



ISSN (E): 2320-3862
ISSN (P): 2394-0530
NAAS Rating: 3.53
JMPS 2019; 7(4): 278-281
© 2019 JMPS
Received: 21-05-2019
Accepted: 22-06-2019

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A review on *Rhodiola rosea* L.: An herb with Anti-stress, anti-oxidant and anti-carcinogenic properties

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Abstract

Rhodiola rosea L. is also called Golden root, Arctic root or Rose root. Its roots are act as adaptogens to help our body adapt to resist physical, chemical and environmental stress. *Rhodiola rosea* are rich in polyphenols, salidroside, tyrosol and other primary bioactive compounds. This review gives the information about the bioactivities it includes in anti-depressant, Anti-oxidant, Antifatigue, Adaptogenic, anticancer activities and its current and future medical applications.

Keywords: Rhodiola, salidroside, bioactive compounds

1. Introduction

Rhodiola rosea L. has more than 200 species. Among 55 species found in China and 30 species found in Tibet. 20 species found in high altitudes (up to 2280 m) Himalayan belt, Europe and North America. *Rhodiola rosea* L. belongs to the plant family is Crassulaceae (Engler A., 1964) [1]. It includes the pharmacological effects to raise their longevity, stimulate their central nervous system that' why it is called "Brain tonic" and it also increase their other activities such as cardiovascular activities, lung disorders, neurogenerative activities, hepatoprotective effects and immunotropic effects. This herb also works on fatigueness, to enhance work performance, prevent high altitude sickness, mountain malhypoxia and anoxia (Petkov VD *et al.*, 1986) [2].

In recent time, *Rhodiola rosea* L. root extracts used in drinks and pharmaceutical preparations. *Rhodiola rosea* L. is not suitable for children. In Adults its dosage ranged from 50-170 mg twice daily for two weeks (Darbinyan V *et al.* 2000) [3]. In various locations in Asia it is used in treatment of cold and flu during winter season. In Mongol it is prescribed in tuberculosis and cancer (Khaidiev Z *et al.*, 1978) [4]. Linnaeus also wrote about *R. rosea* is astringent for the treatment of hernia and leucorrhoea, hysteria and in headache (Linnaeus C., 1749, 1748) [5, 6]. The root extract of *R. rosea* gives the new medicines to treat the cancer, radiation sickness led to the discovery of Flavanoides, Monoterpenes, Triperpenes and various phenolic acids are used.

2. Active components of *Rhodiola rosea* L.

Rhodiola rosea L. has 140 compounds are isolated from its roots and rhizomes. It has glycosides, cyanogenicglycosides, arylglycosides, phenylpropanoids, phenylethanoids, flavonoids, flavonolignans, proanthocyanidins and gallic acid derivatives. The medicinal properties of *Rhodiola rosea* L. have unique pharmacological activities (Panossian A *et al.* 2010; Ali Z *et al.* 2008; Mao Y *et al.*, 2007) [8, 9]. There are eight reference markers are isolated from the *Rhodiola rosea* L. that discriminate from other *Rhodiola rosea* L. species from other plants. These eight compounds are rosarin, rosavin, rosin, salidroside, tyrosol, rhodionin, catechin and gallic acid is present (Grech-Baran M *et al.* 2015) [10].

Salidroside was first isolated from *Salix triandra* L. but it is first detected from *Rhododendron* (Bridel M *et al.*, 1926; Thieme H *et al.*, 1969) [11, 12]. Salidroside has p-hydroxyphenethyl- β -D-glucoside is main active ingredient in *Rhodiola rosea* L. It has many pharmacological properties such as anti-aging, anti- fatigue, antioxidant, antiviral, anti-inflammatory effect and it has neuroprotective and cardiovascular protective effects (Xu MC *et al.*, 2013; Wu T, Zhou H *et al.*, 2009) [13, 14]. Salidroside also used to inhibit the cell proliferation, induce cell apoptosis in lung bladder cancer, Neuroblastoma, Glioma and in human breast cancer cells (Hu X, Zhang X *et al.*, 2010) [15].

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3. Pharmacological and Clinical Studies

The notable research investigate the pharmacological and clinical properties of *R. rosea*. The extensive research is used to identify of *R. rosea* as an adaptogen- a substance that increases the resistance of an organism. Several activities studies in cell cultures, Humans has various adaptogenic effects, anti-mutagenic, anti-arrhythmic, anti-tumour, cardioprotective properties has clinical studies. The chemical composition is responsible for the pharmacological activities of *R. rosea* root, tyrosol, salidroside and cinnamyl, glycoside constituents are important activities (Saratikov SA *et al.*, 1968; Tolonen A *et al.*, 2003; Sokolov S *et al.*, 1985) [16, 17, 18].

a) Adaptogenic Properties

R. rosea help in erythropoiesis and granulocytopenia. In paradoxical sleep deprivation, it leads to the behavioural disorders and changed in haematopoiesis. It also suppress of bone marrow erythropoiesis and activation of granulocytopenia (Provalova NV *et al.*, 2002) [19].

The effects against various stress conditions of *R. rosea* such as (SHR-5; containing rosavin 3.6%, Salidroside 1.6% and p-tyrosol < 0.1%) against other stressors such as menadione, copper and cadmium (Boon-Niermeijer EK *et al.* 2000) [20].

b) Effects upon Central Nervous System

The pharmacological effects of *R. rosea* act as tranquilizers, to enhance the development of avoidance reflexes based on positive amputation (Darbinyan V, *et al.* 2000; Petkov VD *et al.*, 1990; Baranov VB *et al.*, 1994; Komar VV *et al.*, 1981; Stancheva SL *et al.*, 1987; Lazarova MB., *et al.*, 1986) [21, 22, 23, 24, 25, 26]. *R. rosea* stimulated norepinephrine, dopamine, Serotonin and nicotinic cholinergic effects in Central Nervous System. *R. rosea* help in meclizolam, piracetam, citicholine and nootropics to increase the cognition to protect the brain and low toxicity effects. It helps to increase the Serotonin level in frontal cerebral cortex (Petkov VD *et al.*, 1986; Saratikov A *et al.*, 1987; Marina TF *et al.*, 1968) [2, 32]. *R. rosea* release norepinephrine, Serotonin and dopamine activate the cerebral cortex and limbic system (Saratikov AS *et al.*, 1987; Mariana TF *et al.*, 1968). The cognitive functions such as thinking, analyzing, evaluating, calculating and planning functions of cerebral cortex contribute various facets of memory such as encoding, sorting, storage and retrieval. *R. rosea* protects the nervous system from oxidation damage by free radicals. It also exerts positive effects on memory and cognitive stimulation and creates the benefits for both immediate memory performances.

c) Cardioprotective Properties

R. rosea include the prevention of stress- induced cardiac damage, decreased myocardial catecholamines and cyclic adenosine monophosphate i.e. called cAMP level and reduce the level of adrenal catecholamine level (Lishmanov luB *et al.*, 1987; Maslova LV *et al.*, 1994; Maimeskulova LA *et al.*, 1997) [29, 30, 31]. In Adaptogen formula there is the mixture of mono and polyphenolic adaptogen (MMPA). It contains 3mg rhodiolside, 50 mg; 3mg of isofraxidine-syringine and syringaresinoin-glycosides from eleuthero root extract. It helps in both sympathetic and parasympathetic inputs to heart. The autonomous nervous system controls the function of the body. This system follows the fight or flight system to help the organism respond to stress such as increase heart rate, respiratory rate and muscle tone. The parasympathetic nervous system stores the energy such as slowing the heart rate, respiratory rate and metabolism.

d) Endocrine and Reproductive Properties

R. rosea adaptogen increase the thyroid function without causing hyperthyroidism (Maslova LV *et al.*, 1994) [30]. The thymus gland protects the involution the adrenal gland without causing hypertrophy.

R. rosea helps in women amenorrhea that is called loss of menstrual cycle on women with the help of increase the uterine cavity from 5.5cm to 7.0 cm. *R. rosea* help to strong estrogen binding properties to cure amenorrhea in females.

e) Effects on Physical Work Capacity

R. rosea increase the physical work capacity in short time. *R. rosea* increased shooting accuracy, less arm tremor, improved recovery time, strength, endurance, cardiovascular measures and coordination (Saratikov AS *et al.*, 1987) [32]. Adaptogen help to increase the work capacity and use of Central Nervous System depletes brain catecholamines and decrease the conditioned reflexes. It increase the work capacity by a lesser diminution (Panossian A *et al.*, 1999) [33].

R. rosea also increases the energy metabolites, adenosine triphosphate (ATP), creatine phosphate in the muscle and brain mitochondria (Salnik BU *et al.*, 1970) [34]. It also increase the ammonia reassimilation and energy metabolism of the cell to increase the ATP, ribonucleic acid, protein and amino acid synthesis (Adamchuk LB., 1969) [35]. It improves the energy metabolism in the brain (Revina TA., 1969) [36].

f) Antioxidant Properties

R. rosea is rich in phenolic compounds to have strong antioxidant properties (Furmanova M *et al.*, 1998; Bolshakova IV *et al.*, 1997) [37, 38]. It showed singlet oxygen scavenging, Hydrogen peroxides scavenging, Hypochlorite scavenging, Ferric reducing, Ferrous chelating and protein thiol protection activities (Chen TS *et al.* 2008) [39].

R. rosea reduced glutathione levels, glyceraldehyde -3-phosphate dehydrogenase activity and thiobarbituric acid level in human keratinocyte exposed to various oxidative radicals such as Fe²⁺/ascorbate/H₂O₂, and tert-butylhydroperoxide level (Calcabrini C *et al.*, 2010) [40]. *R. rosea* increased the activity of antioxidant enzymes such as catalase, SOD, glutathione peroxidase and glutathione reductase. *R. rosea* increase in time and dose-dependent manner of plasma membrane oxidoreductase to the intracellular redox status in keratinocytes. *R. rosea* extract and salidroside protects the human cortical neurons from oxidative stress and prevents the glutamate- induced cell apoptosis in human cortical cell line (Palumbo DR *et al.*, 2012) [41]. *R. rosea* aglycone, tyrosol has various biological properties such as cancer preventive and anti-inflammatory properties and prevent oxidative-stress-related disorders (Tuck KL *et al.*, 2002; Ko RK *et al.*, 2011) [42, 43].

g) Anticancerous Properties

Rhodiola rosea L. inhibited the growth of transplanted solid Ehrlich adenocarcinoma and Pliss lymphosarcoma, decreased the level of metastases to the liver (Skopinska-Rozewska E., 2008) [44]. *R. rosea* extracts with antitumor agent such as cyclophosphamide to increase the anti-tumor and anti-metastatic efficacy of drug treatment and reduced drug-induced toxicity (Udintsev SN *et al.*, 1991) [45].

R. rosea inhibits cell proliferation and induced cell apoptosis in various cell lines such as human urinary bladder cancer cell line (Liu Z *et al.* 2012) [46], Breast cell lines (Zhao G *et al.* 2015) [47], Colorectal cancer cells (Fan XJ *et al.*, 2016) [48], Gastric cancer cells (Huo J *et al.*, 2013) [49], Glioma cells

(Zhang Y *et al.*, 2013) ^[50], Lung cancer cells (Wang J *et al.*, 2014) ^[51] and Sarcoma (Sun C., 2011). Estrogen receptor negative breast cancer cell line MDA-MB-231 and lung cancer cell line A59 is more sensitive to the cytotoxic effects of salidroside (Hu X *et al.*, 2010) ^[15]. *R. rosea* and salidroside induced the autophagy in bladder, gastric and colorectal cancer cell line (Liu Z *et al.* 2012; Fan XJ *et al.*, 2016; Huo J *et al.*, 2013) ^[46, 48, 49]. *R. rosea* extracts such as Salidroside and Rosavin determine the factor for its anti-cancerous activities.

4) *Rhodiola* in the future

The scientific research is confirmed the preventive and curative benefits of *R. rosea*. *R. rosea* is explored the use in antidepressant, augmentation, memory disorders and cognition, attention deficit disorder, traumatic brain injury, Parkinson's disease, It also protects against arrhythmias, sports performance, aviation and use in space medicine to use in physical and mental performance and reducing stress reactions, endocrine disorders such as infertility, premenstrual disorder, menopause and sexual dysfunction disorders. *R. rosea* also helps in stress response system such as fibromyalgia, chronic fatigue syndrome and post-traumatic stress disorder. It also enhances the chemotherapy/radiation therapy in cancer treatment.

R. rosea are found in harsh conditions in high altitude in cold temperature, low oxygen, little rainfall and intense irradiation from the sun producing the powerful compounds which has beneficial effects in humans. *R. rosea* develops the potential medical applications with their various phytoadaptogens. *Rhodiola rosea* may be expected that the novel therapeutic approach for chronic illness and the therapies are beneficial such as a low risk of side effects, wider availability and lower cost.

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