Rapid Literature Review on Effect of Rhodiola Rosea on physical and mental stress under fatigue

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***Abstract*—Rhodiola rosea is an adaptogen, which is also known as rose root, golden root, or arctic root. It can enhance mental and physical performance under stress and has been traditionally used. Objective: To assess the clinical efficacy of Rhodiola rosea to treat physical and mental fatigue in individuals with stress. Methods: A rapid literature review is conducted on studies to evaluate the effect of Rhodiola rosea on physical and mental stress. Outcomes such as mental performance, fatigue scores, and stress biomarkers are considered. The sample size of a population ranges from as low as 15 participants to 118. Rhodiola rosea doses can range from 100 mg/day to 600 mg/day. Results can be validated by checking a significant improvement in physical and mental performance, and a validated questionnaire. Expected outcome: This literature review showed consistent evidence that supports the efficacy of Rhodiola Rosea in reducing physical and mental stress. It is traditionally used and well-tolerated. it is expected to have no serious side effects. So it can be considered a safe treatment for stress**

1.INTRODUCTION

Rhodiola rosea, or golden root or roseroot, is a medicinal plant belonging to the Crassulaceae family. It grows naturally in high altitudes in dry sandy soil in Arctic regions of Europe and Asia, and coastal regions of North America. The rootstock of the plant is medically used. In the past, Rhodiola rosea has been widely used in traditional systems of medicine to increase physical endurance, mental clarity, and resistance to stress and fatigue. During the past decades, it has gained widespread popularity in modern herbal medicine as an herbal remedy for burnout, lack of focus, and emotional exhaustion. In 2011, Rhodiola rosea was approved as an adaptogen by the European Medicines Agency (EMA) based on its long-term use and numerous scientific studies. An adaptogen is a type of natural substance that helps the body adapt to any type of stress. To be considered an adaptogen, a compound must be non-toxic, help the body increase its resistance to a variety of stressors, and normalize physiological processes. This rapid literature review aims to assess the effect of Rhodiola Rosea on physical and mental stress

2. MECHANISM OF ACTION

Rhodiola Rosea improves physical and mental fatigue mainly through the following mechanisms.

2.1. Regulation of the HPA Axis: The HPA axis (hypothalamic-pituitary-adrenal axis) is the body's central stress response system. In stressful conditions, the hypothalamus activate pituitary gland, which stimulates the adrenal glands to release cortisol. Cortisol is a stress hormone that helps to cope with stress. But if cortisol remains for a longer period, it can cause fatigue. Rhodiola decreases the release of stress hormones like cortisol and reduces fatigue.

2.2. Action on Brain Neurotransmitters: Neurotransmitters in the brain, like dopamine, norepinephrine, and serotonin, will be depleted during stressful conditions. Some bioactive compounds in Rhodiola slow the breakdown of these neurotransmitters and maintain a healthy level. This will enhance mood during periods of mental fatigue.

2.3. Antioxidant Activity: Rhodiola protects the body through its antioxidant properties. Rhodiola's active compounds enhance the actions of natural antioxidant enzymes like superoxide dismutase and glutathione peroxidase. This helps to neutralize the free radicals produced during stressful conditions and protects cells in the brain and muscles. This cellular protection mechanism prevents oxidative damage, supports energy production, and helps in recovery after physical and mental stress.

3.BIOACTIVE CONSTITUENTS AND THERAPEUTIC RELEVANCE

3.1 Family: Crassulaceae, Plant part used: Rhizome and Root, Common name: Golden root, Arctic root and Rose root Over 140 different compounds are found in the Rhodiola Rosea plant. Among the, the most important ones are phenylpropanoids, including rosavin, rosarin, and rosin; phenylethanoids, such as salidrosides and tyrosol; and monoterpenes, including rosiridin. The phenylethanoid salidroside is thought to be the main component responsible for showing adaptogenic and anti-stress properties. Other constituents also show adaptogenic effect, such compounds can also increase energy, stamina, strength, and mental capacity required to withstand physical and environmental stress. (1).

There are many other components like flavonoids, proanthocyanidin, daucosterol, and phenolic acids which show antioxidant, cardioprotective, anti-aging, immune modulating, and anti-inflammatory effects. (2)

Salidroside and tyrosol are major compounds of Rhodiola rosea. Besides adaptogenic and antifatigue effect it has been shown to protect brain ,heart liver and immune system. Rosavin is unique compound in Rhodiola rosea which has brain supporting, antidepressant, anticancer, and liver protecting effects.

4.HOW DOES RHODIOLA IMPROVE PHYSICAL PERFORMANCE WITH SOLID EVIDENCE.

4.1 Physical stress is the body's reaction to any force that strains it. It can be due to exercise, environmental changes, sleep deprivation, and illness. This can activate various mechanisms, like the HPA axis, which leads to a high level of cortisol in the blood, resulting in muscle damage. At the cellular level physical stress can cause oxidative damage which results in muscle fatigue , decreased endurance , and slower recovery. Physical stress is the body's reaction to any force that strains it. It can be due to exercise, environmental changes, sleep deprivation, and illness. This can activate various mechanisms, like the HPA axis, which leads to a high level of cortisol in the blood, resulting in muscle damage. At the cellular level physical stress can cause oxidative damage which results in muscle fatigue , decreased endurance , and slower recovery.

4.2 How Rhodiola rosea fights against physical stress: Rhodiola Rosea acts through multiple mechanisms to improve physical and mental stress, which are explained in earlier modules. It regulates HPA axis -This will maintain a healthy level of cortisol which in turn supports muscle preservation and immune function during physical stress. (3) Antioxidant activity- The bioactive compounds like salidroside and rosavin protect against cell damage and reduce exercise-induced inflammation. (4,5) Improve energy- Rhodiola rosea can increase mitochondrial enzyme and ATP production. This reduce the fatigue onset and enhance endurance capacity. (4) Neurotransmitter regulation- Rhodiola rosea maintains neurotransmitters like dopamine, norepinephrine and serotonin which reduce fatigue. (6)

4.3 Evidence from human clinical studies Rhodiola rosea SHR-5 extract in Stress-Related Fatigue:In the RCT study, subjects under stress shows significant improvement in physical performance after taking the SHR extract supplement. (3). Adaptogenic Effect in Students During Exam Stress: Rhodiola rosea shows significant improvement in physical health when compared to placebo group.(7) Improvement in Night-Shift Physicians' Performance: Rhodiola rosea Reduce general fatigue under stressfull conditions .(6) Burnout Syndrome and Physical Recovery: In this multicentral trial physical complaints were improved, thereby reducing exhaustion in the participants who took Rhodiola Rosea extract. (8) Strength Performance Under Rest: In this trial, the bench press and bench pull exercise performance were improved in participants who took Rhodiola rosea.

5. HOW DOES RHODIOLA ROSEA IMPROVES MENTAL PERFORMANCE WITH SOLID EVIDENCE

5.1 According to WHO Stress can be defined as a state of worry or mental tension caused by a difficult situation. Stress is a natural human response that prompts us to address challenges and threats in our lives. Everyone experiences stress to some degree. The way we respond to stress, however, makes a big difference to our overall well being. How Rhodiola

Study	Intervention	Mechanism and Intervention
RCT trial with adults	SHR-5 extract, 400 mg/day, 28 days	Regulates HPA axis and maintains monoamine, thereby decreasing Fatigue, increasing mental speed, and improving attention (3)
RCT trial with student during exam	SHR-5 extract, 100 mg twice daily, 20 days	Reduced oxidative stress there by increase mental performance. (7)
RCT trial with healthy physicians under night duty	SHR-5 extract, 170 mg/day, 2 weeks	Increased level of dopamine and norepinephrine this increased concentration and calculation speed. (6)
Multicentre open-label study of Adults with burnout symptoms	SHR-5 extract, 400 mg/day, 12 weeks	Reduce cortisol level thereby improved emotional stability. (8)
5.Open-label trial with adults with stress symptoms	WSW 1375 extract, 200 mg twice daily, 4 weeks	cortisol normalization which leads to rapid improvement in stress and mental clarity. (9)

breaks stress cycle Mental stress -------> Elevate cortisol-------> Neurotransmitter imbalance, Oxidative stress and neuronal injury Rhodiola Rosea acts via, HPA axis regulation: Maintain a healthy level of cortisol, Antioxidant defense: Protect brain cells Mitochondrial boost: Improves mental energy This will improve memory, focus, and reduce mental fatigue

5.2.Pre clinical study was conducted using salidroside extract which reduce oxidative stress and results in improvement in spatial memory and learning. (10)

. A pre-clinical study was conducted using salidroside, 20–40 mg/kg which reduced apetite loss. (5)

5.3 Evidence from Human trial table is given below.

6. DOSE AND DOSAGE FORM OF RHODIOLA ROSEA

6.1 In clinical trails, Rhodiola rosea is almost always used in the form of standardized root and rhizome extracts. This ensures a consistent amount of its key active compounds,rosavins and salidroside, which are responsible for most of its adaptogenic effects. Among the many extracts available, SHR-5 and WS 1375 are the most commonly used in studies.

SHR-5 Extract It is a standardized Rhodiola Rosea root extract developed by the Swedish Herbal Institute.It contains: Rosavins: ~3.1% and Salidroside: ~1.0% Available as tablets or capsules, often in 144 mg or 288 mg per unit. (liquid extract is also available but less common)

WS 1375 WS 1375 is a standardized dry extract of Rhodiola rosea root by the German company Dr. Willmar Schwabe GmbH. It contains -Rosavins: 3.0–3.5% and Salidroside: 0.8–1.0% Available as usually film-coated tablets or capsules, each containing 200 mg extract.

6.3 Dosage forms

Tablets - Compressed formulations of standardized extract, often film-coated to improve stability and mask taste. Most common in European trials (e.g., SHR-5, WS 1375)

Capsules - Gelatin or vegetarian capsules containing powdered standardized extract or combination with other plant powders. Sometimes used in dietary supplement formulations

Liquid extract/tincture - Alcohol- or glycerin-based solutions of Rhodiola root extract. Concentrations vary widely. Less common in controlled trials, more in traditional use

Powdered root- Dried, ground root or rhizome powder, either raw or standardized. Mostly in herbal preparations, not often in standardised-dose research.

Trials shows that taking daily doses between 200 and 600 mg per day works best for reducing stress-related

tiredness, and improving mood during burnout or stressful situations.

Lower, short-term doses 100–200 mg can give quick benefits, such as better focus during night shifts and improved stamina in athletes.

For longer use, the most commonly tested amounts are WS®1375 at 400 mg/day and SHR-5 at 576 mg/day, and studies show they are well tolerated.

Higher doses (over 600 mg/day) have been tested for short periods, but there's not enough evidence about their safety over the long term, so they're not usually recommended for regular use.

7. SAFETY AND TOXICITY

7.1 Rhodiola Rosea is a safe and well-tolerated adaptogen. The common dose is 100-600mg/day of standardized extract. Mild side effects reported were listed below: Gastrointestinal: Nausea and gastro intestinal discomfort, Central nervous system: Dizziness and restlessness, Allergic reactions: Rare, usually mild skin reactions .

Clinical Safety Data From clinical and pre-clinical trials Short-term use: Daily doses of ≤600 mg for 4–12 weeks are well tolerated with minimal side effects (3,7,6). High-dose studies: Single or short-term doses of 1,200 mg/day was safe. But long-term safety information is limited (8).

Special populations: Data in pregnant or lactating women are limited so use cautiously. No major interactions with medications have been reported, even though monitoring is required for patients receiving stimulants or antidepressants (9).

Toxicity Studies Animal studies: Acute and subchronic toxicity studies in rodents exhibit very low toxicity. LD50 values are >5 g/kg in rats, without appreciable organ damage at normally employed doses. Genotoxicity and carcinogenicity: Preclinical research shows no genotoxic or carcinogenic

7.2 Rhodiola rosea is a safe adaptogen with a good safety profile. Side effects are mild. It can be concluded that RR extracts have good a safety record in both traditional use and research studies.

8. OVERVIEW OF CLINICAL TRIALS

8.1 Clinical trials consistently show that Rhodiola rosea can help the body cope with both mental and physical stress. Randomized controlled studies in students, physicians, healthy volunteers, and patients with stress related fatigue have reported less fatigue, irritability, and anxiety, together with improvements in mood, attention, cognitive function, and overall well-being, often within 2–8 weeks of use. In situations of physical stress, supplementation has been linked to greater endurance, quicker recovery, and better maintenance of work capacity under fatigue and hypoxia.

Open-label studies in people with burnout or life stress also support its effectiveness and good tolerability. Standardized extracts (200–600 mg/day; 3% rosavins, 1% salidroside) are generally well tolerated, with only mild and short-lived side effects reported. In summary, Rhodiola rosea appears to be a safe and effective adaptogen that improves resilience to stress, reduces fatigue, and supports both mental and physical performance. However, most available studies are relatively small and short-term, so larger and longer trials are still needed—particularly to clarify its role in physical stress adaptation. (11)

9. GLOBAL ACCEPTANCE OF RHODIOLA ROSEA GLOBAL USAGE, AVAILABILITY, AND REGULATORY STANDARDS OF RHODIOLA ROSEA

9.1 Rhodiola Rosea is a well-known adaptogen used traditionally to enhance physical and cognitive performance. Due to consumer demand for adaptogens for last two decades the use of Rhodiola Rosea has increased globally. Now Rhodiola products are commonly available in health stores, pharmacies, and online platforms. Usage Trends:Clinical trials shows benefits in stress-related fatigue, mood,mental performance and physical performance. Scientific backing, along with marketing as a "natural stress reliever," has rises in supplements across the world.

9.2 Availability by Region India: Rhodiola rosea supplements are marketed in India by nutraceutical companies and online stores under Food Safety and Standards Authority of India (FSSAI) regulations for nutraceuticals and health supplement . Rhodiola is marketed as a nutraceutical adaptogen, commonly used as a stress-reduction supplement.

Middle East (UAE, Saudi Arabia, GCC): Rhodiola rosea is available in the Middle East as imported European or US dietary food. Rhodiola rosea is

registered as a herbal dietary supplements under MOHAP (Ministry of Health and Prevention) in UAE. So the products are sold in Pharmacies and health stores as per MOHAP rules. In Saudi Arabia, the supplements are regulated by registration with the Saudi Food and Drug Authority (SFDA), under which Rhodiola is registered as a herbal ingredient in stress/fatigue supplements. This products fall under the category of supplements as this is not traditionally used there. Demand is growing, especially in the wellness and sports nutrition area.

United States: Marketing as a food supplement under DSHEA. Widely available in pharmacies, health food shops, and on the internet. European Union and UK: Ranked as a Traditional Herbal Medicinal Product (THMP/THR) in some countries (e.g., Sweden, UK). Registered products such as Arctic Root are licensed for "relief of stress related fatigue" for temporary use.

Canada: Regulated as a Natural Health Product (NHP) by Health Canada.

Australia: Listed by the Therapeutic Goods Administration (TGA) as an accepted complementary medicine ingredient

Russia: Rhodiola rosea have been traditionally used as a adaptogen in Russia. It is available over the counter as a herbal medicine

9.3 Regulation of Rhodiola in India In India, Rhodiola rosea products are regulated under the Drugs and Cosmetics Act as part of herbal and dietary supplements. This regulation emphasizes safety, quality, and standardisation. The Rhodiola extracts are standardized so that it should contain 3% Rosavin and 1% salidroside to ensure the therapeutic effect. Manufacturers must follow strict quality control tests, including plant identity verification, contaminant testing, and proper labeling. Traceability from the raw material to finished product is also needed. Even though Rhodiola is safe within the recommended dose, compliance should be ensured with Indian Pharmacopoeia standards to ensure product reliability. In summary, Indian regulations mainly focus on ensuring authenticity, safety, and standardization. (13,14)

Rhodiola rosea has global acceptance as safe adaptogen. It is widely used as supplement in US, Canada, India, and Middle East; traditional herbal preparations in Europe and Russia. In the Middle East, demand is increasing, primarily through imported supplement sources, while in India it is from nutraceutical sources. The recent addition to CITES helps to reinforce the need for sustainable supply and enhanced assurance of quality. Rhodiola species have been included in CITES Appendix II since 2023 and it requires permit for international trade in raw materials and extracts to ensure sustainable harvesting

10. DRUG AND FOOD INTERACTION OF RHODIOLA ROSEA

10.1 Rhodiola Rosea is considered a safe adaptogen, but its bioactive compounds, especially Rosavin and salidroside, can cause interactions by influencing metabolic and neurotransmitter pathways. This can cause Drug interaction and Food interaction

10.2 Drug interaction: CNS-active drugs (antidepressants, anxiolytics, stimulants) It was previously discussed in Module 2 (Mechanism of Action) that Rhodiola acts on brain neurotransmitters like Dopamine, Serotonin, and Norepinephrine. When Rhodiola is combined with SSRIs, SNRIs, MAOI's or stimulants, this can increase the risk of additive effects like insomnia, Jitteriness, and rarely serotonin syndrome (12,15). Antihypertensive Due to mild sympathomimetic and adaptogenic effects. Rhodiola can elevate alertness and slightly increase heart rate, which can reduce the antihypertensive effect of the drug, especially beta-blockers and calcium channel blockers. (16) Antidiabetic effect Preclinical studies suggest that Rhodiola increases glucose metabolism and insulin sensitivity. This can cause hypoglycemic effects when taken with hypoglycemic drugs like metformin, sulfonylurea and Insulin.(17) CYP450 substrate Some in vitro studies suggest that Rhodiola inhibits enzymes like CYP2C9 and CYP3A4. This is important for the metabolism of many drugs. This suggests that Rhodiola can interact with warfarin, immunosuppressants and statins even though human clinical studies are limited on this.(18)

10.3 Food Interaction Caffeine and Stimulants Rhodiola is used for mental alertness, so when it is used with stimulants it may cause additive effect this can lead to insomnia and restlessness.(12) Alcohol No direct harmful reactions reported but from the MOA of Rhodiola it is clear that it has CNS activity so as Alcohol also. Alcohol can counteracts it action and can alter mood. High sugar diet Studies shows

that Rhodiola has glucose control effect but high sugar intake can deplete this effect.(17)

11. AVAILABLE BRANDS IN MARKET

11.1 Commonly available brands in India are Trexgenics Rhodiola Rosea 500 mg (500 mg + Piperine; standardized (3% Rosavins, 1% or 3% Salidroside), Adorreal Rhodiola Rosea 60 capsules, NutriJa Rhodiola Rosea 500 mg (500 mg, 3% Rosavins, 1% Salidroside + Bioperine) and Nature's Way Rhodiola Rosea-60 capsules (Standardized extract (typical global brand).

12. LIMITATIONS

12.1 The reviewed studies show Rhodiola rosea has adaptogenic effect, particularly against stress-related fatigue. Human clinical trials, particularly with standardized extracts like SHR-5 or WS 1375, mention symptom relief of fatigue, enhanced mental performance under stress, reduction of cortisol level, enhanced endurance, and enhanced recovery from burnout. Dose administered was from approximately 100-600mg/day for a duration 2 weeks up to 12 weeks. Adults included were who facing work-related stress, chronic fatigue, and academic pressure. Limitations include that sample sizes were typically small and heterogeneous, and thus not generalizable. Longer sample sizes and duration are needed to confirm the safety and efficacy of Rhodiola rosea, especially in chronic stress. Also, long-term side effects can't be accurately summarized. People with different ethnic backgrounds, ages, and health statuses can metabolize and respond to herbal drugs in different ways. So this can't be applied to global populations. Some studies themselves stated a limitation that the dose level was suboptimal. Some studies have a high risk of publication bias. Most studies use subjective stress markers. Objective stress markers with biochemical analysis may provide accurate and more reliable results.

13. FUTURE OF THE STUDY

13.1 Sleep regulation: As discussed in MOA it sis clear that Rhodiola Rosea can modulate hypothalamic pituitary-adrenal (HPA) axis and reducing cortisol levels. Cortisol level is elevated in people with sleep disturbance. This suggests that Rhodiola rosea can be used in people with sleep disturbance and thus can enhance their quality of sleep. Conduct well-designed placebo-controlled studies to confirm Rhodiola's effectiveness, determine the best dose and long-term safety, and understand how it affects sleep and stress.

13.2 Aging and cognitive health: Rhodiola rosea may help protect the brain and slow age-related cognitive decline through its neuroprotective actions, including antioxidant effects and maintaining healthy levels of brain chemicals. Conduct long-term clinical trials in older adults to evaluate Rhodiola's effects on cognitive function, memory, executive performance, and aging-related physiological markers, and explore potential synergistic effects with other neuroprotective compounds.

13.3 Sports performance Rhodiola protects the body through its antioxidant properties. Rhodiola's active compounds enhance the actions of natural antioxidant enzymes like superoxide dismutase and glutathione peroxidase.There by improve energy metabolism by increasing ATP production in muscle cells, reducing oxidative stress, and modulating stress-related hormones like cortisol This cellular protection mechanism prevents oxidative damage, supports energy production, and help in recovery after physical and mental stress Conduct long-term studies to determine the optimal dosing of Rhodiola rosea for endurance, strength, and recovery by evaluating its effects on fatigue, muscle damage, and recovery biomarkers, and compare outcomes professional athletes.

13.4 Combination Therapy: Study how Rhodiola works when combined with other adaptogen to improve mental and physical performance. Find out whether these combinations can better reduce stress, improve sleep, or support brain health.

14. CONCLUSION

Rhodiola rosea is an adaptogenic drug. It is also known as rose root, golden root, or arctic root, which can enhance mental and physical performance under stress, and has been traditionally used. The active compounds of Rhodiola Rosea is Rosavin, Rosin, Rosarin, Salidroside, Tyrosol, and Rosiridin. Rhodiola acts via HPA axis modulation,

neurotransmitter modulation, energy metabolism, and antioxidant activity. HPA axis modulation (the body's central response system), which releases cortisol (stress hormone) under stress. RR regulates this pathway by inhibiting the excess release of cortisol, thereby decreasing stress. RR helps to maintain dopamine and serotonin levels, which in turn enhance mood and focus. RR increases the production of protective proteins like heat shock protein and antioxidants, which protect cells under stressful tiredness conditions. There are studies that include athletes, military cadets, and participants enrolled in cycle ergometer tests that have shown significant improvement in physical performance. There are studies that included participants with stress-related fatigue, students during exams, physicians after night shift, and patients with work-related stress and burnout. They showed better mental performance at the end of the study. RCTs, open label studies, and animal studies were taken. Participants included students, healthy individuals, military cadets, and athletes. All studies suggest that RR has shown significant improvement in both mental and physical fatigue. Dose used was 100-600mg/day. Most commonly used standardized extract was of SHR-5 and WS 1375. RR is considered to be a safe and well-tolerated adaptogen. NO serious ADR were reported. However, long-term studies can help to figure out more. RR is widely used globally. In many countries, it is used as a traditional medicine and has shown significant effects. Limitations include that sample sizes were typically small and heterogeneous, and thus not generalizable. Longer sample sizes and duration are needed to confirm the safety and efficacy of Rhodiola rosea, especially in chronic stress. Also, compound long-term side effects can't be accurately summarized. People with different ethnic backgrounds, ages, and health statuses can metabolise and respond to herbal drugs ways. Future research on RR can expand beyond general physical and mental fatigue. It can be studied in old generation, please with reduced cognitive ability, high stress populations, etc

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