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RHODIOLA ROSEA AS A NATURAL ADAPTOGEN: A REVIEW OF ITS EFFECTS ON STRESS REDUCTION, MOOD ENHANCEMENT, AND COGNITIVE FUNCTION

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ABSTRACT

Introduction: Rhodiola rosea is a widely used adaptogenic herb known for its potential to enhance the body's resistance to physical and psychological stress. Traditionally employed in various medical systems, it has recently gained scientific attention for its beneficial effects on mood regulation, stress reduction, and cognitive performance. The complex phytochemical composition of Rhodiola rosea underpins these effects, yet the precise mechanisms and clinical efficacy remain to be fully elucidated. This review aims to comprehensively summarize current knowledge regarding the phytochemistry, mechanisms of action, preclinical and clinical evidence of Rhodiola rosea's adaptogenic properties, focusing on its impact on stress reduction, mood enhancement, and cognitive function. Mechanisms of action involving modulation of the hypothalamic-pituitary-adrenal (HPA) axis, neurotransmitter systems, and antioxidant pathways are discussed. Despite promising results, further high-quality, large-scale randomized controlled trials are needed to establish standardized protocols for clinical use.

Material and methods: A systematic literature analysis was conducted, including in vitro, animal, and human studies investigating Rhodiola rosea extracts. Emphasis was placed on studies examining biochemical pathways, neurobehavioral outcomes, and clinical trials assessing stress-related parameters, mood states, and cognitive metrics.

Results: Rhodiola rosea exhibits modulatory effects on monoaminergic neurotransmission, enhances antioxidant defenses by upregulating enzymes such as superoxide dismutase and catalase, and improves mitochondrial function, leading to increased cellular energy production. Clinical studies demonstrate significant reductions in perceived stress and fatigue, improvements in mood disorders including mild to moderate depression, and enhanced psychomotor performance and cognitive processing speed. However, variability in extract standardization and study design influences the consistency of findings.

Conclusions: Rhodiola rosea represents a promising natural adaptogen with multifaceted actions supporting stress resilience, mood stabilization, and cognitive enhancement. Standardized extracts with defined phytochemical profiles are essential to ensure reproducible therapeutic effects. Further rigorous clinical investigations are warranted to clarify optimal dosing regimens and long-term safety.

KEYWORDS

Rhodiola Rosea, Adaptogen, Stress Reduction, Mood Enhancement, Cognitive Function

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1. Introduction

Rhodiola rosea L., commonly known as "golden root" or "arctic root," is a perennial plant belonging to the Crassulaceae family, native to cold regions of Europe, Asia, and North America, particularly thriving in the Arctic and mountainous regions such as the Himalayas, Altai, and the Alps. Its use as a medicinal herb dates back to ancient times, with evidence of its application in traditional Chinese, Russian, and Scandinavian folk medicine for enhancing physical endurance, alleviating fatigue, and improving mental capacity under stress. The ancient Greeks and Vikings reportedly utilized Rhodiola to improve stamina and resilience during physical exertion and harsh environmental conditions [1,2]. In recent decades, Rhodiola rosea has garnered increasing scientific interest as a natural adaptogen — a class of substances that help the human body resist various physical, chemical, and biological stressors, thereby restoring homeostasis. Adaptogens are characterized by their ability to produce a non-specific enhancement of the organism's resistance to stress, balancing physiological processes without causing disturbances typical of pharmaceutical stimulants or sedatives. The concept of adaptogens emerged in the mid-20th century from research conducted in the Soviet Union, particularly by the scientist Nikolai Lazarev, who first defined adaptogens as agents that increase "state of non-specific resistance" to stress. Rhodiola rosea was soon recognized as one of the most potent and widely used adaptogenic plants due to its multifaceted biological activities. Modern research has focused on

Rhodiola's potential to mitigate the deleterious effects of chronic stress, including mood disturbances such as anxiety and depression, cognitive impairment, and fatigue. The plant's complex phytochemical profile, including phenylethanoids like salidroside and phenylpropanoids such as rosavins, is believed to mediate these benefits through synergistic interactions**.** Additionally, Rhodiola rosea extracts have found a place in the sports nutrition market, where they are promoted for enhancing endurance, reducing physical and mental fatigue, and accelerating recovery after exercise. The antioxidative properties of Rhodiola further contribute to its protective effects against oxidative stress induced by strenuous physical activity and environmental stressors. Despite growing popularity, the mechanistic understanding of Rhodiola's adaptogenic effects remains incomplete. Current evidence suggests a multifactorial mode of action involving modulation of neurotransmitter systems, enhancement of mitochondrial function and energy metabolism, and regulation of antioxidant defenses. The increasing number of clinical trials and preclinical studies continues to provide insights into the efficacy and safety of Rhodiola-based interventions for stress-related disorders and cognitive enhancement [3-6].

This review aims to comprehensively synthesize the current scientific knowledge on Rhodiola rosea, focusing on its effects on stress reduction, mood enhancement, and cognitive function. Particular emphasis is placed on the influence of cultivation methods on phytochemical composition and biological activity, the molecular mechanisms underpinning adaptogenic effects, and the translational relevance of preclinical and clinical findings.

2. Phytochemistry and Cultivation of Rhodiola rosea

The biological activity of Rhodiola rosea is closely linked to its complex phytochemical composition, which varies depending on the plant's geographic origin, cultivation conditions, and extraction methods. Understanding the phytochemistry and the influence of cultivation is crucial for ensuring consistent quality and efficacy of Rhodiola supplements.

2.1 Key Bioactive Compounds

Among the approximately 140 chemical constituents identified in Rhodiola rosea, phenylethanoids and phenylpropanoids are considered the primary bioactive molecules responsible for the adaptogenic effects. The two most studied groups include:

- Salidroside: A phenylethanoid glycoside recognized for its antioxidant, anti-inflammatory, and neuroprotective properties. Salidroside has demonstrated efficacy in reducing oxidative damage, modulating neurotransmitter levels, and enhancing mitochondrial function in various preclinical models.
- Rosavins: This collective term refers to a group of cinnamyl alcohol glycosides, including rosavin, rosin, and rosarin. Rosavins are unique to Rhodiola rosea and are used as chemical markers to distinguish Rhodiola roseaextracts from those of other species. They contribute to the adaptogenic and antidepressant effects of the plant.

Additional important phytochemicals include flavonoids (such as quercetin derivatives), organic acids, tannins, terpenes, and essential oils, which synergistically augment the plant's physiological effects. Flavonoids, for example, have been implicated in the modulation of antioxidant defenses and mitochondrial biogenesis [7-9].

2.2 Variability in Phytochemical Content

Phytochemical profiles of Rhodiola can vary significantly based on environmental factors such as altitude, soil composition, and climate. Wild-harvested Rhodiola from high-altitude Arctic or mountainous regions tends to exhibit higher concentrations of rosavins and salidroside, correlating with the plant's adaptation to extreme environmental stressors.

In contrast, increasing commercial demand and sustainability concerns have led to the development of controlled cultivation techniques, especially in Central Europe and parts of Asia. Controlled cultivation offers the advantage of standardized growing conditions, such as regulated temperature, humidity, soil nutrients, and light exposure, which can influence phytochemical synthesis.

Studies comparing wild-harvested (RRwh) and controlled cultivation (RRcc) Rhodiola rosea extracts have shown comparable levels of key bioactive components when cultivation protocols are optimized. For example, cultivation at altitudes ranging from 20 to 600 meters with careful selection of seed stock and cultivation environment can yield roots with salidroside and rosavin concentrations similar to those from wild populations [3-4, 10].

2.3 Extraction and Standardization

The therapeutic efficacy of Rhodiola extracts depends not only on the raw plant material but also on extraction methods and standardization. Typically, extracts are prepared from the roots using solvents like 70% ethanol through multi-stage percolation, which efficiently recovers phenolic compounds and glycosides.

Pharmacopoeial standards vary by region, with the United States Pharmacopeia recommending extracts standardized to 0.3% rosavins and 0.08% salidroside, whereas Russian and Australian standards stipulate higher minimum concentrations (up to 1% rosavins and 0.8% salidroside or higher). These standards guide the selection of extracts for clinical and nutraceutical use [11,12].

Due to the complex nature of the phytocomplex and potential synergy among compounds, pure isolated constituents like salidroside or rosavin alone often do not replicate the full adaptogenic activity of the whole extract. This suggests that the combined presence of multiple phytochemicals, including minor constituents like flavonoids and organic acids, contributes to the overall efficacy [5, 13].

2.4 Implications for Supplement Quality

Ensuring consistent phytochemical content is critical for reproducible biological effects and consumer trust. Products that provide certificates of analysis and undergo third-party verification for salidroside and rosavin content help guarantee quality and safety.

The synergy of compounds in well-characterized extracts, combined with controlled cultivation practices, represents a promising avenue to develop reliable Rhodiola rosea supplements that maintain adaptogenic potency while supporting sustainable production [14].

3. Mechanisms of Action

The adaptogenic and multifaceted biological effects of Rhodiola rosea are mediated through complex and interrelated mechanisms that target neurotransmitter systems, antioxidant defenses, anti-inflammatory pathways, and energy metabolism at the cellular and systemic levels. These mechanisms collectively contribute to the enhancement of stress resilience, mood regulation, and cognitive function.

3.1 Neurotransmitter Modulation

One of the key mechanisms underlying Rhodiola's adaptogenic properties involves modulation of monoaminergic neurotransmitter systems, including serotonin, dopamine, and norepinephrine pathways. These neurotransmitters play pivotal roles in regulating mood, motivation, cognitive function, and the physiological response to stress.

Rhodiola extracts have been shown to influence the availability and activity of serotonin, a neurotransmitter critical for mood stabilization and anxiety regulation. By modulating serotonin levels, Rhodiola may exert anxiolytic and antidepressant effects, contributing to improved emotional resilience under stress. Similarly, the herb affects dopamine pathways, which are essential for motivation, reward processing, and motor control. Enhanced dopaminergic signaling supports improved mood, increased energy, and better cognitive focus. Norepinephrine, which governs the sympathetic nervous system response and alertness, is also modulated by Rhodiola, helping to optimize the balance between arousal and calmness during stressful situations [5, 8].

In addition to monoamine modulation, Rhodiola impacts neuropeptide signaling and opioid receptor activity. Neuropeptides such as beta-endorphins are involved in pain modulation and stress relief, and Rhodiola may enhance their release or receptor sensitivity, contributing to improved tolerance to physical and psychological stressors. The interaction with opioid receptors further supports analgesic effects and modulates mood and stress responses, reinforcing the herb's adaptogenic profile. This multi-targeted approach to neurotransmitter regulation allows Rhodiolato exert broad-spectrum effects on the central nervous system, improving stress coping and emotional stability [10-14].

3.2 Antioxidant and Anti-inflammatory Effects

Oxidative stress is a major contributor to cellular damage under physiological and pathological stress conditions. Excess reactive oxygen species (ROS) lead to lipid peroxidation, protein oxidation, DNA damage, and ultimately cellular dysfunction. The antioxidant properties of Rhodiola are crucial for mitigating these effects and maintaining cellular homeostasis.

Rhodiola enhances the endogenous antioxidant defense system by increasing the expression and activity of key antioxidant enzymes, including superoxide dismutase (SOD), catalase, and glutathione peroxidase

(GPx). These enzymes play essential roles in neutralizing ROS and protecting cellular components. SOD catalyzes the dismutation of superoxide radicals into hydrogen peroxide, which is then decomposed to water and oxygen by catalase and GPx. By upregulating these enzymes, Rhodiola significantly reduces oxidative damage within cells, particularly in tissues vulnerable to oxidative stress such as muscle and brain [15, 16].

Moreover, Rhodiola exerts anti-inflammatory effects by modulating inflammatory signaling pathways. It reduces the production of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukins IL-1β and IL-6, which are typically elevated in stress and chronic inflammation. By dampening inflammatory responses, Rhodiolaprotects tissues from damage induced by prolonged inflammatory states, which can exacerbate oxidative stress and impair cellular function.

The combined antioxidant and anti-inflammatory actions of Rhodiola form a protective network that safeguards mitochondrial integrity, membrane lipids, and nucleic acids, thereby preserving cell viability and function. This protection is particularly relevant in the nervous and muscular systems, where oxidative stress and inflammation are key contributors to fatigue, cognitive decline, and muscle damage [1, 2, 15].

3.3 Energy Metabolism and Mitochondrial Function

Mitochondria are central to cellular energy metabolism, producing adenosine triphosphate (ATP) through oxidative phosphorylation. Efficient mitochondrial function is essential for meeting the energy demands of cells, especially in high-demand tissues like muscle and brain. Rhodiola has been demonstrated to enhance mitochondrial bioenergetics, supporting energy production and cellular resilience.

In vitro studies show that Rhodiola extracts stimulate ATP synthesis by improving mitochondrial respiratory chain activity. This enhancement results in increased cellular energy availability, which is crucial for sustaining physical and cognitive performance during stress. Improved mitochondrial function also reduces the generation of excessive ROS by optimizing electron transport and minimizing electron leakage, thereby further mitigating oxidative stress.

Beyond direct mitochondrial effects, Rhodiola modulates metabolic pathways that support energy homeostasis. One such pathway is the folate cycle, which plays a key role in nucleotide biosynthesis, methylation reactions, and redox balance. By influencing folate metabolism, Rhodiola promotes DNA repair, epigenetic regulation, and cellular detoxification processes. Additionally, the herb affects polyamine metabolism, which is involved in cell proliferation, differentiation, and stress response signaling. Polyamines contribute to stabilizing DNA and modulating ion channels, influencing cell growth and survival under adverse conditions.

The interaction of these metabolic pathways underlies the systemic adaptogenic effects of Rhodiola, promoting cellular energy efficiency, repair capacity, and stress resistance. This comprehensive enhancement of energy metabolism contributes to improved endurance, faster recovery, and sustained cognitive function [6, 7, 10, 15-20].

3.4. Influence on Muscle Cell Differentiation and Repair

Recent cellular studies reveal that Rhodiola rosea extracts influence muscle cell homeostasis and regeneration. In vitro experiments using human skeletal myoblasts indicate that treatment with standardized extracts modulates the expression of myogenic transcription factors such as Pax7 and MyoD, which are critical for muscle cell differentiation and repair.

By promoting these pathways, Rhodiola may accelerate recovery from exercise-induced muscle damage and support muscle regeneration. Furthermore, the extract enhances intracellular ATP levels and mitochondrial respiration in muscle cells, providing bioenergetic support essential for tissue repair processes [1, 21,22].

3.5. Modulation of Metabolic Pathways

Metabolomic analyses reveal that Rhodiola affects metabolic fluxes, particularly within antioxidant enzyme systems and the folate/polyamine pathway. Folate metabolism is essential for nucleotide synthesis, methylation reactions, and cellular repair, while polyamines are involved in cell proliferation and stress responses.

Through these interactions, Rhodiola may optimize cellular metabolism under stress conditions, contributing to improved physiological resilience and performance. This novel insight suggests that beyond direct antioxidant effects, Rhodiola fine-tunes metabolic networks to enhance systemic adaptation [23].

3.6. Immunomodulatory Effects

Although less extensively studied, Rhodiola rosea also exerts immunomodulatory actions. Limited human trials indicate that supplementation may reduce susceptibility to viral infections following intense exercise, potentially by modulating innate immune responses. These effects are clinically relevant for athletes, as acute illnesses negatively impact training continuity and competitive performance [9, 15].

3.7. Safety and Pharmacokinetics

Rhodiola is generally well-tolerated, with a favorable safety profile documented in human and animal studies. Toxicological assessments indicate low risk of adverse effects at commonly used doses. However, potential interactions with pharmaceuticals and other supplements remain to be fully elucidated.

Pharmacokinetic studies show that salidroside and rosavins are bioavailable following oral ingestion, with peak plasma concentrations occurring within 1–2 hours. Metabolic pathways primarily involve hepatic biotransformation, and elimination is rapid, suggesting the need for sustained dosing to maintain therapeutic levels [23,24].

4. Preclinical Evidence

The preclinical evaluation of Rhodiola rosea encompasses a broad spectrum of in vitro and animal model studies that elucidate its adaptogenic, antioxidant, and regenerative properties. These investigations provide critical insight into the molecular and cellular mechanisms through which Rhodiola exerts its beneficial effects, particularly regarding muscle cell homeostasis, stress resilience, and cardiovascular protection.

4.1 In vitro Studies

In vitro research employing primary human skeletal muscle myoblasts has revealed that Rhodiola rosea extracts modulate key transcription factors involved in muscle differentiation and regeneration. Notably, Rhodiola influences the expression of Pax7 and MyoD, two essential regulators of myogenesis. Pax7 is a marker of muscle satellite cells, responsible for the maintenance and renewal of muscle tissue, while MyoD promotes the commitment of these precursor cells to differentiation pathways. Treatment with controlled cultivation Rhodiola extracts leads to an upregulation of Pax7 and a balanced modulation of MyoD expression, suggesting a role in enhancing muscle stem cell proliferation and subsequent differentiation. This modulation supports the repair and regeneration processes essential for muscle homeostasis, particularly under stress or injury conditions.

Beyond transcriptional effects, Rhodiola extracts demonstrate significant influence on cellular metabolism. Experimental data indicate that Rhodiola enhances mitochondrial respiration and increases intracellular ATP production in myoblast cultures. This mitochondrial stimulation is critical in muscle cells, where high energy demand necessitates efficient oxidative phosphorylation. The improved bioenergetic status promotes not only muscle cell viability but also functional capacity during periods of increased physiological demand.

Moreover, Rhodiola exhibits potent antioxidant properties at the cellular level. By upregulating antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx), Rhodiola counters oxidative stress induced by reactive oxygen species (ROS). This effect is particularly relevant in muscle cells subjected to oxidative damage following intense physical activity or metabolic stress. The herb's antioxidant capacity protects cellular components from lipid peroxidation, protein oxidation, and DNA damage, thereby preserving muscle integrity and function.

Untargeted metabolomic analyses have further revealed that Rhodiola treatment modulates the folate and polyamine metabolic pathways within myoblasts. These pathways are crucial for nucleotide synthesis, methylation reactions, and cellular proliferation. The enhanced activity in these metabolic routes indicates a systemic effect of Rhodiola on cellular renewal and defense mechanisms, contributing to the overall adaptogenic response at the muscle tissue level [20-25].

4.2 Animal Models

Animal studies have corroborated and extended the in vitro findings, demonstrating the adaptogenic and protective effects of Rhodiola rosea in vivo. Various rodent models subjected to physical and psychological stress provide a framework for understanding how Rhodiola mitigates stress-induced physiological alterations.

In models of chronic stress and fatigue, Rhodiola supplementation has been shown to improve endurance, reduce behavioral signs of fatigue, and normalize stress hormone levels. These effects are

accompanied by improvements in cognitive performance and mood-related behaviors, reinforcing the herb's central nervous system adaptogenic properties. Importantly, these benefits occur alongside biochemical changes indicative of reduced oxidative stress and inflammation.

The cardioprotective effects of Rhodiola have been highlighted in animal models of myocardial injury and hypertrophy. Supplementation with Rhodiola extracts reduces cardiac dysfunction by attenuating myocardial fibrosis, hypertrophy, and inflammation. These protective effects are mediated through antioxidant mechanisms that reduce oxidative damage within cardiac tissue and through modulation of signaling pathways involved in fibrotic remodeling. By mitigating inflammation and preserving cardiac structure and function, Rhodiola contributes to the resilience of the cardiovascular system under stress conditions.

In addition, Rhodiola exhibits anti-inflammatory properties in animal models, demonstrated by decreased levels of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β. This immunomodulatory activity supports tissue repair and reduces chronic inflammation, which is often a consequence of prolonged stress and contributes to various pathologies.

Collectively, these preclinical studies underpin the adaptogenic profile of Rhodiola rosea, confirming its role in enhancing muscle regeneration, improving cellular bioenergetics, counteracting oxidative damage, and providing cardioprotection and anti-inflammatory effects. The integration of in vitro cellular assays with in vivo animal models offers a comprehensive understanding of Rhodiola's biological activities, setting a foundation for translational clinical research [12, 19, 23-26].

5. Clinical Evidence: Stress Reduction and Mood Enhancement

The clinical investigation of Rhodiola rosea has progressively expanded to encompass various populations characterized by elevated stress levels, mood disturbances, and related cognitive complaints. These groups primarily include healthy adults exposed to occupational stress, athletes undergoing intense physical and psychological demands, and patients suffering from mild to moderate depression and anxiety. Collectively, these studies provide a comprehensive perspective on the adaptogenic potential of Rhodiola in real-world settings, highlighting its role in alleviating stress-related symptoms and improving mood.

5.1 Populations Studied

Research involving healthy adults under psychological and physical stress has demonstrated that Rhodiola roseasupplementation can significantly mitigate perceived stress and improve well-being. Occupational stress models frequently recruit individuals working in high-demand professions, such as healthcare workers, military personnel, or corporate employees, where sustained mental exertion and emotional strain are prevalent. In these cohorts, Rhodiolasupplementation has been associated with reductions in stress-related symptoms, including fatigue, irritability, and sleep disturbances.

Athletes represent another critical group studied for the effects of Rhodiola on stress and mood. The physiological stress imposed by rigorous training and competition often leads to overreaching and burnout, conditions characterized by diminished performance and mood deterioration. Intervention studies have explored whether Rhodiola can buffer these effects by enhancing recovery and supporting mental resilience [24].

Clinical trials including patients diagnosed with mild to moderate depression or anxiety disorders have also been conducted, although these remain fewer and with more heterogeneous methodologies. These trials investigate the potential of Rhodiola as a complementary or alternative treatment to conventional pharmacotherapy, particularly for individuals experiencing stress-related mood symptoms or those seeking non-pharmaceutical options [17].

5.2 Dosage and Preparations

The efficacy of Rhodiola rosea in clinical contexts is closely tied to the standardization and quality of the extracts used. Most studies utilize extracts standardized to contain specific percentages of key bioactive compounds, primarily salidroside and rosavins, to ensure reproducibility and comparability of results. Commonly used extracts meet pharmacopeial standards, with rosavins content ranging between 1% and 3% and salidroside between 0.5% and 1.5%.

Dosage regimens vary considerably depending on the population and study design, but typical daily doses range from 200 mg to 600 mg of standardized extract. The duration of supplementation spans from acute single doses to chronic administration over several weeks or months. Both dosing strategies have been explored, with evidence suggesting that longer-term supplementation tends to provide more consistent benefits in stress reduction and mood improvement.

Administration timing relative to daily activities or exercise also influences outcomes. Some studies administer Rhodiola in the morning to capitalize on its potential energizing effects, while others divide doses throughout the day to maintain stable plasma levels. The form of supplementation—capsules, tablets, or liquid extracts—does not appear to significantly affect efficacy, provided that the extract is properly standardized [1-3, 14].

5.3 Effects on Perceived Stress and Fatigue

A substantial body of clinical evidence supports the role of Rhodiola rosea in reducing perceived stress and fatigue. Placebo-controlled trials in healthy adults subjected to chronic occupational stress have consistently reported significant reductions in self-reported fatigue and improvements in overall quality of life following Rhodiola supplementation. These benefits often emerge within the first few weeks and are sustained with continued use.

Mechanistically, the alleviation of fatigue is linked to Rhodiola's ability to modulate the hypothalamic-pituitary-adrenal (HPA) axis, leading to more balanced cortisol secretion patterns and reduced physiological stress markers. This hormonal regulation contributes to a subjective sense of increased energy and decreased exhaustion, both mental and physical.

Meta-analyses synthesizing available randomized controlled trials corroborate these findings, revealing medium to large effect sizes in fatigue reduction and mood enhancement. Improvements are reported across multiple domains, including cognitive function, emotional well-being, and sleep quality, underscoring the multifaceted nature of Rhodiola's adaptogenic effects.

Notably, the reduction in fatigue is often accompanied by improvements in cognitive symptoms such as concentration, memory, and mental clarity, which further contribute to enhanced daily functioning. These effects are particularly relevant in populations experiencing chronic stress, where cognitive impairments are commonly reported [27-30]

5.4 Effects on Depression and Anxiety

The therapeutic potential of Rhodiola rosea in mood disorders has garnered increasing interest, particularly as a natural alternative or adjunct to standard antidepressant treatments. Clinical trials targeting patients with mild to moderate depression have documented reductions in depressive symptoms, as measured by standardized rating scales. These studies suggest that Rhodiola may exert anxiolytic and mood-stabilizing effects, possibly through its influence on monoaminergic neurotransmitter systems.

Proposed mechanisms include the modulation of serotonin, dopamine, and norepinephrine pathways, as well as the attenuation of inflammatory processes implicated in the pathophysiology of depression. Additionally, Rhodiola's antioxidant properties may protect neuronal integrity and function, further supporting mood regulation.

Despite promising results, the heterogeneity of study designs, sample sizes, and diagnostic criteria limit definitive conclusions. Some trials report modest or no significant improvements, highlighting the need for larger, well-controlled studies. Moreover, the placebo effect, common in mood disorder research, complicates interpretation.

Nevertheless, the favorable safety profile of Rhodiola combined with its multifactorial mechanism of action positions it as a valuable option for patients seeking complementary therapies. Its use in anxiety disorders, while less studied, shows preliminary evidence of benefit, particularly in reducing symptoms of generalized anxiety and stress-related manifestations [4, 6, 23, 31].

5.5 Conflicting Results and Possible Explanations

While the majority of clinical data support the adaptogenic and mood-enhancing properties of Rhodiola rosea, inconsistencies across studies are evident. Variability in results may stem from methodological differences including sample size, participant selection, extract composition, dosing, and duration of treatment.

Standardization issues represent a significant challenge. Variations in salidroside and rosavin content, as well as the presence of other synergistic phytochemicals, influence bioactivity and clinical outcomes. Inadequate quality control or the use of non-standardized products can result in reduced efficacy and poor reproducibility.

Differences in participant baseline characteristics such as severity of stress or mood symptoms, comorbidities, and concurrent medication use also affect responsiveness. Moreover, subjective outcome measures and the psychological nature of stress and mood complicate objective assessment.

Future research should aim to address these limitations by employing rigorous trial designs, larger cohorts, and standardized intervention protocols. Investigations into pharmacokinetics, dose-response relationships, and long-term safety will further clarify the clinical utility of Rhodiola rosea [18, 32].

6. Cognitive Function and Mental Performance

Cognitive decline and impaired mental performance are common consequences of both acute and chronic stress, often manifesting as reduced attention, slower reaction times, and diminished executive function. The adaptogenic herb Rhodiola rosea has attracted scientific interest for its potential to improve various aspects of cognitive functioning, ranging from psychomotor speed to memory and higher-order cognitive processes. Clinical and preclinical evidence supports the role of Rhodiola in enhancing mental performance through multiple neurobiological mechanisms, including modulation of neurotransmitter systems, mitochondrial protection, and antioxidant effects within the central nervous system.

6.1 Psychomotor Function and Reaction Time

Psychomotor performance, encompassing the speed and accuracy of motor responses to sensory stimuli, serves as a fundamental measure of cognitive efficiency and neurological integrity. In clinical research, both simple and complex reaction time tests are employed to evaluate the effects of Rhodiola on this domain. Simple reaction time tasks require a straightforward motor response to a single stimulus, while complex reaction tasks involve discriminating between multiple stimuli and executing differentiated responses, thus engaging attention and processing speed more extensively.

Multiple randomized controlled trials have demonstrated that supplementation with standardized Rhodiola roseaextracts leads to a statistically significant reduction in reaction times. These effects are observed in healthy adults exposed to stress-inducing conditions, such as prolonged cognitive work or sleep deprivation, suggesting that Rhodiolamay counteract the cognitive slowing commonly associated with stress and fatigue. Additionally, improvements in accuracy accompany faster responses, indicating enhanced processing efficiency rather than impulsivity.

The mechanisms underlying these effects likely involve Rhodiola's modulation of central monoaminergic pathways, particularly dopamine and norepinephrine, which are critically implicated in attention and motor control. By maintaining optimal neurotransmitter levels and receptor sensitivity, Rhodiola facilitates rapid and accurate psychomotor responses. This is further supported by preclinical data showing increased expression of genes related to synaptic plasticity and neural signaling in response to Rhodiola constituents [33].

6.2 Memory, Attention, and Executive Functions

Beyond psychomotor speed, Rhodiola rosea appears to benefit cognitive domains that require more complex processing, such as working memory, sustained attention, and executive function. Working memory, essential for temporarily holding and manipulating information, often suffers under stress, leading to impaired decision-making and problem-solving. Clinical trials investigating Rhodiola's effects on these cognitive facets report improvements in memory recall, task switching, and concentration, especially in populations experiencing chronic stress or mental fatigue.

The enhancement of attentional capacity is particularly noteworthy given the central role of attention in virtually all cognitive tasks. Rhodiola supplementation has been linked to increased alertness and reduced distractibility, facilitating better performance in activities requiring prolonged mental effort. Similarly, executive functions, including planning, inhibitory control, and cognitive flexibility, show positive responses to Rhodiola, contributing to improved overall mental performance.

These cognitive enhancements likely arise from Rhodiola's combined effects on neurotransmission and cellular energy metabolism. By optimizing mitochondrial function and reducing oxidative stress in neuronal populations, Rhodiolasupports the energetic demands of cognitively demanding tasks. Furthermore, its impact on neurotransmitters such as serotonin and acetylcholine may enhance synaptic communication and neuroplasticity, critical for memory consolidation and attention regulation [33-35].

6.3 Neurobiological Mechanisms Supporting Cognitive Effects

At the cellular level, Rhodiola rosea exerts neuroprotective actions that underlie its cognitive benefits. One key mechanism involves the preservation and enhancement of mitochondrial function within neurons. Mitochondria, as cellular powerhouses, provide the ATP necessary for synaptic transmission and plasticity. Stress and aging often impair mitochondrial efficiency, leading to neuronal dysfunction and cognitive decline.

Studies using in vitro and animal models demonstrate that Rhodiola extracts stimulate mitochondrial biogenesis and respiratory chain activity, thereby increasing ATP production. This bioenergetic support helps maintain neuronal integrity under conditions of oxidative stress and metabolic challenge. Additionally, Rhodiola's antioxidant properties mitigate the accumulation of reactive oxygen species (ROS) in the brain, which are known to damage lipids, proteins, and DNA, contributing to neurodegeneration.

The herb's influence on the folic acid and polyamine metabolic pathways further supports neuronal health. These pathways are crucial for DNA repair, methylation reactions, and the regulation of ion channels, all of which impact cognitive function. By enhancing the activity of antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase, Rhodiola reduces oxidative damage and fosters a neuroprotective environment conducive to optimal cognitive performance.

Moreover, Rhodiola's ability to modulate stress hormones, particularly by normalizing cortisol levels, alleviates the detrimental effects of chronic stress on the hippocampus and prefrontal cortex—brain regions integral to learning, memory, and executive function. Chronic elevation of cortisol is associated with dendritic atrophy and synaptic loss in these areas; thus, Rhodiola's adaptogenic action indirectly preserves cognitive faculties.

At the molecular signaling level, Rhodiola impacts pathways involved in synaptic plasticity, including those mediated by brain-derived neurotrophic factor (BDNF) and cyclic AMP response element-binding protein (CREB). These factors are essential for long-term potentiation, the cellular correlate of learning and memory. By upregulating these signaling molecules, Rhodiola facilitates the strengthening of synaptic connections and cognitive resilience [30-37].

In summary, the cognitive benefits observed in clinical studies of Rhodiola rosea arise from a complex interplay of enhanced neurotransmission, improved cellular energy metabolism, antioxidant defense, and neuroendocrine regulation. This multifactorial mechanism underlines Rhodiola's potential as a natural agent for supporting mental performance, especially in populations exposed to stress and cognitive fatigue.

7. Effects on Physical Performance and Recovery

Rhodiola rosea has been extensively studied for its potential to enhance physical performance and facilitate recovery, particularly in contexts involving both aerobic and anaerobic exercise. The plant's adaptogenic properties contribute to improved endurance, strength, and resilience to fatigue, mechanisms that are of particular interest in sports medicine and physical rehabilitation.

7.1 Influence on Endurance and Strength

Studies investigating the effects of Rhodiola rosea on aerobic endurance have demonstrated significant improvements in exercise capacity and time to exhaustion. The ergogenic benefits are largely attributed to enhanced mitochondrial efficiency and increased ATP production, which translate into sustained energy availability during prolonged physical activity. Supplementation with Rhodiola rosea extracts has been shown to delay the onset of fatigue in both trained athletes and recreational exercisers. For example, experimental protocols involving treadmill running and cycling time trials report improvements in oxygen consumption efficiency and decreased lactate accumulation, which are indicative of better aerobic metabolism.

Anaerobic performance, involving short bursts of high-intensity effort, also appears to benefit from Rhodiola roseasupplementation, though the evidence is somewhat more limited and mixed. Some studies suggest increases in peak power output and muscle strength, potentially mediated by improved muscle oxygenation and reduced oxidative damage to contractile proteins. The effects on anaerobic capacity may also be influenced by the modulation of neurotransmitters involved in muscle activation and fatigue perception.

Dosage and duration of supplementation are critical factors in the manifestation of ergogenic effects. Clinical trials typically utilize standardized extracts containing specific concentrations of salidroside and rosavins, with doses ranging from 200 to 600 mg daily over periods varying from a few days to several weeks. The timing of administration relative to exercise appears to influence outcomes, with some evidence supporting acute pre-exercise dosing, while others favor chronic supplementation to build physiological resilience. The synergistic action of multiple bioactive compounds within the extract likely contributes to the variability in response and suggests that whole-plant preparations may be more effective than isolated constituents [7-11, 20-22, 29-31].

7.2 Resistance to Fatigue and Muscle Recovery

Beyond performance enhancement, Rhodiola rosea demonstrates significant potential in mitigating exercise-induced fatigue and promoting muscle recovery. Fatigue resistance is partially mediated by the plant's antioxidant capacity, which counteracts the excessive production of reactive oxygen species (ROS) generated during intense physical activity. By scavenging free radicals and upregulating endogenous antioxidant enzymes such as superoxide dismutase and catalase, Rhodiola helps preserve cellular integrity and maintain metabolic homeostasis in muscle tissue.

Markers of muscle damage, including creatine kinase (CK) and lactate dehydrogenase (LDH), are often elevated following strenuous exercise and serve as indicators of tissue injury and inflammation. Supplementation with Rhodiola rosea has been associated with reductions in these biomarkers, reflecting decreased muscle membrane disruption and improved recovery kinetics. Histological analyses in animal models support these findings, revealing attenuated muscle fiber necrosis and enhanced regeneration.

Inflammation following exercise is a natural physiological response; however, excessive or prolonged inflammation can impair recovery and performance. Rhodiola exhibits anti-inflammatory effects by modulating cytokine production, reducing levels of pro-inflammatory mediators such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6). This immunomodulatory action not only facilitates muscle repair but may also protect against chronic inflammation associated with overtraining syndromes.

Furthermore, Rhodiola rosea influences hormonal responses relevant to fatigue and recovery. Cortisol, a catabolic hormone elevated by physical stress, is often attenuated by Rhodiola supplementation, which contributes to a more favorable anabolic-catabolic balance conducive to muscle repair. The modulation of the hypothalamic-pituitary-adrenal axis by Rhodiola is consistent with its adaptogenic classification and supports resilience to both physical and psychological stressors [38].

7.3 Immunomodulation in the Context of Physical Exertion

Intense physical exercise imposes considerable stress on the immune system, often leading to transient immunosuppression and increased susceptibility to infections, particularly upper respiratory tract infections. The immunomodulatory properties of Rhodiola rosea may counteract these effects, promoting immune homeostasis during periods of heightened physical demand.

Preclinical and clinical data indicate that Rhodiola modulates both innate and adaptive immunity. It enhances the function of natural killer (NK) cells and macrophages, which are frontline defenders against pathogens, while also influencing T and B lymphocyte activity to support long-term immune competence. These effects are partly mediated through the regulation of cytokine networks, with a shift towards anti-inflammatory profiles that prevent excessive immune activation and tissue damage.

In athletes and physically active individuals, supplementation with Rhodiola rosea has been linked to a reduction in the frequency and severity of infections during intensive training cycles. This protective effect may derive from the combined antioxidant, anti-inflammatory, and hormonal regulatory actions of the phytocomplex. By attenuating exercise-induced immunosuppression, Rhodiola not only preserves health but also ensures consistent training and performance.

The immunomodulatory effects also extend to the regulation of oxidative stress within immune cells themselves, supporting their viability and function under strenuous conditions. This holistic influence on immune resilience underscores the value of Rhodiola rosea as a natural adaptogen capable of maintaining physiological balance during physical challenges [12, 37].

8. Safety, Quality Control, and Standardization

The safety profile of Rhodiola rosea has been investigated through various toxicological studies conducted both in animal models and in human populations. Animal studies generally report a wide margin of safety, with acute toxicity tests demonstrating high LD50 values, indicating low acute toxicity. Subchronic and chronic toxicity assessments have not revealed significant adverse effects at doses relevant to human use. No evidence of mutagenicity or genotoxicity has been observed in standard in vitro and in vivo assays, which further supports the plant's safety for human consumption. Studies in rodents have also evaluated reproductive and developmental toxicity, with results indicating no teratogenic or reproductive harm at typical exposure levels. These findings align with traditional use and modern clinical data, which report a favorable tolerance profile even with prolonged administration.

Human clinical trials, while often limited in size and duration, consistently report mild and infrequent adverse effects. The most common side effects include mild gastrointestinal discomfort, dizziness, and dry

mouth, but these are usually transient and resolve without intervention. There are isolated reports of allergic reactions, yet these remain rare and unpredictable. Importantly, no severe toxicities or clinically significant laboratory abnormalities have been associated with Rhodiola rosea supplementation in well-controlled clinical studies. This safety evidence supports its use as an over-the-counter nutraceutical, although caution is advised when used concomitantly with other pharmacological agents due to potential herb-drug interactions, especially involving the cytochrome P450 enzymatic system and monoaminergic neurotransmission pathways [39,40].

Despite this overall positive safety profile, concerns related to the quality and consistency of commercially available Rhodiola rosea supplements remain significant. The variability in phytochemical content across products is well-documented and primarily arises from differences in plant material origin, harvesting practices, extraction methods, and standardization protocols. The presence and concentration of key bioactive markers, notably salidroside and rosavins, can vary widely. Some supplements fail to meet pharmacopeial standards or even lack detectable levels of these compounds, undermining their efficacy and raising concerns about consumer deception. Additionally, adulteration with other Rhodiola species or unrelated plants has been reported, which further complicates quality assurance and can potentially introduce safety risks.

The lack of stringent regulatory oversight in many jurisdictions allows for such disparities, resulting in inconsistent product quality. Variations in cultivation conditions, such as altitude, soil composition, and climate, influence the phytochemical profile of Rhodiola rosea roots, and uncontrolled wild harvesting exacerbates this issue. Controlled cultivation methods have been developed to mitigate these factors, aiming to produce more consistent and standardized raw materials. Nonetheless, without uniform quality control procedures across the industry, the reproducibility of clinical effects remains questionable [41, 42].

Given these challenges, the establishment of comprehensive quality control and standardization frameworks is critical. Pharmacopeial monographs, such as those developed by the United States Pharmacopeia (USP), Russian Pharmacopoeia, and Australian standards, provide minimum thresholds for active compounds and set guidelines for extraction and preparation. However, enforcement of these standards varies, and many commercial products do not conform fully. Advanced analytical techniques, including high-performance liquid chromatography (HPLC), mass spectrometry, and nuclear magnetic resonance (NMR) spectroscopy, have been employed to authenticate extracts, quantify bioactives, and detect adulterants. Routine application of such methodologies is essential for ensuring product integrity.

Certification programs and third-party testing represent additional layers of quality assurance, offering consumers and healthcare providers confidence in supplement composition and safety. Labels indicating compliance with Good Manufacturing Practices (GMP), organic cultivation, or allergen-free status contribute to transparency. Moreover, post-market surveillance for adverse events and ongoing toxicological evaluations help identify rare safety concerns. These practices are increasingly recognized as necessary, particularly as Rhodiola rosea gains popularity worldwide.

In conclusion, while Rhodiola rosea exhibits a favorable toxicological profile supported by both preclinical and clinical data, issues related to product quality and standardization pose significant barriers to its reliable therapeutic use. The development and strict implementation of robust certification, analytical testing, and regulatory frameworks are paramount to safeguard consumers and maximize the plant's medicinal potential. Future research and policy efforts should prioritize harmonizing standards internationally and promoting transparency in the herbal supplement market to fully realize the benefits of Rhodiola rosea as a natural adaptogen [4-8, 37-42].

9. Limitations and Future Perspectives

Despite the promising results observed in both preclinical and clinical studies, the current body of evidence on Rhodiola rosea is not without limitations. A critical examination of the existing research reveals several methodological and conceptual issues that must be addressed to fully establish its efficacy, safety, and mechanisms of action.

One of the primary limitations is the heterogeneity of clinical trials in terms of study design, sample size, and endpoints. Many studies evaluating the effects of Rhodiola rosea on stress, mood, or cognitive function involve small sample sizes, often below 100 participants, which reduces statistical power and generalizability. Additionally, there is a lack of multicenter, randomized, double-blind, placebo-controlled trials that adhere to high methodological standards, making it difficult to compare results across studies or perform robust meta-analyses. Another concern is the variability in the composition and standardization of Rhodiola rosea extracts used in research. Different studies have employed a variety of commercial preparations, with varying ratios of key bioactive compounds such as salidroside and rosavins. Some products

contain a high salidroside-to-rosavin ratio, while others use a more balanced or rosavin-dominant profile. The lack of consistent phytochemical standardization creates challenges in replicating findings and drawing general conclusions about efficacy or optimal dosing. Moreover, in many clinical trials, the composition of the extract is either incompletely reported or entirely unspecified, making it impossible to assess the quality of the intervention. A further limitation involves the duration of supplementation in clinical trials. Most studies have examined short-term use, typically lasting between one to twelve weeks. While some beneficial effects may manifest within this time frame, long-term outcomes and safety profiles remain largely unknown. Chronic use of adaptogens such as Rhodiola roseamay involve complex physiological adaptations that require extended observation periods to fully understand [8, 35-43].

The inclusion criteria and participant populations used in clinical trials also contribute to the limitations of the current evidence. Many studies involve healthy volunteers or individuals with mild symptoms, which may not reflect the full spectrum of potential users, including patients with clinically significant anxiety, depression, or cognitive impairment. There is also a lack of stratification based on demographic variables such as age, sex, and ethnicity, despite evidence suggesting that these factors can influence both pharmacodynamics and therapeutic outcomes. Pharmacokinetic data on Rhodiola rosea and its major constituents remain scarce. The absorption, distribution, metabolism, and excretion (ADME) profiles of salidroside, rosavins, and other compounds are not fully characterized in humans. This gap hinders our understanding of dosage optimization, onset and duration of action, and potential for drug interactions. Additionally, studies addressing the bioavailability of specific compounds, their metabolism in the liver and brain, and their transport across the blood-brain barrier are limited and require further exploration using modern analytical tools.

There is also limited research on possible interactions between Rhodiola rosea and conventional pharmaceuticals. Given its influence on monoaminergic systems and stress-related pathways, potential interactions with antidepressants, anxiolytics, or stimulants must be carefully evaluated. This is particularly important in clinical settings where patients may be using polypharmacy. Without systematic studies, clinicians and consumers are left without clear guidelines regarding safety in these contexts. Gender-specific and age-related responses to Rhodiola rosea have not been adequately studied. Although some preclinical data suggest potential differences in hormonal modulation and stress response pathways between sexes, most human trials do not perform subgroup analyses by gender or age. This represents a missed opportunity for precision in the application of adaptogenic interventions, particularly for vulnerable populations such as older adults, adolescents, or individuals with hormonal imbalances [44, 45].

In addition to these limitations, publication bias may also influence the current body of literature. Positive findings are more likely to be published than negative or null results, which could skew the perceived effectiveness of Rhodiola rosea. Moreover, the increasing commercial interest in adaptogens might incentivize selective reporting or industry-sponsored studies, raising concerns about conflicts of interest and data transparency. Despite these limitations, the existing research provides a compelling foundation for future studies. Several promising directions can be identified. First, there is a need for large-scale, well-controlled clinical trials using standardized Rhodiola rosea extracts with clearly defined phytochemical profiles. Such trials should include diverse populations, stratified by age, sex, and relevant health conditions, and should assess both short-term and long-term outcomes. Second, pharmacokinetic and pharmacodynamic studies are urgently needed to clarify the metabolism and mechanisms of action of key constituents, as well as their interactions with human enzymes and receptors. Advances in metabolomics, proteomics, and systems biology offer powerful tools to dissect the complex interplay between Rhodiola rosea and physiological networks. Third, research should explore the potential of Rhodiola rosea in combination with other adaptogens or nootropic agents. Synergistic effects may enhance efficacy or reduce required doses, and studying such combinations could open new avenues in integrative approaches to mental health and cognitive enhancement. Fourth, preclinical models should continue to investigate mitochondrial function, oxidative stress pathways, and neuroinflammation, particularly in relation to age-related cognitive decline and neurodegenerative diseases. Rhodiola rosea may hold promise as a supportive intervention in early stages of Alzheimer's disease or other dementias, but this requires rigorous experimental validation. Finally, researchers should prioritize transparency and data sharing. The development of open-access phytochemical databases, standardized testing protocols, and independent quality control frameworks will help to reduce variability and improve the reproducibility of results across different laboratories and populations.

In conclusion, while the body of evidence supporting Rhodiola rosea is growing, critical gaps remain. Addressing these limitations will require coordinated efforts across pharmacology, clinical medicine, and systems biology. With rigorous methodology and collaborative research, the full potential of Rhodiola rosea as a natural adaptogen can be more clearly defined and responsibly applied in clinical practice [40-45].

10. Conclusions

Rhodiola rosea has emerged as one of the most extensively studied natural adaptogens, with a growing body of evidence suggesting its potential to support stress resilience, enhance mood, and improve cognitive performance. Rooted in centuries of traditional use across Eurasia, it has garnered contemporary scientific interest due to its multifaceted biological effects, low toxicity profile, and relevance to modern health challenges.

The extract of Rhodiola rosea, particularly when standardized to key bioactive compounds such as salidroside and rosavins, demonstrates measurable effects on several physiological systems implicated in the stress response. These include modulation of the hypothalamic-pituitary-adrenal axis, protection of mitochondrial function, antioxidant activity, and influence on monoaminergic neurotransmission. Such broad-spectrum actions contribute to its adaptogenic properties, allowing organisms to maintain homeostasis under a variety of psychological and physiological stressors. Clinical studies have reported improvements in symptoms of fatigue, burnout, mild to moderate depression, and cognitive impairment—especially under conditions of acute stress or sleep deprivation. Positive effects have been observed in both healthy individuals and certain patient populations, although the strength of evidence varies depending on the outcome measured and the methodological rigor of individual trials. At the same time, critical limitations remain. The heterogeneity of study designs, the inconsistent standardization of extracts, and the lack of long-term safety data underscore the need for more rigorous and coordinated research. The absence of large-scale, multicenter trials and insufficient pharmacokinetic profiling hinder the translation of findings into clinical practice. Moreover, potential drug interactions, gender-specific responses, and the effects of chronic supplementation require further investigation. Despite these gaps, the current evidence supports the cautious use of Rhodiola rosea as a well-tolerated, potentially effective intervention for managing stress-related symptoms and enhancing mental performance. It may be particularly valuable in contexts where conventional pharmacotherapy is either not indicated or poorly tolerated.

Moving forward, a more systematic, interdisciplinary research agenda is necessary to fully elucidate the therapeutic role of Rhodiola rosea. Advances in phytochemistry, molecular biology, and clinical trial design can contribute to a more nuanced understanding of this plant's adaptogenic mechanisms and its place within evidence-based integrative medicine. If such efforts are undertaken, Rhodiola rosea may find a more definitive role as a bridge between traditional wisdom and modern scientific inquiry.

Disclosure

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