et al, 1968). In their book (p. 71) and monograph on Rhodiola, Brown et al mention that any treatment that increases energy has the potential to induce mania in bipolar individuals, so therefore would be ill advised (Brown and Gerbarg, 2004) (Brown et al, 2002).
- **Drug Interactions** – Brown et al, referring once again to the stimulant action of Rhodiola, indicate that Rhodiola may have additive effects with other stimulants (Brown et al, 2002). Similar to other strong adaptogenic and tonic herbs, use with caffeine and other stimulants should be avoided (Morgan and Bone, 2005).
- **Pregnancy and lactation** - no adverse effects noted in the literature
- **Side Effects** – few side effects, however, a small clinical study showed an increase in symptoms of a subgroup of depressed/bipolar patients as indicated above in contraindications (Morgan and Bone, 2005); some insomnia noted in some individuals (De Bock et al, 2004); based on personal experience with patients, Brown et al (practicing Psychiatrists) note that Rhodiola rosea can interfere with sleep or cause vivid dreams in some individuals in the first two weeks of ingestion so should be taken early in the day; Clinical feedback in their respective practices indicate that at doses of 1.5 to 2.0 grams and above, Rhodiola rosea extract standardized for 2% rosavin, might cause an increase in irritability and insomnia within several days. (Brown et al, 2002)
- **Overdose (if known)** – none noted in the literature
- **Ability to drive and use machinery** – no adverse effects noted in the literature



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Commercial Sources

Rhodiola rosea has traditionally been harvested from wild sources, usually in Russia (Herbalgram, 2006) and Finland (Richter, 2004). However, commercial demand is threatening the health of the wild plant populations. According to the Herb Research Foundation, herb suppliers need to develop sustainable sources of Rhodiola, so that this herb is available in the future. Already destructive harvesting practices have decimated Rhodiola plants in some parts of Russia. Although Russian forestry experts have established controls to monitor the harvesting of wild Eleutherococcus for example, no such controls have been put into place for Rhodiola. (Leigh, 2006) Rhodiola rosea is agriculturally sustainable. To harvest the root, the whole plant must be destroyed, so farmers in Russia, some former Soviet republics, and Scandinavia are developing commercial Rhodiola rosea farms, where high quality roots may be cultivated without destroying the wild Rhodiola. (Blumenthal, 2005) The Canadian government, in order to meet growing demand, is also promoting Rhodiola cultivation, growing hundreds of thousands of Rhodiola seedlings in greenhouses and then distributing to 33 farms to create 400 acres in Alberta by the year 2009 (Herbalgram, 2006).

SHR-5 is a proprietary standardized extract (standardized to 3% rosavin and 0.8% salidroside) from Rhodiola rosea root from the Swedish Herbal Institute, Vastra Frolunda, Sweden. This same extract was approved in Denmark in 2001 as an herbal medicine product. Several clinical studies have also studied SHR-5 as mentioned in this monograph. (Shevtsov et al, 2003) (Spasov et al, 2000) (Oliff, 2004)

APPENDIX

ADAPTOGENS

Introduction and Overview

Rhodiola rosea is considered one of the original adaptogens as designated and studied by Russian and Scandinavian researchers for approximately 40 years (Kelly, 2001). In their 1968 review of 189 medicinal plants, the Soviet researchers Brekhman and Dardymov identified *Rhodiola rosea* as one of the plants that met their criteria for an adaptogen (Brekhman et al, 1968). Some of the other plants cited as conforming to the requirements were *Eleutherococcus senticosus*, *Panax ginseng*, *Raponticum carthamoides*, and *Schisandra chinensis* (Brekhman et al, 1968).

The following is a discussion of adaptogens, including history, definition, and criteria for inclusion. Stress and the stress response will be discussed, including information on homeostasis, the H-P-A axis and the more modern concept of allostasis. All of this is important when referencing adaptogens, as they are key plants to consider when a person is in an acute or chronically hyperaroused state from stress or the perception of stress.

History of Adaptogens

In 1947, N.V. Lazarev, a pharmacologist, was the first to use the term adaptogen to describe the unexpected effects of an arterial dilator developed in France, dibazol (2-benzylbenzimidazol) (Panossian et al, 1999). Lazarev discovered that dibazol increased the resistance of organisms to stress (Panossian et al, 1999). Dibazol was found to be effective in medication for damage to different regions of the nervous system and to increase non-specific resistance to adverse influences. This new group of medicinal substances contributed to “a state of nonspecifically increased resistance” or SNIR of the organism. These medicinal substances that caused SNIR were named “adaptogens”. (Brekhman et al, 1968)

Approximately 35-40 years ago, the former USSR conducted much research on adaptation and stress and the mechanism of action in such situations as high-altitude hypoxia, physical load training, with emphasis on finding ways to increase adaptation in a number of highly stressful situations, seeking to develop methods and pharmacological agents that would help humans to ultimately adapt and cope. (Panossian et al, 1999). In the USSR the study of adaptogens actually morphed into a field of biomedical research, specifically targeting stress research, and mapping or screening biologically active substances of natural origin, mainly from plants (Panossian et al, 1999)

Although in 1947 Lazarev first coined the term adaptogen, traditional medicine has been using plants for these adaptogenic purposes for a long time (Brekhman et al, 1968). Tonic plants are some of the most ancient medicinal remedies of folk medicine in many parts of the world and in many different cultures. Brekhman and colleagues analyzed 158 complex prescriptions of folk medicine in different Asian countries and found 116 of

these included plants of tonic action (Brekhman et al, 1968). They chemically analyzed the plants and found that glycosides were prevalent in these tonic plants, as well as alkaloids in a smaller percentage of cases. In looking at the current and past use of these plants in folk medicine, they found that corroborative action was prevalent in treatment for hypertension, atherosclerosis, diabetes, cancer, tuberculosis, anemia and other diseases. (Brekhman et al, 1968)

General Adaptation Syndrome

When stress is discussed in these works, it is used as defined by Hans Selye's theory about stress, which is defined as a state of threatened homeostasis. In 1936, Selye conducted experiments on rats and found that various stressors (cold, heat, noise, chemicals, etc.) induced the same "non-specific" generalized physiological response of the organism (stomach and colon ulceration, atrophy of immune system tissue and increase of adrenals) – he named this 'stress'. (Panossian et al, 1999).

Selye identified three phases of an organism's stress response (McCance, 2004).

1. First is the alarm phase, when a stimulus triggers the body's stress response system. Activation of the Sympathetic Nervous System results in increased secretion of epinephrine and norepinephrine. These stress hormones prepare the body for 'flight or fight'. Attention and memory are heightened, as well as problem-solving skills. The Hypothalamus-Pituitary-Adrenal (HPA) axis directs the adrenal glands to secrete more cortisol. Cortisol, another stress hormone, directs the body to increase energy by released stored fat as triglycerides, converting stored energy to glucose and breaking down proteins. (McCance, 2004) (Spelman, 2004) (Brown and Gerbarg, 2004)
2. Second phase is the resistance phase. If a stressor continues, the damaged cells from the alarm phase are repaired and rebuilt via anabolism, which also prepares the body for future stressors. (McCance, 2004) (Brown and Gerbarg, 2004)
3. Third phase is the exhaustion phase (McCance, 2004), which happens when the stressor continues beyond the body's capacity to resist it (Brown and Gerard, 2004). It is in this phase where continual stress leads to breakdown and depletion of homeostasis (Spelman, 2004) and breakdown of compensatory mechanisms (McCance, 2004). Per Selye, this phase is considered the most detrimental to health and marks the onset of certain diseases (McCance, 2004).

Selye referred to these three phases as the General Adaptation Syndrome. These phases describe a stereotypic non-specific response to stressor signals from variable sources. This adaptation response gives an organism the ability to resist against stressors and to adapt to environmental challenges and changes. Selye ascertained that the factor limiting adaptability was the organisms 'adaptation energy', which is the capacity of the organism to resist adverse environmental influences. This capacity is finite and declines with increasing and or continuous exposure to stressors. Faulty adaptation leads to disease. (Wagner et al, 1994)

The Stress Response

Stress is simply a fact of nature as all organisms are constantly interacting with their environments (external and internal), both physically and behaviorally. In stress a demand exceeds a person's ability to cope, with the result being disturbances of cognition, emotion, and behavior which can adversely impact well-being (McCance, 2004). Stressors come in a variety of forms including environmental (heat, cold, radiation), chemical (pesticides, pollutants, free radicals and other waste products of metabolism), biological (bacteria and viruses) and /or psychological (a major life event such as divorce or death or a loved one, job loss, etc., socioeconomic status (Spelman, 2004) (Brown and Gerard, 2004). Many studies show clearly that negative stressors produce biological changes in almost all systems of the body, and a complex chain of biological and psychological processes are involved (Syvalahti, 1987).

If the brain perceives any stimuli as a cause for alarm, the stress response system is activated (McCance, 2004), including activation of the sympathetic branch of the autonomic nervous system and the Hypothalamus-Pituitary-Adrenal axis (HPAA) (McCance, 2004). The HPAA refers to our neuroendocrine system, which is one of our major auto-regulatory systems and consists of seven small glands. The HPAA is able to sense what is going on within and around us and then prioritize how our limited energy should be directed. (Yance, 2005) (McCance, 2004) The neuroendocrine network is a very complex, integrated system, replete with feedback control mechanisms, and an overriding control of the whole system by internal biological rhythms or external events impacting the hypothalamus (Syvalahti, 1987).

The balance of the HPAA is critical to optimum health. Over time, if an organism is under prolonged stress conditions, hormone balance is shifted towards a catabolic process of constantly shifting to release more stress hormones in order to attempt to adapt to the stressful situation. (Yance, 2005). Profound changes may occur in the secretory patterns of hormones (Syvalahti, 1987). This shifting of hormones is detrimental to health as it causes more oxidative damage and lowers the levels of anabolic hormones needed for building up. As a result, the whole endocrine system is thrown out of balance (including the thyroid, pancreas, reproductive, thymus, etc.). Anabolic metabolism determines muscle mass, influences immunity, protein synthesis, cell proliferation, bioenergetics, cell communication, endocrine function, and of course mind, mood and behavior. (Yance, 2005)

While the sympathetic nervous system is upregulated, the parasympathetic nervous system is downregulated, thus allowing all energies to be diverted to the need to 'fight or flight'. The body is amazingly prepared to deal with such emergency situations so that when there is an acute danger, all body systems rally and coordinate to protect vital processes and systems. Once the threat or perceived threat is gone, then under normal conditions, the body returns to a balanced state, whereby the maintenance of homeostasis or stability through change is maintained. This maintenance of stability through change is called allostasis (McEwen, 1999).

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The problem occurs when the body is in a constant state of hyperarousal, which occurs frequently in our modern day society. The body is not equipped to deal with being constantly in the fight or flight mode, and after chronic hyperarousal, systems start breaking down, as being chronically aroused comes at a metabolic expense and uses critical organ reserve (Spelman, 2004). When the body is constantly trying to fight the tiger because it is constantly stressed, be it real or perceived, then what energy is normally reserved to keep the set points in a set range and in homeostasis or allostasis, is now being sacrificed to fight the enemy. There is a wear and tear exacted on the body, also called allostatic load, as the body is constantly trying to achieve allostasis (McEwen, 1999). An example of this is when the body is constantly secreting high levels of cortisol and catecholamines, and becomes less efficient in turning on or shutting off these stress responses (McEwen, 1999). The HPA system becomes dysregulated, resulting in a constant secretion of cortisol (Spelman, 2004) and other hormones/neurotransmitters. Organ reserve is being depleted. Organ reserve includes protein synthesis, blood flow, and mitochondria. Loss of organ reserve includes a loss of enzyme activity (due to loss of enzyme protein) as well as loss of activity of the respiratory chain that occurs during aging (Spelman, 2004). The loss of the respiratory chain may be responsible for the loss of skeletal and heart muscle that occurs often during aging (Spelman, 2004). Deletions of the mitochondrial genome have been found in the aged human tissue in the skeleton, myocardium, brain, external eye muscles, liver and more (Spelman, 2004). Often the enemy is a function of our own decisions on lifestyle, nutrition, reaction to life, etc.

The sharper, keener problem-solving skills that occur in acute stress actually dull during Selye's exhaustion stage mentioned above. Prolonged stress also often results in depression and anxiety; sleep disorders, dysrhythmia, chronic headaches, backaches, maladaptive coping behavior (i.e. overworking, hyperactivity, overeating) and hypertension to name a few (Spelman, 2004).

The short-term effects of glucocorticoid hormones include inhibition of sexual motivation, regulation of the immune system, increased gluconeogenesis, and increased foraging behavior. Long-term adaptation results in inhibition of reproduction, suppression of the immune system, promotion of protein loss, and suppression of growth (Spelman, 2004).

Adaptogens Defined

Brekhman and Dardymov studied adaptogenic plants and further defined the term adaptogen as follows:

1. An adaptogen must be innocuous, and cause minimal disorders in the physiological functions of an organism (Brekhman et al, 1968). It must not influence normal body functions more than required (Wagner et al, 1994).
2. The action of an adaptogen should be nonspecific, i.e. it should increase resistance to adverse influences of a wide range of physical, chemical and biological factors (Brekhman et al, 1968).



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3. An adaptogen may possess normalizing action independent of the nature or direction of the pathologic changes or state (Brekhman et al, 1968) (Wagner et al, 1994). If a body parameter is high, the adaptogen brings the parameter towards normal; if it is low, the adaptogen tends to bring it up towards normal (Brown et al, 2002).

Adaptogens tend to reinforce the non-specific power of resistance against stressors, increase overall capacity to manage situations of stress, and protect against disease caused by overstress (Wagner et al, 1994). In their studies of adaptogenic plants, Brekhman and Dardymov found that *Rhodiola rosea*, along with *P. Ginseng*, *Eleutherococcus senticosus* and *Raponticum carthamoides* contributed to a more sparing use of carbohydrates and to increased resynthesis of glycogen and high-energy phosphorus compounds (Brekhman et al, 1968). This action was apparent during physical strain. The results also showed an anabolic action as shown with increases of body weight, restoration of blood albumin after massive bleeding, and on immune system enhancement.

One of the more important actions of adaptogens noted by Brekhman was the capacity of adaptogens, including *Rhodiola rosea*, to increase efficiency both after a single (stimulant action) or prolonged (tonic action) administration. The difference between the stimulant actions of the plant preparations used and Bazedrine-like compounds was that the plants had low toxicity and no pronounced excitant action. The plants also didn't lead to sleep problems, either falling asleep or waking in the middle of the night. (Brekhman et al, 1968) In more recent research, after a single dose, *Rhodiola rosea* was found to be more active than the adaptogens *Schizandra chinensis* and *Eleutherococcus senticosus*, producing within 30 minutes of intake a stimulating effect that continued for 4-6 hours (Panossian and Wagner, 2005).



In 1978, Roger Porsolt and other Russian scientists developed a forced swimming test to measure nonspecific resistance to stress. The Porsolt test involved a mouse or rat being forced to swim to exhaustion (approximately 15 minutes). The rodent would initially frantically try to stay afloat, and after this initial period, would adopt a characteristic immobile posture (one I've seen often in humans!), making only the most minimal movements to stay alive and above water. Refer to the picture of the rat for this characteristic posture of immobility after 10 minutes immersion in water (Porsolt et al, 1978) This test initially became a screening test for antidepressants by pharmaceutical companies (Brown et al, 2002).

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Adaptogens and antidepressants have been found to increase the duration of time that rats are able to keep swimming actively (Brekhman et al, 1968) (Brown et al, 2002). Brekhman found that in stress, adaptogens may actually increase nonspecific resistance rather than lessen it. They did an experiment where two groups of rats were made to swim in water. Eleutherococcus (0.2 ml/g) was injected intraperitoneally into one half of the rats. After five hours half of the rats were killed, and a comparison of the adrenals was made. In comparing the adrenals of rats that were not made to swim, a five-hour swimming caused marked hypertrophy of the adrenals in the controls, which was almost completely prevented with the Eleutherococcus treated group. There was a clear anti-alarm action seen with the Eleutherococcus extract, and increased resistance, as the treated rats were able to swim 52 minutes longer (9.2%) until complete fatigue (death). (Brekhman et al, 1968)

Brekhman also observed a number of effects of these plant adaptogens on the cell. Many of the effects noted were anabolic (influencing the processes of biosynthesis of protein and nucleic acids, including stimulating the production of immune bodies) and protective. Many of the plants studied showed antioxidant action, including *Rhodiola rosea*. (Brekhman et al, 1968)

Adaptogens and the Stress Response

As elucidated earlier, through various studies of plant adaptogens, Brekhman showed that adaptogens have the ability to regulate the stress response in a variety of ways. Adaptogens are considered a new class of natural, metabolic regulators which have been shown through repeated studies to increase the ability of an organism to adapt to and avoid damage from environmental stressors (Panossian et al, 1999). The adaptogenic effect is seen to increase the basal level of dynamic equilibrium (homeostasis) (Panossian et al, 1999) or allostasis (McEwen & Seeman, 1999) of switch on and off systems, including activators NO, PAF, and catecholamines and such inhibitors as cortisol and PGE₂ (Panossian et al, 1999). Adaptogens affect many regulatory systems in the organs and tissues, such as the immune, hormonal, Central Nervous System, cardiovascular, and muscular systems (Brown et al, 2002). Adaptogens alter the systems' reactivity to stress, i.e. the defense system, including the HPA axis and the Sympatho-adrenal system (SAS) (Brown et al, 2002) (Panossian et al, 1999). In this way, adaptogens may reduce the damage from stressors, including the HPA axis and the SAS (Panossian et al, 1999).

The End.

Rhodiola Rosea