KUTNIK, Karolina, SIKORA, Gabriela, WOŹNIAK, Martyna, KOGUC, Karolina, KUSIBAB, Karolina, CZECHOWSKI, Michał, SKÓRSKA, Gabriela, SŁOMIANNY, Marcela, KOLADA, Karolina and SAJDA, Małgorzata. Rhodiola rosea as a Medicinal Adaptogen: A Review of Its Antidepressant, Anti-Stress, and Performance-Enhancing Effects. Quality in Sport. 2025;46:66551. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.46.66551
https://apcz.umk.pl/QS/article/view/66551

The journal has been awarded 20 points in the parametric evaluation by the Ministry of Higher Education and Science of Poland. This is according to the Annex to the announcement of the Minister of Higher Education and Science dated 05.01.2024, No. 32553. The journal has a Unique Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).
The authors declare that there is no conflict of interest regarding the publication of this paper.
Received: 06.11.2025. Revised: 16.11.2025. Accepted: 16.11.2025. Published: 17.11.2025.

Rhodiola rosea as a Medicinal Adaptogen: A Review of Its Antidepressant, Anti-Stress, and Performance-Enhancing Effects

Karolina Kutnik

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

karolinakutnik98@gmail.com

https://orcid.org/0009-0008-2250-1232

Gabriela Sikora

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

gabriela.sikora1029@gmail.com

https://orcid.org/0009-0002-4627-7403

Martyna Woźniak

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

m.wozniak912@gmail.com

https://orcid.org/0009-0002-2518-4531

Karolina Koguc

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

karolinakoguc@gmail.com

https://orcid.org/0009-0004-0762-7356

Karolina Kusibab

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

karolinakusibab00@gmail.com

https://orcid.org/0009-0004-9743-8734

Michał Czechowski
Medical University of Silesia, Poniatowskiego 15, 40-055 Katowice, Poland
michat.czechowski@gmail.com
https://orcid.org/0009-0009-7038-6731

Gabriela Skórska
Medical University of Silesia, Poniatowskiego 15, 40-055 Katowice, Poland
gabrielaskorska12@gmail.com
https://orcid.org/0009-0008-2197-3414

Marcela Słomianny
Medical University of Silesia, Poniatowskiego 15, 40-055 Katowice, Poland
slomiannymarcela@gmail.com
https://orcid.org/0009-0004-8029-1422

Karolina Kolada
Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland
karolinakolada2001@gmail.com
https://orcid.org/0009-0005-4960-9604

Małgorzata Sajda
Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland
m.skura15@gmail.com
https://orcid.org/0009-0004-6836-0704

Abstract

Background: *Rhodiola rosea* L. is a traditional medicinal plant recognized for its adaptogenic properties, particularly in enhancing the body's resistance to physical, chemical, and biological stress. Its pharmacological activity has been attributed mainly to phenylpropanoids such as rosavin and salidroside, which influence stress adaptation mechanisms and central neurotransmission.

Aim: The review of the pharmacological action, bioactive compounds, and therapeutic applications of *Rhodiola rosea*, with a particular focus on its potential role in supporting physical and mental performance under stress-related conditions.

Methodology: A review was conducted using PubMed and Google Scholar. Studies investigating the chemical composition, mechanisms of action, and effects of *Rhodiola rosea* on stress, fatigue, cognitive function, and homeostasis were analyzed and synthesized.

Results: *Rhodiola rosea* has demonstrated benefits in reducing fatigue, improving cognitive function, enhancing physical performance, and stabilizing mood. It also possesses a favorable safety profile, with minimal adverse effects.

Conclusions: *Rhodiola rosea* represents a well-tolerated and biologically active adaptogen with promising applications in managing stress-related fatigue and enhancing resilience to physical and psychological challenges. Further controlled clinical trials are warranted to define its efficacy, optima dosage, and mechanisms of action more precisely.

Keywords: *Rhodiola rosea*, adaptogen, depression, stress, anxiety, physical activity, salidroside, rosavin, cognitive function

1. Introduction

Adaptogens are a unique class of natural compounds known for their ability to enhance the body's resilience to various stressors, including physical, chemical, and biological challenges. These substances have garnered considerable interest in recent years due to their potential in improving mental and physical performance, reducing fatigue, and supporting overall homeostasis [1,2,3]. Originally rooted in traditional medicine systems, adaptogens have been extensively studied to understand their molecular mechanisms and clinical benefits.

The concept of adaptogens emerged from research aimed at identifying substances that promote nonspecific resistance to stress, thereby improving the organism's ability to adapt without causing harm or over-stimulation [1,3]. Key adaptogenic plants, such as *Rhodiola rosea*, *Withania somnifera* (Ashwagandha), and *Eleutherococcus senticosus*, contain bioactive compounds that modulate stress-response pathways, including neuroendocrine and immune systems. These plants have demonstrated efficacy in reducing stress-induced fatigue, enhancing cognitive function, and supporting mood stabilization [4,5].

At the molecular level, adaptogens influence several signaling pathways involved in cellular stress responses, such as the hypothalamic-pituitary-adrenal (HPA) axis and oxidative stress regulation [6,7]. Their multifaceted actions include antioxidant effects, modulation of neurotransmitter levels, and regulation of gene expression related to inflammation and apoptosis [4]. These effects contribute to the normalization of physiological functions during periods of increased stress.

Current research emphasizes the importance of standarized extracts and well-characterized bioactive markers to ensure consistent efficacy and safety of adaptogenic preparations [8].

Moreover, emerging evidence from clinical trials suggests that adaptogens may serve as effective complementary agents in managing chronic stress-related conditions and fatigue syndromes [9]. Despite the growing body of evidence, further investigations are necessary to elucidate precise mechanisms and optimize therapeutic protocols.

In summary, adaptogens represent promising natural compounds with significant potential to enhance resilience to stress through complex biochemical and physiological interactions. This work aims to provide a comprehensive review of their mechanisms of action, focusing on recent advances and integrating molecular insights with clinical observations.

2. Methodology

This narrative review was conducted to synthesize current knowledge on the pharmacological properties, adaptogenic mechanisms, and therapeutic applications of *Rhodiola rosea*. Relevant scientific literature was identified through a comprehensive search of databases including PubMed and Google Scholar. Keywords used in the search included: *Rhodiola rosea*, adaptogen, salidroside, rosavin, stress, fatigue, cognitive function, physical activity. Studies published between the years 2000 and 2024 were considered for inclusion in the review. Particular emphasis was placed on research examining the extract's effects on stress-related fatigue, cognitive performance, mood regulation, and physiological adaptation to external stressors.

3. Botanical and Phytochemical Profile

Rhodiola rosea L., commonly known as golden root or Arctic root, is a perennial flowering plant belonging to the *Crassulaceae* family. It naturalny grows in cold regions such as the Arctic, mountainous areas of Europe, and Asia [1]. The plant is characterized by its fleshy root system, which is the main part used in traditional medicine. *R. rosea* thrives in harsh environmental conditions, including high altitude and cold temperatures, which contribute to its unique biochemical composition [10].

Historically, *R. rosea* has been used for centuries in traditional medicine systems across Russia, Scandinavia, and China to combat fatigue, improve physical endurance, and enhance mental performance [11]. It has also been employed as an adaptogen, a substance believed to help the body resist physical, chemical, and biological stressors [12].

The pharmacological properties of *R. rosea* are primarily attributed to its complex mixture of bioactive compounds [13]. The most studied bioactive components include phenylpropanoids, salidroside, flavonoids, phenolic acids. Rosavin, rosin, and rosarin are considered marked compounds of *R. rosea*. These phenylpropanoids are often used to standardize extracts [14]. Salidroside is a glycoside with significant antioxidant and neuroprotective properties, playing a key role in the plant's adaptogenic effects [1]. Flavonoids such as quercetin and kaempferol derivatives, contributing to the anti-inflammatory and antioxidant activity [10]. Phenolic acids including gallic and chlorogenic acids, which exhibit free radical scavenging abilities [1].

The content of active compounds in *R. rosea* can vary significantly depending on factors such as geographic origin, harvest time, and extraction methods [15]. Standardized extracts typically contain 3% rosavins and 1% salidroside to ensure consistent pharmacological activity [12].

Several analytical methods have been developed for the identification and quantification of *R. rosea* constituents. The most widely used technique is high-performance liquid chromatography (HPLC) [14]. Additionally, mass spectrometry and nuclear magnetic resonance (NMR) spectroscopy provide structural information critical for confirming compound identity [10].

4. Mechanisms of Action

Rhodiola rosea is classified as a powerful adaptogen due to its ability to enhance the body's resistence to various stressors – whether physical, chemical, or biological. This effect is primarily attributed to the modulation of the hypothalamic–pituitary–arenal (HPA) axis, which plays a central role in managing the stress response through cortisol regulation [1,16]. By helping to maintain stable cortisol levels, *Rhodiola* supports physiological balance (homeostasis) and helps prevent early depletion of energy resources during prolonged stress.

Furthermore, *R. rosea* influences brain chemistry by modulating levels of key neurotransmitters, particularly serotonin, dopamine, and norepinephrine. These changes contribute to improved mood, reduced anxiety, and enhanced resistance to mental fatigue [10,17]. One proposed mechanism involves the inhibition of monoamine oxidase (MAO), the enzyme responsible for breaking down these neurotransmitters, resulting in higher concentrations in the brain. Moreover, *Rhodiola* appears to stabilize the GABAergic system,

promoting a calming effect and better sleep quality. Together, these action support better cognitive functioning, increased focus, and sustained mental energy throughout the day [12].

Rhodiola improves the body's readiness for stress without overstimulating the nervous system. This differentiates *Rhodiola* from many other stimulatory adaptogens and explains its popularity in enhancing physical performance and reducing perceived fatigue during intense exertion [17].

One of the most notable features of *R. rosea* is its neuroprotective capacity, largely driven by its active compounds – particularly salidroside. This phytochemical contributes to the protection of neurons against oxidative damage and inflammation [4]. Research shows that salidroside supports neurogenesis and synaptic plasticity, which are essential for memory retention and cognitive function [12].

The plant also exhibits anti-inflammatory effects by suppressing key signaling pathways involved in cytokine production, particularly those related to TNF-α, IL-6, and IL-1β [18]. This effect is largely attributed to inhibition of the transcription factor NF-κB, a central regulator of inflammation [19].

Reducing systemic inflammation is critical in preventing and managing chronic inflammatory diseases such as arthritis, cardiovascular disorders, and neuroinflammation. Notably, these anti-inflammatory effects often act synergistically with *Rhodiola*'s antioxidant activity, reinforcing its protective role at the cellular level [20].

Animal studies also suggest that salidroside may reduce neuronal apoptosis triggered by toxic stimuli, making it a promising agent in the context of neurodegenerative disease prevention, including Alzheimer's disease. Additionally, *Rhodiola* enhances cerebral blood flow, improving the delivery of oxygen and nutrients to the brain, which may account for observed improvements in alertness and mental clarity [21,22,23].

R. rosea has emerged as a potential natural selective estrogen receptor modulator (SERM) with relevance for managing menopause-related symptoms. Evidence suggests that its bioactive constituents, particularly salidroside, interact selectively with estrogen receptor subtypes, preferentially activating ERβ pathways. This selective modulation may afford neuroprotective, cardioprotective, and osteoprotective benefits without eliciting the proliferative effects on reproductive tissues that are commonly associated with conventional hormone replacement therapy [24].

The antioxidant properties of *R. rosea* are rooted in its rich content of phenolic compounds such as rosavin, salidroside, and a variety of flavonoids. These compounds help neutralize reactive oxygen species (ROS), thereby protecting lipids, and DNA from oxidative damage [10].

In addition to its direct antioxidant effects, *Rhodiola* boosts the activity of endogenous antioxidant enzymes like superoxide dismutase (SOD), catalase, and glutathione peroxidase. This dual mechanism strengthens the body's natural defense system, which may slow cellular aging and reduce the risk of chronic diseases associated with oxidative stress, such as cardiovascular conditions and metabolic disorders [22,25].

R. rosea supports cardiovascular health through several interrelated mechanisms. It enhances myocardial energy metabolism and protects heart cells from ischemic damage [1]. Its active compounds improve oxygen utilization by cardiac muscle cells, increasing their efficiency and resilience under stress [26].

In paralel, the plant's antioxidant and anti-inflammatory actions help preserve endothelial integrity, reduce oxidative stress in blood vessels, and lower the risk of atherosclerosis. Some studies suggest that *Rhodiola* may also contribute to improved lipid profiles and reduced cholesterol levels, further enhancing its cardiovascular benefits [10,27,28].

5. Antidepressant Effects

Rhodiola rosea has shown promising antidepressant properties in both clinical and preclinical contexts, primarily through multiple complex mechanisms that influence mood and emotional regulation.

Key active constituents in *R. rosea* – namely salidroside and rosavin – are believed to enhance mood by modulating levels of serotonin, dopamine, and norepinephrine in the brain. These compounds have been show to inhibit monoamine oxidase (MAO), the enzyme responsible for breaking down these neurotransmitters, resulting in elevated synaptic concentrations associated with positive mood states and reduced depressive symptoms [29,30,31].

Chronic stress frequently causes HPA-axis dysregulation, leading to persistently elevated cortisol levels – a hallmark of many depressive disorders. *R rosea* has been shown to offset this imbalance, reducing excessive cortisol release and normalizing HPA function. There effects contribute to its antidepressant action, as supported by controlled clinical investigations [32,33].

Adaptogens like *R. rosea* and related plants have been shown to upregulate protective proteins such as heat-shock protein 72 (Hsp72), boosting cellular resilience to stressors [29]. Additionally, neuroprotective mechanisms – including stimulation of neurogenesis and mitigation of oxidative damage – further suport mood stability and resilience [29,34].

Several randomized clinical trials have examined *R. rosea*'s effects on depression. A 12-week, double-blind, placebo-controlled trial in mild-to-moderate depression showed significant improvement using standardized *R. rosea* extract compared to placebo, with reductions in depression scale stores [35].

In a comparative trial against sertraline, both treatments reduced depressive symptoms; although sertraline was slightly more effective, R. rosea demonstrated better tolerability [36]. Synergistic benefits were observed in studies where *R. rosea* was combined with sertraline, resulting in enhanced symptom relief compared to either treatment alone [37]. These studies used extract doses ranging from 340 to 680 mg per day over 6 to 12 weeks. Despite some inconsistencies, results generalny indicato meaningful mood improvements and favorable safety profiles [35,36,37].

R. rosea has been well tolerated with few reported side effects, primarily mild gastrointestinal disturbances or headache. Its side effect profile compares favorably with standard antidepressants, with the added advantage of lower risk of sedation or sexual dysfunction [38].

Despite encouraging data, limitations exist: many clinical trials feature small sample sizes and limited duration, with varying extract formulations and dosage regimens. Consequently, clinical guidelines (e.g. CANMAT) do not currently endorse *R. rosea* as a first-line treatment for major depressive dis order [39]. More rigorous, large-scale randomized controlled trials are required to firmy establish it as a viable antidepressant option.

6. Antistress and Anxiolytic Properties

Rhodiola rosea is a well-studied adaptogenic plant recognized for its ability to enhance the body's resilience to various stressors. Its psychotropic activity is associated with modulating the hypothalamic–pituitary–arenal (HPA) axis, regulating neurotransmitter levels, and improving cellular stress responses [32,33].

Chronic stress disrupts the function of the HPA axis, leading to elevated cortisol levels and impaired feedback mechanisms. Animal studies indicate that administration of *R. rosea* extracts

reduces plasma corticosterone and corticotropin-releasing factor (CRF), potentially normalizing stress responses by modulating glucocorticoid receptor expression in the brain [40]. Furthermore, it was shown to attenuate stress-induced activation of the locus coeruleus and amygdala – key regions involved in anxiety and arousal [1,40].

The adaptogenic effects of *R. rosea* are partially attributed to upregulation of cellular protective proteins such as heat shock proteins (Hsp70), which are involved in maintaining protein integrity during stress exposure. Salidroside, a key bioactive compound in *R. rosea*, also influences redox balance by enhancing antioxidant enzyme activity and reducing oxidative stress markers in the central nervous system [40,41]. This molecular activity supports neuronal survival under stress conditions and contributes to its anxiolytic properties.

In a 10-week open-label pilot trial, patients with generalized anxiety disorder (GAD) who received 340 mg per day of *R. rosea* extract experienced moderate improvements in anxiety symptoms as assessed by the Hamilton Anxiety Rating Scale (HAM-A) [40]. Although limited by the lack of a control group, the results suggest therapeutic potential for anxiety-related disorders.

Another randomized, placebo-controlled study involving individuals with mild anxiety symptoms demonstrated that a two-week supplementation with 400 mg per day of *R. rosea* significantly reduced scores related to anxiety, stress, anger, and confusion [42]. Participants also reported improved mental performance under stress, supporting its application in occupational or academic stress contexts.

A multicenter, open-label trial suggests that daily supplementation of *R. rosea* extract over 12 weeks may significantly reduce burnout-related symptoms – especially fatigue, stress perception, and emotional exhaustion – often within the first week. It also supports improvements in mood, sexual health, cognitive alertness, and daily functioning [43].

R. rosea demonstrates a high safety profile in human studies. Adverse events are rare and typically mild, such as transient dizziness or dry mouth. Compared to pharmaceutical anxiolytics, the absence of sedative effects or dependency risk makes it a promising alternative for long-term use in stress and anxiety management [40,42,44].

7. Effects on Physical and Cognitive Performance

Rhodiola rosea is widely studied for its capacity to improve both physical endurance and cognitive functions, particularly under conditions of stress and fatigue.

Studies have shown that *R. rosea* supplementation can improve physical endurance by reducing perceived exertion and enhancing recovery. In randomized controlled trials, subjects receiving standarized *R. rosea* extract demonstrated increased time to exhaustion during exercise tests compared to placebo [35]. The adaptogenic properties are attributed to improved mitochondrial efficiency and reduced oxidative damage in muscle tissues, resulting in better energy metabolism [1]. Several studies have demonstrated that *R. rosea* supplementation leads to significant reductions in biomarkers indicative of muscle damage and inflammation. Specifically, decreases in C-reactive protein (CRP) were observed at 5 hours and 5 days post-exercise. Additionally, reductions in lactate and creatine kinase (CK) levels were particularly evident in trained athletes [45].

Moreover, *R. rosea* may contribute to faster recovery by modulating stress hormones such as cortisol, which typically increase during intense physical activity. Reduced cortisol levels lead to less muscle catabolism and inflammation, thus supporting better regeneration after excersise [41].

Cognitive performance, particularly attention, memory, and mental fatigue, can be impaired under stress. Clinical studies reveal that *R. rosea* intake improves mental performance during fatigue-inducing conditions by enhancing focus, memory recall, and mental endurance [42]. For instance, participants undergoing mentalny demanding tasks showed faster reaction times and better accuracy after *R. rosea* supplementation compared to placebo [46].

These cognitive benefits are linked to *R.rosea*'s ability to modulate neurotransmitter systems which play key roles in attention and mood regulation [40]. Furthermore, by reducing the subjective feeling of fatigue, *R. rosea* helps sustain cognitive function in stressful or exhausting situations [42].

At the cellular level, salidroside and rosavin – the main active compound of *R. rosea* – have antioxidant and anti-inflammatory effects that protect neurons from damage incuced by oxidative stress [1]. These effects preserve brain function and support sustained cognitive activity. Animal models have demonstrated that *R. rosea* reduces markers of oxidative stress and improves neurotransmitter balance in brain regions responsible for learning and memory [41].

In a study involving physical exercise, *R. rosea* extract improved endurance by approximately 20% and reduced fatigue perception [35]. Cognitive tests performer during periods of mental stress showed significant improvements in concentration and memory recall

after supplementation with *R. rosea* [42,46]. Daily dosing (1,500-2,400 mg/day) for 4-30 days demonstrated ergogenic effects in both trained and untrained adults – improving sprint cycles and resistance-training performance [47].

Variability in results across studies may be due to differences in dosage, bioactive compound content, participant fitness, and exercise type. No significant adverse effects were reported, supporting its use as a safe cognitive and physical enhancer [35,42,47].

8. Summary of Medical Applications and Clinical Relevance

Rhodiola rosea has been widely studied for its potential to address various medical conditions, particularly those related to stress, fatigue, mood disorders, and cognitive impairment. As an adaptogen, it supports the body's resilience to physical and psychological stressors, thus improving overall health and functional capacity.

One of the most prominent clinical applications of *R. rosea* is in the treatment of fatigue and burnout syndrome. Clinical trials have demonstrated that supplementation with *Rhodiola* extracts can significantly reduce symptoms of chronic fatigue and improve energy metabolism in affected individuals [4,33,43]. These effects are attributed to its ability to modulate stress hormones such as cortisol and enhance mitochondrial function, resulting in improved cellular energy production [6,10].

Moreover, *R. rosea* exhibits antidepressant and anxiolytic properties, which have been validated in randomized controlled trials. Patients suffering from mild to moderate depression reported improved mood, reduced anxiety, and enhanced quality of life following *Rhodiola* administration, with a favorable safety profile [35,38].

R. rosea shows potential as a complementary treatment for insomnia, primarily due to its adaptogenic effects that mitigate stress and improve overall sleep quality [48].

In the realm of cognitive performance, *Rhodiola* has shown promise in enhancing mental clarity, focus, and memory. Several studies indicato that *Rhodiola* supplementation can improve cognitive function, especially under stressful conditions, by reducing mental fatigue and supporting neuroplasticity [49]. These benefits make it a candidate for adjunct therapy in neurodegenerative diseases and age-related cognitive decline [21]. Some results underscore the therapeutic potential of salidroside as a promising candidate for mitigating neurodenegeration associated with Parkinson's disease [50].

Beyond neuropsychiatric conditions, *Rhodiola*'s adaptogenic effects extend to cardiovascular health, where it contributes to improved endurance and recovery in patients with ischemic heart disease. It exerts cardioprotective effects through anti-inflammatory and antioxidant pathways, potentially lowering the risk of cardiac events during stress [10,51].

Research on *R. rosea* extract in experimental models of arthritis indicates that its administration leads to a significant reduction in clinical symptoms and histopathological markers of joint inflammation, accompanied by downregulation of key pro-inflammatory cytokines. These results support the potential of *R. rosea* as an adjunctive therapeutic agent in the treatment of inflammatory conditions such as rheumatoid arthritis [52].

R. rosea shows promising anticancer properties through antioxidant protection, inflammation reduction, apoptosis induction, and tumor suppression in preclinical studies. While not a cure or standalone therapy, it may have preventive or supportive benefits in cancer care, pending further human research [43].

Salidroside confers neuroprotective effects in a rat model of cerebral ischemia/reperfusion injury, primarily through the modulation of oxidative stress pathways and the dopaminergic system. These findings underscore the potential of salidroside as a therapeutic candidate for the treatment of ischemic stroke [53].

R. rosea is increasingly recognized as a natural compound with selective estrogen receptor modulating properties, potentially beneficial in addressing menopausal symptoms [24].

The clinical relevance of *R. rosea* is further supported by its minimal adverse effects and low toxicity profile, which contrast favorably with conventional pharmacological agents used in managing depression and fatigue [10,41]. This makes it an attractive complementary treatment option in integrative medicine.

In summary, *R. rosea*'s multifaceted pharmacological action underpin its medical applications, particularly in stress-related disorders, mood regulation, cognitive enhancement, and cardiovascular support. Ongoing research continues to elucidate its full therapeutic potential and optimize its clinical use.

9. Limitations and Future Perspectives

Despite the promising therapeutic potential of *Rhodiola rosea*, several limitations currently restrict its broader clinical application and understanding. One major challenge is the variability in the quality and standarization of *Rhodiola* extracts used across different studies.

Differences in extraction methods, plant origin, and active compound concentrations (such as rosavin and salidroside) can significantly impact the consistency and reproducibility of clinical outcomes [1,33]. This variability complicates direct comparison of results and the formulation of standarized dosing guidelines.

Another limitation lies in the relatively small scale and heterogeneity of clinical trials investigating *Rhodiola*'s effects. Many studies suffer from limited sample sizes, short intervention durations, and diverse participant populations, which can restrict the generalizability of findings [35,38]. Furthermore, most trials have focused on mild to moderate conditions, leaving a gap in knowledge about *Rhodiola*'s efficacy in severe or chronic illnesses, as well as its long-term safety profile [54].

While the molecular mechanisms underlying *Rhodiola*'s adaptogenic effects have been partially elucidated, there is still incomplete understanding of its pharmacodynamics and interactions with other medications, especially in populations with comorbidities or polypharmacy [6]. More comprehensive pharmacokinetic and mechanistic studies are needed to optimize therapeutic regimens and ensure safety.

Looking forward, future research should prioritize large-scale, multicenter, randomized controlled trials with standardized *Rhodiola* preparations to validate clinical efficacy and establish evidence-based dosing recommendations. Investigating *Rhodiola*'s potential synergistic effects with conventional therapies could also enhance its application in integrative medicine [55]. Additionally, exploring its benefits in neurodegenerative diseases, cardiovascular conditions, and immune regulation presents promising avenues for expanding its clinical relevance [1,40,41].

Advancements in bioanalytical techniques and molecular biology will further elucidate *Rhodiola*'s bioactive compounds and their mechanisms of action, potentially leading to the development of novel derivatives or formulations with improved efficacy and safety profiles. Moreover, personalized medicine approaches considering genetic, metabolic, and environmental factors may optimize *Rhodiola*-based interventions tailored to individual patient needs [1,13,40].

In conclusion, while *R. rosea* shows significant potential as an adaptogen with diverse medical applications, addressing current limitations through rigorous research will be essential to fully harness its therapeutic benefits and integrate it into mainstream clinical practice.

10. Conclusions

Rhodiola rosea is a promising adaptogenic herb with a broad spectrum of beneficial effects on physical and cognitive performance, stress resilience, and overall health. The accumulated evidence from clinical and preclinical studies demonstrates its potential in alleviating fatigue, improving mood disorders such as mild to moderate depression, and enhancing cognitive functions, especially under stress [4,12,33]. Its pharmacological actions – mediated through modulation of stress hormones, neurotransmitter systems, mitochondria protection, and antioxidant effects – provide a plausible biological basis for its efficacy [6,35,46].

Moreover, *R. rosea*'s favorable safety profile and low toxicity make it an attractive adjunct or alternative to conventional therapies for stress-related conditions and neuropsychiatric disorders [36,38]. Its role in supporting cardiovascular health and potentially slowing cognitive decline in aging and neurodegeneration further expands its clinical relevance [13,33,40,41].

Despite these positive findings, limitations such as variability in extract standarization, limited large-scale clinical trials, and incomplete understanding of its pharmacokinetics and long-term effects call for further rigorous research [12,40,41]. Future studies should focus on optimizing dosing regiments, confirming efficacy in diverse populations, and exploring synergistic use with established therapies.

In conclusion, *R. rosea* stands out as a valuable natural adaptogen with multifaceted therapeutic applications. Continued investigation and standarized clinical evaluation will be crucial for integrating this ancient medicinal plant into modern evidence-based medical practice.

Disclosure:

Author Contribution Statement

Conceptualization: Karolina Kutnik, Gabriela Sikora, Karolina Kusibab, Karolina Kolada;

Methodology: Karolina Kutnik, Martyna Woźniak, Gabriela Skórska

Formalanalysis: Karolina Koguc, Karolina Kolada

Investigation: Martyna Woźniak, Gabriela Sikora, Marcela Słomianny, Karolina Kutnik, Karolina Kolada, Karolina Koguc, Karolina Kusibab, Michał Czechowski, Gabriela Skórska

Resources: Karolina Kutnik

Data curation: Karolina Kutnik, Martyna Woźniak, Gabriela Skórska, Marcela Słomianny

Writing – rough preparation: Karolina Kutnik, Gabriela Sikora, Marcela Słomianny, Karolina Kusibab, Karolina Kolada, Karolina Koguc, Michał Czechowski, Gabriela Skórska, Martyna Woźniak

Writing – review and editing: Karolina Kolada, Karolina Kutnik, Gabriela Sikora

Visualization: Martyna Woźniak, Michał Czechowski

Supervision: Karolina Kutnik, Karolina Koguc, Karolina Kusibab

Project administration: Karolina Kutnik

All authors have read and agreed with the published version of the manuscript.
Funding Statement. The authors did not receive special funding.
Institutional Review Board Statement: Not applicable.
Informed Consent Statement: Not applicable.
Data Availability Statement: Not applicable.
Conflict of Interest Statement: The authors declare no conflict of interest.

References

1. Panossian A, Wikman G. Effects of Adaptogens on the Central Nervous System and the Molecular Mechanisms Associated with Their Stress-Protective Activity. Pharmaceuticals (Basel). 2010, 3(1), 188–224. https://doi.org/10.3390/ph3010188

2. Panossian AG, Efferth T, Shikov AN, et al. Evolution of the adaptogenic concept from traditional use to medical systems: Pharmacology of stress- and aging-related diseases. Med Res Rev. 2021;41(1):630-703. https://doi.org/10.1002/med.21743

3. Panossian A. Understanding adaptogenic activity: specificity of the pharmacological action of adaptogens and other phytochemicals. *Ann N Y Acad Sci*. 2017;1401(1):49-64. https://doi.org/10.1111/nyas.13399

4. Panossian A, Wikman G. Evidence-based efficacy of adaptogens in fatigue, and molecular mechanisms related to their stress-protective activity. Curr Clin Pharmacol. 2009 Sep;4(3):198-219. https://doi.org/10.2174/157488409789375311

5. Kennedy DO, Scholey AB. The psychopharmacology of European herbs with cognition-enhancing properties. Curr Pharm Des. 2006;12(35):4613-4623. https://doi.org/10.2174/138161206779010387

6. Panossian A, Wikman G, Kaur P, Asea A. Adaptogens exert a stress-protective effect by modulation of expression of molecular chaperones. Phytomedicine. 2009;16(6-7):617-622. https://doi.org/10.1016/j.phymed.2008.12.003

7. Szopa A, Ekiert R, Ekiert H. Current knowledge of Schisandra chinensis (Turcz.) Baill. (Chinese magnolia vine) as a medicinal plant species: a review on the bioactive components, pharmacological properties, analytical and biotechnological studies. Phytochem Rev. 2017;16(2):195-218. https://doi.org/10.1007/s11101-016-9470-4

8. Zeng J, Tan M, Peng X, Luo Q. (2011). Standardization and Quality Control of Herbal Extracts and Products. Traditional Herbal Medicine Research Methods. 2011. https://doi.org/10.1002/9780470921340.ch9

9. Tóth-Mészáros A, Garmaa G, Hegyi P, Bánvölgyi A, Fenyves B, Fehérvári P, Harnos A, Gergő D, Nguyen Do To U, Csupor D. The effect of adaptogenic plants on stress: A systematic review and meta-analysis. Journal of Functional Foods. 2023;108,105695. https://doi.org/10.1016/j.jff.2023.105695

10. Bernatoniene J, Jakstas V, Kopustinskiene DM. Phenolic Compounds of Rhodiola rosea L. as the Potential Alternative Therapy in the Treatment of Chronic Diseases. Int J Mol Sci. 2023;24(15):12293. https://doi.org/10.3390/ijms241512293

11. Ivanova Stojcheva E, Quintela JC. The Effectiveness of *Rhodiola rosea L*. Preparations in Alleviating Various Aspects of Life-Stress Symptoms and Stress-Induced Conditions-Encouraging Clinical Evidence. Molecules. 2022;27(12):3902. https://doi.org/10.3390/molecules27123902

12. Panossian A, Wikman G, Sarris J. Rosenroot (*Rhodiola rosea*): traditional use, chemical composition, pharmacology and clinical efficacy. Phytomedicine. 2010;17(7):481-493. https://doi.org/10.1016/j.phymed.2010.02.002

13. Chiang HM, Chen HC, Wu CS, Wu PY, Wen KC. *Rhodiola* plants: Chemistry and biological activity. J Food Drug Anal. 2015;23(3):359-369. https://doi.org/10.1016/j.jfda.2015.04.007

14. Ganzera M, Yayla Y, Khan IA. Analysis of the marker compounds of *Rhodiola rosea L*. (golden root) by reversed phase high performance liquid chromatography. Chem Pharm Bull (Tokyo). 2001;49(4):465-467. https://doi.org/10.1248/cpb.49.465

15. Elameen A, Kosman VM, Thomsen M, Pozharitskaya ON, Shikov AN. Variability of Major Phenyletanes and Phenylpropanoids in 16-Year-Old *Rhodiola rosea L*. Clones in Norway. Molecules. 2020;25(15):3463. https://doi.org/10.3390/molecules25153463

16. Panossian A, Hambardzumyan M, Hovhanissyan A, Wikman G. The adaptogens *rhodiola* and schizandra modify the response to immobilization stress in rabbits by suppressing the increase of phosphorylated stress-activated protein kinase, nitric oxide and cortisol. *Drug Target Insights*. 2007;2:39-54. https://doi.org/10.1177/117739280700200011

17. Ivanova Stojcheva E, Quintela JC. The Effectiveness of *Rhodiola rosea L*. Preparations in Alleviating Various Aspects of Life-Stress Symptoms and Stress-Induced Conditions-Encouraging Clinical Evidence. Molecules. 2022;27(12):3902. https://doi.org/10.3390/molecules27123902

18. Lee Y, Jung JC, Jang S, et al. Anti-Inflammatory and Neuroprotective Effects of Constituents Isolated from *Rhodiola rosea*. Evid Based Complement Alternat Med. 2013;2013:514049. https://doi.org/10.1155/2013/514049

19. Xu W, Yang T, Zhang J, Li H, Guo M. *Rhodiola rosea*: a review in the context of PPPM approach. EPMA J. 2024;15(2):233-259. https://doi.org/10.1007/s13167-024-00367-3

20. Pu WL, Zhang MY, Bai RY, et al. Anti-inflammatory effects of *Rhodiola rosea L.*: A review. Biomed Pharmacother. 2020;121:109552. https://doi.org/10.1016/j.biopha.2019.109552

21. Zhang N, Nao J, Dong X. Neuroprotective Mechanisms of Salidroside in Alzheimer's Disease: A Systematic Review and Meta-analysis of Preclinical Studies. J Agric Food Chem. 2023;71(46):17597-17614. https://doi.org/10.1021/acs.jafc.3c06672

22. Zhuang W, Yue L, Dang X, et al. Rosenroot (*Rhodiola*): Potential Applications in Aging-related Diseases. Aging Dis. 2019;10(1):134-146. https://doi.org/10.14336/AD.2018.0511

23. Wang H, Li Q, Sun S, Chen S. Neuroprotective Effects of Salidroside in a Mouse Model of Alzheimer's Disease. *Cell Mol Neurobiol*. 2020;40(7):1133-1142. https://doi.org/10.1007/s10571-020-00801-w

24. Gerbarg PL, Brown RP. Pause menopause with *Rhodiola rosea*, a natural selective estrogen receptor modulator. *Phytomedicine*. 2016;23(7):763-769. https://doi.org/10.1016/j.phymed.2015.11.013

25. Calcabrini C, De Bellis R, Mancini U, et al. *Rhodiola rosea* ability to enrich cellular antioxidant defences of cultured human keratinocytes. Arch Dermatol Res. 2010;302(3):191-200. https://doi.org/10.1007/s00403-009-0985-z

26. Chen Y, Tang M, Yuan S, et al. *Rhodiola rosea*: A Therapeutic Candidate on Cardiovascular Diseases. Oxid Med Cell Longev. 2022;2022:1348795. https://doi.org/10.1155/2022/1348795

27. Leung SB, Zhang H, Lau CW, Huang Y, Lin Z. Salidroside improves homocysteine-induced endothelial dysfunction by reducing oxidative stress. Evid Based Complement Alternat Med. 2013;2013:679635. https://doi.org/10.1155/2013/679635

28. Zhou Q, Han X, Li R, et al. Anti-atherosclerosis of oligomeric proanthocyanidins from *Rhodiola rosea* on rat model via hypolipemic, antioxidant, anti-inflammatory activities together with regulation of endothelial function. Phytomedicine. 2018;51:171-180. https://doi.org/10.1016/j.phymed.2018.10.002

29. Panossian A, Wikman G, Kaur P, Asea A. Adaptogens stimulate neuropeptide y and hsp72 expression and release in neuroglia cells. Front Neurosci. 2012;6:6. https://doi.org/10.3389/fnins.2012.00006

30. Dimpfel W, Schombert L, Panossian AG. Assessing the Quality and Potential Efficacy of Commercial Extracts of *Rhodiola rosea L*. by Analyzing the Salidroside and Rosavin Content and the Electrophysiological Activity in Hippocampal Long-Term Potentiation, a Synaptic Model of Memory. Front Pharmacol. 2018;9:425. https://doi.org/10.3389/fphar.2018.00425

31. Yang Z, Huang X, Lai W, et al. Synthesis and identification of a novel derivative of salidroside as a selective, competitive inhibitor of monoamine oxidase B with enhanced neuroprotective properties. Eur J Med Chem. 2021;209:112935. https://doi.org/10.1016/j.ejmech.2020.112935

32. Dinel AL, Guinobert I, Lucas C, et al. Reduction of acute mild stress corticosterone response and changes in stress-responsive gene expression in male Balb/c mice after repeated administration of a *Rhodiola rosea L*. root extract. Food Sci Nutr. 2019;7(11):3827-3841. https://doi.org/10.1002/fsn3.1249

33. Olsson EM, von Schéele B, Panossian AG. A randomised, double-blind, placebo-controlled, parallel-group study of the standardised extract shr-5 of the roots of *Rhodiola rosea* in the treatment of subjects with stress-related fatigue. Planta Med. 2009;75(2):105-112. https://doi.org/10.1055/s-0028-1088346

34. Burns J. Common herbs for stress: The science and strategy of a botanical medicine approach to self-care. J Interprof Educ Pract. 2023;30:100592. https://doi.org/10.1016/j.xjep.2022.100592

35. Darbinyan V, Aslanyan G, Amroyan E, Gabrielyan E, Malmström C, Panossian A. Clinical trial of *Rhodiola rosea L*. extract SHR-5 in the treatment of mild to moderate depression

[published correction appears in Nord J Psychiatry. 2007;61(6):503]. Nord J Psychiatry. 2007;61(5):343-348. https://doi.org/10.1080/08039480701643290

36. Mao JJ, Xie SX, Zee J, et al. *Rhodiola rosea* versus sertraline for major depressive disorder: A randomized placebo-controlled trial. Phytomedicine. 2015;22(3):394-399. https://doi.org/10.1016/j.phymed.2015.01.010

37. Gao L, Wu C, Liao Y, Wang J. Antidepressants effects of *Rhodiola* capsule combined with sertraline for major depressive disorder: A randomized double-blind placebo-controlled clinical trial. J Affect Disord. 2020;265:99-103. https://doi.org/10.1016/j.jad.2020.01.065

38. Mao JJ, Li QS, Soeller I, Xie SX, Amsterdam JD. *Rhodiola rosea* therapy for major depressive disorder: a study protocol for a randomized, double-blind, placebo- controlled trial. J Clin Trials. 2014;4:170. https://doi.org/10.4172/2167-0870.1000170

39. Sarris J, Ravindran A, Yatham LN, et al. Clinician guidelines for the treatment of psychiatric disorders with nutraceuticals and phytoceuticals: The World Federation of Societies of Biological Psychiatry (WFSBP) and Canadian Network for Mood and Anxiety Treatments (CANMAT) Taskforce. World J Biol Psychiatry. 2022;23(6):424-455. https://doi.org/10.1080/15622975.2021.2013041

40. Amsterdam JD, Panossian AG. *Rhodiola rosea L.* as a putative botanical antidepressant. Phytomedicine. 2016;23(7):770-783. https://doi.org/10.1016/j.phymed.2016.02.009

41. Ishaque S, Shamseer L, Bukutu C, Vohra S. *Rhodiola rosea* for physical and mental fatigue: a systematic review. BMC Complement Altern Med. 2012;12:70. https://doi.org/10.1186/1472-6882-12-70

42. Cropley M, Banks AP, Boyle J. The Effects of *Rhodiola rosea L.* Extract on Anxiety, Stress, Cognition and Other Mood Symptoms. Phytother Res. 2015;29(12):1934-1939. https://doi.org/10.1002/ptr.5486

43. Li Y, Pham V, Bui M, et al. *Rhodiola rosea L.:* an herb with anti-stress, anti-aging, and immunostimulating properties for cancer chemoprevention. *Curr Pharmacol Rep*. 2017;3(6):384-395. https://doi.org/10.1007/s40495-017-0106-1

44. Bystritsky A, Kerwin L, Feusner JD. A pilot study of *Rhodiola rosea* (Rhodax) for generalized anxiety disorder (GAD). J Altern Complement Med. 2008;14(2):175-180. https://doi.org/10.1089/acm.2007.7117

45. Lu Y, Deng B, Xu L, Liu H, Song Y, Lin F. Effects of *Rhodiola Rosea* Supplementation on Exercise and Sport: A Systematic Review [published correction appears in Front Nutr. 2022 Jun 20;9:928909. https://doi.org/10.3389/fnut.2022.856287

46. Spasov AA, Wikman GK, Mandrikov VB, Mironova IA, Neumoin VV. A double-blind, placebo-controlled pilot study of the stimulating and adaptogenic effect of *Rhodiola rosea* SHR-5 extract on the fatigue of students caused by stress during an examination period with a repeated low-dose regimen. Phytomedicine. 2000;7(2):85-89. https://doi.org/10.1016/S0944-7113(00)80078-1

47. Tinsley GM, Jagim AR, Potter GDM, Garner D, Galpin AJ. *Rhodiola rosea* as an adaptogen to enhance exercise performance: a review of the literature. *Br J Nutr*. 2024;131(3):461-473. https://doi.org/10.1017/S0007114523001988

48. Sarris J, Panossian A, Schweitzer I, Stough C, Scholey A. Herbal medicine for depression, anxiety and insomnia: a review of psychopharmacology and clinical evidence. *Eur Neuropsychopharmacol*. 2011;21(12):841-860. https://doi.org/10.1016/j.euroneuro.2011.04.002

49. Ma GP, Zheng Q, Xu MB, et al. *Rhodiola rosea L*. Improves Learning and Memory Function: Preclinical Evidence and Possible Mechanisms. Front Pharmacol. 2018;9:1415. https://doi.org/10.3389/fphar.2018.01415

50. Li T, Zhang W, Kang X, et al. Salidroside protects dopaminergic neurons by regulating the mitochondrial MEF2D-ND6 pathway in the MPTP/MPP^+-induced model of Parkinson's disease. *J Neurochem*. 2020;153(2):276-289. https://doi.org/10.1111/jnc.14868

51. Chen Y, Tang M, Yuan S, et al. *Rhodiola rosea*: A Therapeutic Candidate on Cardiovascular Diseases. Oxid Med Cell Longev. 2022;2022:1348795. https://doi.org/10.1155/2022/1348795

52. Drafi F, Bauerova K, Chrastina M, et al. *Rhodiola rosea* L. Extract, a Known Adaptogen, Evaluated in Experimental Arthritis. *Molecules*. 2023;28(13):5053. https://doi.org/10.3390/molecules28135053

53. Zhong ZF, Han J, Zhang JZ, et al. Neuroprotective Effects of Salidroside on Cerebral Ischemia/Reperfusion-Induced Behavioral Impairment Involves the Dopaminergic System. *Front Pharmacol*. 2019;10:1433. https://doi.org/10.3389/fphar.2019.01433

54. Li X, Chen W, Xu Y, et al. Quality Evaluation of Randomized Controlled Trials of *Rhodiola* Species: A Systematic Review. Evid Based Complement Alternat Med. 2021;2021:9989546. https://doi.org/10.1155/2021/9989546

55. Hung SK, Perry R, Ernst E. The effectiveness and efficacy of *Rhodiola rosea L.*: a systematic review of randomized clinical trials. Phytomedicine. 2011;18(4):235-244. https://doi.org/10.1016/j.phymed.2010.08.014