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### **PHYTO-ADAPTOGEN**

#### ***Rhodiola imbricata* Edgew. syn. *R. rosea* Linn.**

**Author(s):- *Dr. Brahma Singh,***

#### **Abstract**

Rose root, *Rhodiola imbricata* syn. *R. rosea* Linn. is being used by Amchis (Traditional Medical Practitioners of Ladakh) for treatment of high altitude sicknesses since ancient times. Phytochemistry of the root revealed the presence of phenylpropanoids, phenylethanol derivatives, flavanoids, monoterpenes, triterpenes, and phenolic acids. Root extracts have been found to favourably affect a number of physiological functions; its constituents rosavins and salidroside, occurring in the ratio of 3:1 have been reported to exhibit adaptogenic properties. An extensive study on this plant by Defence Research Development Organization, Delhi, India for development of an effective adaptogen has been reviewed.

#### **Introduction**

Phyto-adaptogen or adaptogen (earlier called *rasayana* or rejuvenating product) is a commonly used term by scientists, physiologists, wellness experts and herbalists to refer to a natural herb product which is potent to resist against or recover from physical, chemical, biological and environmental stress, fatigue, trauma or anxiety. In India and China this concept of adaptogens dates back thousands of years but scientific evaluation and confirmation of their potentials started in the latter half of the twentieth century. Adaptogens are non-toxic in normal doses and have defensive or normalizing influence on the body against stress. Important adaptogenic plants identified in Ayurveda or time tested traditional medicines, are: *Codonopsis pilosula* (dang shen), *Eleutherococcus senticosus* (eleuthero), *Glycyrrhiza glabra* (licorice), *Gynostemma pentaphyllum* (jagulan), *Lepidium meyenii* (maca), *Ocimum sanctum* (holy basil), *Panax ginseng* (ginseng), *Rhodiola imbricata* (rose root), *Schisandra chinensis* (Schisandra), *Tinospora cordifolia* (guduchi) and *Withania somnifera* (aswagandha). There are several other less known phyto-adaptogens. Scientific studies have now validated that the above herbs are capable of balancing endocrine hormones, immune system, maintaining homeostasis and preventing hypo and hyper functioning of human systems under stress.

**Rhodiola imbricata** Edgew. syn. *R. rosea*, *R. scopolii*, *Sedum imbricatum* (Family *Crassulaceae* ; sub-Family *Sedoideae*); ROSE ROOT, GOLDEN ROOT, ARCTIC ROOT, STONE PLANT, AARON ROD.

A large genus of nearly 200 species; its current taxonomical status needs attention so as to facilitate availability of uniform quality of *Rhodiola* and its products. *Rhodiola* is widely found in nature at very high altitudes, dry regions of arctic areas in Asia and Europe. Most commonly used and highly experimented species is *R. imbricata*. Twenty more species of *Rhodiola* have been used in traditional and modern medicine sparingly.



*Rhodiola imbricata* Edgew.

The plant is a perennial, 30cm in height, grows even at an altitude of 16,000ft. It has underground rhizome with several thick cylindrical golden color roots (a reservoir of adaptogens), which possess rose like fragrance. Leaves are thick, flowers mostly yellow, dioecious. In India, pioneering research and development at DIHAR (Defence Institute of High Altitude<sup>1</sup>Research, DRDO) led to an extensive investigation of this plant as adaptogen. *R. imbricata* was found growing wild in Ladakh region. Other species identified in this region were *R. tibetica*, *R. heterodonta*, *R. crenulata*.

**Traditional Uses:** India and China used this plant in several preparations to combat mountain sickness and as general health booster (aphrodisiac) covering number of reproductive disorders and debilities. Siberians have used the plant to increase physical endurance, work productivity, longevity, resistance to high altitude sickness and to treat fatigue, depression, anemia, impotence, gastrointestinal ailments, infections, nervous system disorders, cold flu, tuberculosis, cancer, hernia, leucorrhoea, hysteria, amenorrhoea, asthenia, insomnia, schizophrenia, sexual dysfunctions specially in males, headache, scurvy, haemorrhoids and inflammations. The plant survives in extreme cold, intense radiation, wind, drought and reduced oxygen level and pressure which perhaps makes it potential for its exceptional healing power. This traditional knowledge led to examine it for its chemicals and their use as medicine in several countries.

**Phytochemistry:** In 2002, Brown, Gerbarg and Ramazanov published a comprehensive phyto-medicinal overview on the species which revealed the presence of about 28 compounds classified into the following six distinct groups (Saratikov and Krasnov, 1987; Kurkin and Zapesochnaya, 1985):

Phenylpropanoids: rosavin, rosin, rosarin (specific to *R. rosea*);

Phenylethanol derivatives: salidroside (rhodioloside), tyrosol;

Flavanoids: rodiolin, rodionin, rodiosin, acetylrodalgin, triclin;

Monoterpenes: rosiridol, rosaridin;

Triterpenes: daucosterol, beta-sitosterol;

Phenolic acids: chlorogenic, hydroxycinnamic, and gallic acids.

Rhizomes from Norway contained 0.05% essential oil with monoterpene hydrocarbons (25.4%), monoterpene alcohols (23.61%),

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\* Author served as Director of the organization at Leh during 1991-1995 and remained actively associated with the plant till 2001

straight chain aliphatic alcohols (37.54%), *n*-Decanol (30.38%), geraniol (12.49%), and 1,4-*p*-menthadien-7-ol (5.10%) as the most abundant volatiles.

Geraniol has been identified as the most important rose like odorous compound besides geranyl formate, geranyl acetate, benzyl alcohol and phenylethyl alcohol. A large number of antioxidant compounds have been identified including *p*-tyrosol, organic acids (gallic acid, caffeic acid and chlorogenic acid) and flavonoids (catechins and pro-anthocyanidins) of which Rosavin, rosin and rosarin glycosides are specific to *R. rosea* (= *R. imbricata*).

**Adaptogenic, Aphrodisiac and Associated Properties:** In 1968 Soviet pharmacologists Brekhman and Dardymov surveyed the literature on several medicinal plants and identified five (including rose root) that met the three following defining criteria for an adaptogen.

1. An adaptogen should be innocuous and cause minimal disturbance of the normal physiological functions of an organism;
2. The action of an adaptogen should be nonspecific (i.e., it should increase resistance to adverse influences of a wide range of harmful factors of physical, chemical, and biological nature);
3. An adaptogen may possess normalizing action irrespective of the direction of the preceding pathological changes (i.e., if a body parameter is high, the adaptogen brings it down towards normal; if a parameter is low, the adaptogen brings it up towards normal).

Brown *et al* (2002) explained in their overview particularly the nonspecific resistance imparted by rose root in adaptation of human beings and other biological entities under stress conditions. Neuroendocrine animal studies showed that the plant, like other adaptogens, enhanced thyroid function without causing hyperthyroidism. In addition, the thymus gland functioned better and was protected from the involution that occurs with aging. The adrenal glands functioned with better reserve and without the kind of hypertrophy caused by other psychostimulants. In a study in Russia, forty women suffering from amenorrhea were given rose root extract (either 100 mg extract orally twice a day for 2 weeks, or 1 ml rhodosin intramuscularly for 10 days). In some subjects the

treatment cycle was repeated 2-4 times. Normal menses were restored in 25 women, 11 of whom became pregnant. In those with normal menses, the mean length of the uterine cavity increased from 5.5 cm to 7.0 cm (normal) after the treatment (Saratikov and Krasnov, 1987).

Brown in 2002 reported that he treated with rose root several women (who had failed to conceive with standard fertility drugs); they became pregnant within months of treatment. *R. imbricata* syn. *R. rosea* extract showed strong estrogen binding properties (Brown *et al*, 2002).

In an open study, 26 out of 35 men with erectile dysfunction and/or premature ejaculation (of 1-20 years duration) responded to rose root (150-200 mg/day for 3 months) with substantially improved sexual function, normalization of prostatic fluid, and an increase in 17-ketosteroids in urine (Saratikov and Krasnov, 1987).

Kelly (2001) was of the view that *Rhodiola* supplementation helps in amenorrhea, asthenia, cancer, colds and flu, depression, fatigue, headaches, hypertension, insomnia, schizophrenia, sexual dysfunction (male) and helps in adaptation.

Spasov *et al* (2000) investigated the effects of SHR-5 (standardized extract of *R. rosea*) on male medical students during an examination period. Forty students were randomized to receive either 50 mg SHR-5 or placebo twice daily for a period of 20 days. The students receiving SHR-5 demonstrated significant improvements in physical fitness, psychomotor function, mental performance, and general wellbeing and a greater motivation to study and statistically significant reduction in mental fatigue, need for sleep, etc.

Ramazanov (2002) summarizes the adaptogenic benefits of *Rhodiola rosea*, verified in the human and animal trials (mostly Russian), as:

Improves memory and mental performance, and has anti-fatigue, anti-stress and antidepressant properties;

Improves physical performance, reducing exhaustion and accelerating recovery after heavy training workloads, and increases muscle energy production, protein synthesis and anabolic activity;

Improves erectile dysfunction and /or premature ejaculation in men;

Activates lipolytic (fat breakdown) processes and mobilizes fat from adipose tissue;

Reduces or prevents stress-induced heart damage.

Reduces liver toxicity from various anticancer drugs while enhancing their anticancer action;

Enhances thyroid function without causing hyperthyroidism, protects the thymus gland from the shrinkage that comes with stress and aging, and increases adrenal gland reserve without causing adrenal gland reserve without causing adrenal hypertrophy;

Has antioxidant effects, reducing lipid peroxidation and preventing intestinal damage after acute x-ray exposure; and is incredibly safe; with an estimated LD50 (lethal dose for 50 percent of test animals) for humans of 235 gm for a 154-pound person.

Soviet/Russian sports professionals have used *R. rosea* for decades with excellent results. Russian research shows that the plant increases muscle anabolic activity, stimulates production of ATP (adenosine triphosphate, the key energy source in the body) and creatine phosphate (energy reserve) and prolongs stamina during periods of intense physical stress. *R. rosea* also reduces cardiovascular recovery time, even after strenuous muscular / physical workouts.

Recent studies in life science laboratories of DRDO have also confirmed adaptogenic potential of golden root. Mishra *et al* (2006 & 2007) demonstrated immunomodulatory potentials of aqueous rhizome extract of *R.imbricata* of Ladakh region.. Mishra *et al* (2006) investigated the effect of aqueous extract of *R. imbricata* rhizome (RAE), on Toll-like receptor-4 (TLR-4) and intracellular granzyme-B expression in mouse splenocytes. Furthermore, TH1/TH2 cytokine profile was analyzed in RAE-treated human peripheral blood mononuclear cells (PBMCs) using multiplex flow cytometry kit. The findings suggest that RAE induces TLR-4 expression and intracellular granzyme-B in treated splenocytes while RAE stimulated IL-1 $\beta$ , IL-6, and TNF- $\alpha$  in human PBMCs. Another study suggests that RAE stimulates the innate immune pathway and has potent immunostimulatory activity, which can be used in modulating the immune system of immunocompromised individuals.

To examine the dose dependent adaptogenic activity, aqueous extract of *R.imbricata* root was orally administered in rats at different doses, 30 min prior to cold (5°C)–hypoxia (428 mm Hg)–restraint (C–H–R) exposure. These results suggest that aqueous extract of *R. imbricata* root possesses potent adaptogenic property with no acute and sub-acute toxicity. The mechanism of action was studied in rats. The results suggest that *Rhodiola* extract treatment in rats shifted anaerobic metabolism to aerobic, during C-H-R exposure and post stress recovery (Gupta *et al*, 2009).

**Cardioprotective property:** Golden root has been shown to moderate against stress-induced damage and dysfunction in cardiovascular tissue. Treatment with *R.rosea* extract prevents the decrease in cardiac contractile force secondary to environmental stress in the form of acute cooling and contributes to stable contractility. In animals, acute cooling leads to a decrease in myocardial contractile activity that partially recovers during the first 18 hours after the cold-stress is removed. This recovery is viewed as only partial, since the heart tissue is incapable of stable contractility during perfusion. Pretreatment with *R. rosea* extracts appears to create a beneficial adaptive response in this type of stress. When pretreated rats were exposed to acute cooling, the decrease in contractility was prevented and stable contractility of heart tissue occurred during perfusion (Kelly, 2001).

Other reports suggest that administration of *R. rosea* protects cardiovascular tissue from stress-induced catecholamine release and mitigates against adrenaline-induced arrhythmias in rats. The antiarrhythmic effect is suggested to be secondary to an ability to induce opioid peptide biosynthesis and related to the stimulation of peripheral kappa-opioid receptors (Kelly, 2001).

**Wound healing, anticancer, radioprotection, antioxidant properties:** In a study, *R imbricata* rhizome ethanol extract (rich in polyphenols) was used in rat excision wound models; treated wounds healed much faster as indicated by the improved rate of wound contraction and decreased time taken for epithelialization. (Gupta *et al*, 2007). The anti-proliferative effects of *Rhodiola* aqueous extract (RAE) were studied in human erythroleukemic cell line K-562 using MTT cell proliferation assay. The proliferation of K-562 was significantly decreased after 72 h incubation with RAE at 100 and 200  $\mu$ g/ml. However, almost no suppressive effects could be detected in normal human peripheral blood lymphocytes or mouse macrophage cell line RAW-264.7. RAE was also found to induce intracellular reactive oxygen species (ROS) in K-562 cells at 200  $\mu$ g/ml, when incubated overnight. The increased ROS generation may cause apoptosis, which was observed in AnnexinV-FITC and propidium iodide (PI) staining of treated cells. RAE arrested cell cycle progression in G2/M phase in early and late period of exposure. The anti-cancer activity of RAE was

also confirmed by increased NK cell cytotoxicity. These observations suggest that aqueous extract of *R. imbricata* rhizome has very potent anti-cancer activities, which might be useful in leukemia cancer treatment (Mishra, 2007). Arora *et al* (2005) reported that *R. imbricata* renders *in vitro* and *in vivo* radioprotection via multiple mechanisms that act in synergistic manner.

Gupta *et al* (2009) reported that aqueous extract of roots of *R. imbricata* is a potent source of natural antioxidants and is a free radical scavenger.

**Utilization:** Proper *R. rosea* (= *R. imbricata*) extract is made only from the roots, and as stated earlier, is standardized to contain at least 0.8 per cent salidroside and 3 per cent rosavins.

Typical dosages used in human studies have ranged from 50 to 250 mg taken two or occasionally three times daily. *R. imbricata* should always be taken as advised by competent medical practitioners only. It is best taken 30 minutes before breakfast and lunch, with a third dose before an afternoon workout if necessary. It is best not to take it after dinner or in the evening, as it can be stimulating and may cause insomnia. Those suffering from mania or bipolar disorder should not take it without medical supervision. It may potentiate the action of stimulants, so should not be taken with them. Extremely sensitive individuals may need to reduce the dosage to as low as 50 mg twice daily, and work up slowly to higher doses.

### **Rose root Products**

DIHAR has come up with chavanpras, herbal tea and beverage containing *Rodiola imbricata* root extracts. Efforts are on to develop *Rhodiola* based adaptogen.

### **Conclusion**

*Rhodiola imbricata* grows wild in abundance in India. In the course of evolution it has adapted to the harsh conditions of cold and arid high altitudes by producing protective phyto-molecules that are useful in human and animal adaptation and helping in meeting prevalent common challenges there. It needs to be cultivated by developing appropriate agro-technologies in remote high altitudes of Indian Himalayas or elsewhere in the world. Its adaptogenic potentials have been amply demonstrated in animal and human model. Several *Rhodiola* preparations are available in different countries. There is need to isolate gene(s) from this plant which help in adaptation for use in human wellness or bio-molecule(s) which can be synthesized for use by the masses. *In vitro* production of t and its useful molecules needs to be attempted to develop cheaper and effective adaptogens and drugs.

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