Investigating the effect of adaptogens on anxiety, stress and injury: a systematic review

Maryam Hajipoor, 1 Motahhareh Heydati Kebriti2, Bagher Sadeghiyan *3

Abstract:

Introduction: Adaptogens are a group of plants known for their innate ability to fortify the body's nervous system. They achieve this by influencing the hypothalamus-pituitary-adrenal axis, regulating cortisol secretion (stress hormone) and enhancing endorphin production. By bolstering the body's resilience against fatigue, adaptogens hold promise in improving the overall quality of life. However, it is imperative to substantiate their efficacy through rigorous scientific investigation, thereby fostering tranquility and enhancing societal well-being. Consequently, this study aims to examine the impact of utilizing plant adaptogens on three key phenomena: anxiety, stress, and fatigue.

Method: The current study takes the form of a comprehensive systematic review, where an assortment of trials and studies were meticulously gathered using well-defined search terms. These were sourced from both internal and external databases, with a particular emphasis on article titles. The inclusion criteria encompassed articles published in either English or Farsi between the years 2000 to 2023. Moreover, the focus primarily revolved around the clinical trial aspect. Additionally, the articles selected for analysis were those that involved a combined intervention of chemical medicine. To aid in the screening and management of resources, EndNote version 7 software was employed diligently.

Findings: Out of the 2707 pertinent articles, a meticulous examination led to the inclusion of 27 fully qualified articles in this study. The comprehensive evidence substantiates the efficacy of botanical adaptogens in bolstering performance, enhancing the body's resilience against fatigue, and fostering mental well-being in the face of stress.

Conclusion: By affording appropriate opportunities for the utilization of these plants in the human diet or medicinal formulations, a significant stride is taken towards enhancing the collective mental well-being of society.

Keywords: adaptogens, anxiety, fatigue, stress

Received: 30/ August/ 2023 Accepted: 11/ October/ 2023

Citation: Hajipoor M, heydari kebriti M, Sadeghiyan B. Investigating the effect of adaptogens on anxiety, stress and injury: a systematic review, Family and health, 2023; 13(3): 24-42

© 2020 The Author(s). This work is published by family and health as an open access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by-nc/4.0/). Non-commercial uses of the work are permitted, provided the original work is properly cited.

¹ - PhD student in counseling, Yazd Branch, Islamic Azad University, Yazd, Iran, maryamhaj70@gmail.com

² - Master of Family Counseling, Payam Noor University, Semnan, Iran, motahharehheidari@gmail.com

³ - Doctoral student of health care management, Faculty of Health, Tehran, Iran (**corresponding author**) bsadeghian@yahoo.com tell: 09138548456

Introduction:

The term "adaptogen" emerged in the clinical and scientific realm in the late 1940s, attributed to a Russian toxicologist named Lazarus. In 1947, Lazarus defined an adaptogen as a synthetic compound that enhances resistance to stress. The essence of an adaptogen lies in its ability to: a) augment the body's resilience against physical, chemical, and biological stressors such as anxiety, fatigue, and stress; b) exert a normalizing influence regardless of the stressor's origin; and c) ensure its effects are harmless, without disrupting normal bodily functions beyond necessity [3].

An adaptogen, by definition, refers to a plant-derived substance possessing antioxidant properties that fortify the body's resistance against stressors, injuries, blood sugar imbalances, anxiety, weakness, and fatigue [4]. These adaptogens fall into two main categories: plant-based adaptogens and synthetic adaptogens, the latter also known as active preservatives. While plant adaptogens have been employed since ancient times [5], herbalists commonly use phytoadaptogens (often referred to as "adaptogens") as herbal remedies to mitigate the adverse impact of chronic stress on overall health [6]. Herbal adaptogens serve to enhance the body's stamina and mitigate stress and anxiety-related disorders. By regulating stress hormones, such as cortisol, and other detrimental psychological factors, these adaptogens aid in maintaining equilibrium [7].

On the other hand, humans have long grappled with challenges such as anxiety, stress, and fatigue, seeking remedies to alleviate and overcome these issues [8]. A survey reveals that a significant percentage of individuals experience social anxiety disorder (ranging from 20% to 70%), panic disorder (50%), post-traumatic stress (48%), and general anxiety (43%) at some point in their lives [9]. The urgency to discover novel and natural solutions to manage and reduce these afflictions arises from the fact that they all have detrimental effects on overall quality of life, causing profound harm to the body, mind, social relationships, and professional and educational pursuits. They hinder the attainment of holistic well-being [8].

Anxiety and stress manifest through various symptoms, including premature fatigue, irritability, muscle tension, sleep disturbances, impaired social and occupational functioning, apathy, anhedonia, diminished concentration and attention, palpitations, and restlessness [10]. Moreover, stress and anxiety are recognized as triggers for numerous conditions, such as neurological disorders (e.g., Alzheimer's disease), cardiovascular ailments (e.g., hypertension and heart disease), and lifestyle diseases (e.g., diabetes and obesity). Given our current stress-laden lifestyles, effective management strategies should encompass a range of adaptogens devoid of adverse effects. Conventional pharmaceuticals, on the other hand, have demonstrated side effects and the potential for dependency [11]. Thus, interventions for these phenomena necessitate the utilization of adaptogens, which offer a promising avenue with minimal side effects [12].

While adaptogens are presently utilized in traditional practices by a segment of the population, their effectiveness necessitates scientific and systematic studies and research to validate their efficacy. Given the aim of minimizing side effects and drug resistance, it appears more reasonable to explore the utilization of these natural medicinal substances as opposed to artificial compounds. Additionally, considering the extensive historical usage of medicinal and herbal plants spanning thousands of years, investigating the role of these plants in anxiety, stress, and fatigue has captivated the attention of numerous researchers. However, comprehensive investigations are required to ascertain the effects of these plants. Should they prove efficacious, these plants may serve as suitable alternatives to chemical drugs, given their minimal or nonexistent side effects. Moreover, with the growing

population and the emergence of numerous challenges in people's daily lives, culminating in anxiety and stress with their deleterious consequences, it becomes imperative to regulate and attenuate their effects in order to foster tranquility and ultimately enhance societal quality of life. Notably, no comprehensive study has been conducted in this realm thus far, and disparate studies have identified various adaptogens as influential factors in anxiety, depression, and fatigue. Consequently, this study endeavors to conduct a systematic review of prior research to identify effective adaptogens.

Research Method:

The present study constitutes a systematic review that encompasses a comprehensive examination of various trials and studies conducted on the effects of adaptogens on stress, anxiety, and fatigue. The search for relevant literature included English sources and information databases such as PubMed, EMBASE, SCIENCE DIRECT, MEDLINE, SCOPUS, CHEMICAL ABSTRACTS, Google Scholar, Web of Science, as well as Persian sources in the SID information bank. The search utilized specific keywords such as Adaptogen, Ectoprotectors, plant adaptogens, Panax ginseng, adaptogen hydroxyecdysone, Eleutherococcus senticosus, Schisandra chinensis, Leuzea carthamoides, Rhodiola rosea, Rhaponticum carthamoides, Eukaryota, Viridiplantae, Streptophyta, Embryophyta, Tracheophyta, Magnoliopsida, Araliaceae, Eleutherococcus, and various combinations thereof. Additionally, the search included terms like Adaptogenic properties of ginseng, adaptogenic properties, adaptogenic properties of carthamoid, adaptogenic properties of ecdysterone, Fatigue, Mental Fatigue, Alert Fatigue, Health Personnel, Compassion Fatigue, Overtraining Syndrome, Psychological Stresses, Stresses, Life Stresses, Psychological Stressor, Crowding, Life Change Events, Behavior and Behavior Mechanisms, Behavioral Symptoms Stress, Burnout Psychological, Burnout Professional, Caregiver Burden, Stress, Occupational Stress, Historical Trauma, along with their Persian equivalents. The search spanned the years 2000 to 2023, encompassing all articles published during this 23-year period. This meticulous approach aimed to retrieve a comprehensive collection of records pertaining to the history, properties, and applications of plant adaptogens.

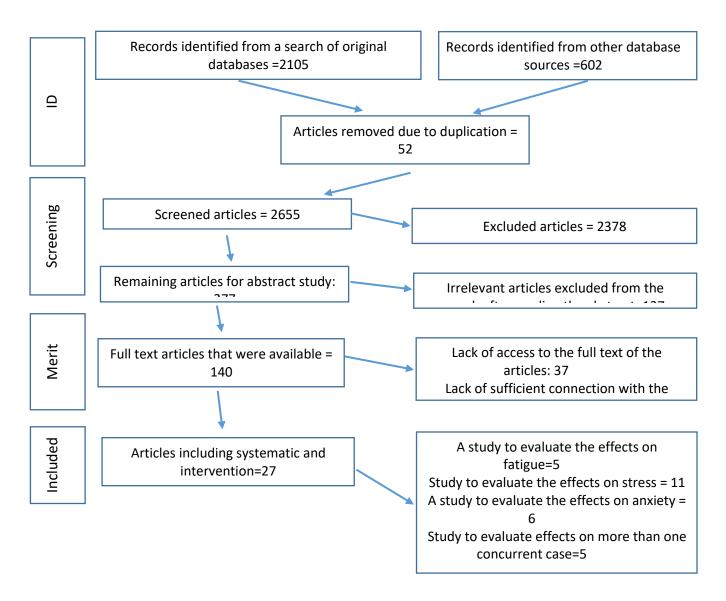
In the initial phase of the screening process, our focus was on identifying eligible studies that met specific criteria. Articles with language restrictions were taken into consideration. The study selection criteria included the following:

- 1. The presence of trials and studies on adaptogens.
- 2. Examination or explanation of the effects of trials and studies on fatigue, anxiety, and stress.
- 3. Conducted within the timeframe of 2000 to 2023.
- 4. Emphasis on clinical trial studies.
- 5. Publication in either English or Farsi.

On the other hand, we excluded studies that involved interventions combining chemical drugs. Our aim was to solely focus on adaptogenic plants and their therapeutic dimensions and effects.

Moving to the second step, we followed the systematic review framework outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) as our guide [13]. This

framework ensured a structured and comprehensive approach to conducting the systematic review, as depicted in the following:



In the third stage of our study, we proceeded to select articles deemed worthy for inclusion. Out of the total of 2707 articles identified (2112 in English and 595 in Persian), we carefully screened 277 related articles based on their abstracts. After thorough screening, 137 articles were excluded due to their focus on irrelevant outcomes, leaving us with 140 full-text articles. Ultimately, 27 articles met the eligibility criteria and were included in our systematic review.

Findings:

Based on our findings, we discovered that studies conducted on adaptogens, particularly the cow's tongue flower extract, have demonstrated reduced anxiety-like behaviors in rats [14-15]. Sayah and colleagues found that the use of cow's tongue plant also led to a reduction in anxiety symptoms in mice [14]. Furthermore, research has indicated that the aqueous extract of cow's tongue flower can reduce blood pressure and heart rate [16]. These studies collectively suggest that cow's tongue has

potential in reducing anxiety, stress, blood pressure, and heart rate. Additionally, Erfani et al. explored the effects of the herbal drug Hyperian on students' anxiety and stress, revealing a positive impact in reducing anxiety in the experimental group [17]. Similarly, Rezaei et al. found that flower extract of Rai possesses calming, anti-anxiety, and stress-relieving effects [18]. Stanley et al. conducted a study demonstrating that lavender scent can effectively reduce anxiety and pre-operative stress in cataract surgery patients [19]. Kuchta et al. discovered that kava plant can alleviate anxiety disorders in elderly individuals [20]. Holy basil, known for its various chemical compounds, including oleanolic acid, rosmarinic acid, ursolic acid, eugenol, linalool, carvacrol, elemen, caryophyllene, and germacrene, has been shown to improve swimming time and exhibit anti-stress effects in a study by Maitio and colleagues [22]. This adaptogen is revered as the "queen of plants," "unique," and the "mother of nature's medicine" due to its numerous advantages. Holy basil aids in adapting to stimuli and maintaining physiological homeostasis [23]. Rhodiola rosea, a traditional medicine with significant antioxidant properties, has been extensively studied in clinical treatments. Phytochemical analysis has revealed the presence of phenylpropanoids, phenylethanol/benzyl alcohol derivatives, flavonoids, cyanogenic glycosides, and terpenoids in this plant [24]. Parisi et al. conducted a placebocontrolled study to investigate the long-term effects of Rhodiola rosea supplementation on physical performance and endurance. The results showed that Rhodiola rosea significantly improved physical performance by reducing free fatty acids in the body plasma [25]. Cropley et al. found that individuals with mild anxiety responded positively to Rhodiola rosea [26]. In a study by Mao et al., participants with anxiety and stress disorders were administered adaptogenic herbs in supplement and tablet forms, resulting in significant anti-anxiety and stress effects [27].

The study conducted by Talbot et al. reveals that daily supplementation with Tongat root extract enhances stress hormone regulation and improves certain mood parameters. Traditional treatment studies also support the notion that this approach of safeguarding the body against the detrimental effects of stress aids in combating chronic and modern-day stressors, including those arising from diet and lack of sleep. Extensive laboratory research, animal nutrition studies, and human supplementation have confirmed the wide range of health benefits associated with Tongat Ali root extract, including improved physical performance, reduced fatigue, increased energy, enhanced mood, and a sense of well-being. Consequently, Tongat Ali has been utilized in traditional medicine and Southeast Asian medical systems for centuries to alleviate lethargy, manage stress, and enhance psychological well-being in individuals facing various modern stressors. Moreover, Tongat Ali aids in restoring hormonal balance by regulating cortisol and testosterone levels [28].

The primary aromatic compound in saffron is safranal, which constitutes approximately 60% of the volatile components of saffron. While this substance exists as stable picrocrocin in fresh saffron, it decomposes into the volatile safranal aldehyde over time and when exposed to heat [29]. Akhundzadeh et al. compared the efficacy of saffron plant extract with imipramine, a commonly prescribed antidepressant, in the treatment of mild to moderate depression. The research findings demonstrated that saffron extract exhibited comparable effectiveness to imipramine without the associated side effects [30]. Studies have also confirmed the anti-anxiety, stress-reducing, and fatigue-alleviating effects of saffron through the consumption of both aqueous and ethanol extracts, as well as saffron petals. These effects can be attributed to the presence of compounds such as crocin and safranal, which play a pivotal role in the antidepressant effect of saffron extract. Crocin inhibits

the reabsorption of dopamine and norepinephrine, while safranal inhibits the reabsorption of serotonin [31]. Ashwagandha, a well-known adaptogen, exerts a significant impact on stress management and has the potential to restore a balanced lifestyle by reducing stress and preventing the onset of various life-threatening diseases. Recent studies have extensively explored the effects of Ashwagandha. Vitania et al. conducted a study on mice to evaluate the anti-stress properties of Ashwagandha root extract, and the results demonstrated that Ashwagandha enhanced the body's resistance to stress and improved immunity [32]. Another article revealed that rats pre-treated with an aqueous suspension of Ashwagandha root extract exhibited reduced levels of adrenal cortisol and ascorbic acid, indicating decreased stress levels [33]. Ashwagandha holds significant medicinal value and consistently affects human health. Research findings indicate that eight weeks of Ashwagandha root aqueous extract consumption significantly reduces stress levels and improves overall quality of life. Therefore, utilizing this medicinal plant as a supplement to manage stress and anxiety proves to be an excellent alternative [11]. Ginseng extract is widely available in numerous products, with many being utilized as food supplements and others in medicinal forms. Ginseng root is included in European and US pharmaceuticals, and it typically possesses a cylindrical shape, occasionally branching, with a length of up to 20 cm and a diameter of 2.5 cm. In white ginseng, the surface appears pale yellow or cream, while red ginseng exhibits a red-brown hue. The lower portion of white ginseng is abundant in roots, which are generally absent in red ginseng. When transformed into powder form, it assumes a bright yellow color [34]. Additionally, Siberian ginseng, introduced by Porfiry Krylov in the 19th century, is among the other adaptogens that have been discovered. Its extract aids in adapting to external factors, improving mental and physical conditions, and enhancing memory functions [36-37]. The extensive research conducted on potent adaptogens such as ginseng, Maral plant, and Rhodiola rosea underscores their remarkable and multifaceted roles. Further details regarding adaptogen studies can be found in the provided tables.

Table 1 provides a summary of various studies that highlight the primary benefits associated with the consumption of white ginseng and Siberian ginseng extracts.

Table 1: Panax ginseng studies.

Study Objectives	Study Design	Main Results	References
Evaluation of the effects on subjective mood and memory of a single and subchronic <i>Panax</i> ginseng dose.	Thirty adults, aged 22.87 ± 4.01 years, participated in the study. They received a placebo, 200 or 400 mg <i>Panax ginseng</i> extract per day for 3 treatments—8 days with 6 days washout. Period of the study—32 days.	Improved calmness, mood, and mental health.	[38]
•	Twelve men, aged 20–24 years, participated in the study. All participants received 200 mg ginseng extract or a placebo one hour before the exercise.	Increased endurance time, blood glucose and insulin levels, catalase, superoxide- dismutase, and total	[<u>39</u>]

Study Objectives	Study Design	Main Results	References
Evaluation of benefits on fatigue in multiple sclerosis with <i>Panax</i> ginseng treatment.	Fifty-two women, aged 18–50 years, participated in the study. There were 26 participants who received 500 mg daily of Korean ginseng tablets and 26 were in the placebo group.Period of the study—3 months.	Reduced fatigue. Improved quality of life.	[<u>40</u>]
Evaluation of the efficacy of a combination of <i>Panax ginseng</i> and vitamins on physical and mental stress.	One-hundred and fourteen women and men, aged 30–60 years, participated in the study. There were 59 participants who received 200 mg daily of ginseng dried extract and vitamins; 55 were in the placebo group. Period of the study—8 weeks.	Increased quality of life, without a difference in blood pressure and heart rate.	[<u>41</u>]
Evaluation of the effects of <i>Panax ginseng</i> on sleep.	Fifteen men, aged 19–25 years, participated in the study. There were eight participants who received 4.5 g of ginseng extract daily; seven participants were in the placebo group. Period of the study—2 weeks.	Increased deep sleep. Decreased shallow sleep.	[<u>42</u>]
Evaluation of anti-fatigue effects of <i>Panax ginseng</i> .	Eighty-eight men and women 20–60 years of age participated in the study. There were 30 participants who received 1 g of ginseng extract daily; 29 participants had an intake of 2 g of ginseng extract daily. There were29 participants who were in the placebo group. Period of study—2 months.	Reduced the severity of fatigue. Increased glutathione reductase and total glutathione.	[<u>43</u>]
Examine the effects of Eleutherococcus senticosus extract on physical working capacity.	Six men, aged 21–22 years, participated in the study. They were in the control group, placebo group, and the group that received 2 mL ethanol extract (125 mg dried extract) Eleutherococcus senticosus twice daily. Period of study—8 days.	oxygen uptake, oxygen pulse, total work, and	[<u>44]</u>
Examine the effects of a dietary supplement containing Eleutherococcus senticosus extract on burnout symptoms.	Eighty-seven volunteers, aged 27–63 years, participated in the study. There were 44 participants who had an intake of 100 mg dry extract from Eleutherococcus senticosus; 43 were in the placebo group. Period of study—12 weeks.	Decreased fatigue score and Beck depression.	[<u>45</u>]

Study Objectives	Study Design	Main Results	References
Assessment of the impact of Eleutherococcus senticosus on quality of life.	Twenty volunteers, aged over 65 years, participated in the study. There were 10 participants who received 300 mg/day Siberian ginseng extract and 10 participants who were in placebo group. Period of study—2 months.	Improved mental health and social functioning, but prolonged use decreased these improvements. Blood pressure was not affected.	[<u>46</u>]

The research findings indicate that the consumption of white ginseng extracts yields numerous benefits, including heightened energy levels, increased strength, and reduced fatigue. Moreover, the consumption of white ginseng extract not only enhances physical power but also improves cognitive function and memory, while alleviating conditions such as physical and mental stress and anxiety. Importantly, the consumption of white ginseng extract is not associated with any significant side effects [38 and 47]. Similarly, the findings highlight that the consumption of Siberian ginseng supports physical performance, reduces fatigue, and promotes mental well-being by mitigating the effects of stress and anxiety. Furthermore, long-term consumption of Siberian ginseng extract does not pose any serious side effects [44-48].

Another noteworthy adaptogenic plant is the Maral plant extract, known by its scientific name. This extract offers various beneficial effects on human health, such as increased physical endurance and performance against fatigue, neuroprotective properties, and the ability to facilitate adaptation to diverse stressors that the body may encounter [49].

Table 2 provides a comprehensive overview of studies investigating the utilization and effects of Maral plant extract.

Table 2: Rhaponticum carthamoides studies.

Study Objectives	Study Design	Main Results	References
Evaluation of the effects of an increased dose of <i>Rhaponticum carthamoides</i> during the training process.	Twenty women, aged 25–40 years, participated in the study. There were 12 of them whoreceived 5–15 mg/kg/day ecdysterone; 8 were in controlled group.	Increased physical endurance and performance.	[<u>50</u>]
Examine the effect of ecdysterone-containing products on sport physical exercises.	Forty-six men, aged 25.6 ± 3.7 years, participated in the study. There were 12 participants whohad an intake of 200 mg ecdysterone; 10 participants received 800 mg ecdysterone, 12 participants received the placebo, and 12 of the participants were in the control group—they had an	body weight, muscle mass. Increased power and strength of performance. Without negative effects on creatinine, glutamate—oxaloacetate transaminase, gamma-	[<u>51</u>]

Study Objectives	Study Design	Main Results	References
	intake of 200 mg ecdysterone without training. Period of study—10 weeks.	and glutamate-pyruvate transaminase. Did not affect steroid profile.	
Evaluation of the effectiveness of ecdysterone in athletes.	Twenty-six women aged 18–22 years participated in the study. There were 12 participants who received ecdysterone from 37.5 to 50 mg; 14 participants were in the controlled group. Period of study—9 moths.	Increased VO2 lactate, performance activity.	[<u>52</u>]
Evaluation of the effectiveness of ecdysterone from <i>Rhaponticum</i> carthamoides leaves in athletes.	Ç î	Increased resistance to disease, physical, and mental endurance.	[<u>53</u>]
Assessment of effects of methoxyisoflavone, 20-hydroxyecdysone, and sulfopolysaccharides intake on training adaptation and markers of muscle anabolism and catabolism.	daily, the	No change in training adaptation and in anabolic and catabolic effect in training.	[<u>54</u>]
Evaluation of the effects of the combination of <i>Rhaponticum</i> carthamoides and <i>Rhodiola</i> rosea on performance fatigability and reactions before and after training.	Twenty-seven men, aged 22.3 ± 4.1 years, participated in the study. The participants received a 350 mg tablet which contains 70:30 <i>Rhaponticum</i> carthamoides extract and <i>Rhodiola rosea</i> extract, or a tablet containing	No change in muscle strength and total work.	[<u>55</u>]

Study Objectives	Study Design	Main Results	References
	175 mg maltodextrin, and 175 m	g	
	Rhaponticum carthamoides and Rhodiola rosea extract in ratio 70:30 oplacebo.	or	

The data reveals that the consumption of Maral plant extract elicits anabolic effects, leading to an increase in body mass, augmented muscle strength, and a positive impact on fatigue reduction [56].

Rhodiola Rosea, on the other hand, serves as an adaptogen and exerts its influence by enhancing body endurance, mitigating fatigue, stress, anxiety, and various other disorders [57]. The beneficial effects of Rhodiola Rosea, as supported by studies, have been succinctly summarized in Table 3.

Table 3: Rhodiola rosea studies.

Study Objectives	Study Design	Main Results	References
Studying the effects of short- term supplementation with <i>Rhodiola rosea</i> .	Eleven women, aged 19.4 ± 0.8 years, participated in the study. They had an intake of 1.5	Increased anaerobic capacity, anaerobic power, and total work. No change in	[58]
	g/day <i>Rhodiola rosea</i> extract or placebo for 3 days. A 500 mg additional dose of <i>Rhodiola rosea</i> extract was taken before each trial.	fatigue index.	
Examine hormonal and oxidative stress of <i>Rhodiola</i> rosea supplementation and the effects on mental and physical performance.	Twenty-six men participated in the study. Thirteen of them had an intake of 600 mg/day extract of <i>Rhodiola rosea</i> and 13 were in placebo group. Period of study—4 weeks.	Improved reaction and response time. Increased antioxidant capacity. Without changes in hormone profile and endurance exercise capacity.	[<u>59</u>]
Examine the levels of inflammatory C-reactive protein and creatinine kinase in blood after intake of <i>Rhodiola rosea</i> .	Thirty-six volunteers aged 21–24 years participated in the study. Twelve of them had an intake of 340 mg Rhodiola rosea extract twice a day, 12 participants were in the placebo group, and 12 participants were in the control group. Period of study—36 days.	Increased levels of C-reactive protein and creatinine kinase.	[60]
Examine the effects and safety of Rho tolar for 4 weeks of treatment.	There were 101 women and men, aged 30–60 years, who participated in study. All participants had an intake	Improved mood, stress symptoms, and quality of life.	[<u>61</u>]

Family and health

	of Rhodiola rosea extract 400	
	mg/day.	
	Period of the study—1 month.	
Examine the effects of a	There were 121 men aged 19–	Improvement in the [62]
	· ·	
single dose of	21 years participated in the	anti-fatigue index.
standardized Rhodiola	study; 41 participants received	
rosea extract.	370 mg dry	
	extract Rhodiola rosea, 20	
	participants received 555 mg	
	dry extract of <i>Rhodiola</i>	
	rosea before test, 40 of	
	*	
	participants were in the	
	placebo group,	
	20 participants were in the	
	controlled group.	
Examine the effects of	Eighty-nine women and men,	Improved in overall [63]
standardized Rhodiola rosea	aged 18–70 years, participated	depression, insomnia,
extract in patients suffering	in the study. Thirty-one	somatization, and
from depression.	participants received 340	emotional instability. No
nom depression.	• •	
	mg/day extract of Rhodiola	improvements in self-
	rosea,	belief.
	29 participants received 680	
	mg/day extract of Rhodiola	
	rosea, and 29 participants	
	were in the placebo group.	
	Period of study—42 days.	
Evaluating the changes of	There were 48 men and	Increased myoglobin, [64]
Rhodiola	women, aged 25–60 years,	creatine phosphokinase,
		* *
rosea supplementation on	who participated in the study.	aspartate
muscle damage and	Twenty-four participants	aminotransferase, alanine
inflammation.	received a 300 mg capsule per	aminotransferase, and
	day containing <i>Rhodiola</i>	interleukin (IL-6, IL-8,
	rosea extract, and 24	IL-10) without a
	participants	difference in both groups.
	were in the placebo group.	Ç 1
	Period of study—38 days.	
Examine the effects	Twenty-two men aged 20.4 ±	Decreased levels of [65]
of Rhodiola		
	1.2 participated in the study.	superoxide
rosea supplementation on	Eleven of them had an intake	dismutase. Increased
selected redox parameters	of	total
in athletes.	200 mg/day <i>Rhodiola</i>	antioxidant capacity.
	rosea extract,	
	and 11 were in the placebo	
	group.Period of study—4	
	weeks. Decreased levels of	
	superoxide dismutase.	

	Increased total		
	antioxidant capacity.		
Examine the effects of	Fourteen men, aged 25 ± 5	Decreased free fatty acids [66]	
chronic intake of Rhodiola	years, participated in the study.	levels, blood lactate, and	
rosea on	All of the participants received	creatinine kinase levels.	
physical performance and	a	No change in VO2max.	
antioxidant capacity during	placebo; after that, all of them		
exercise in athletes.	received		
	170 mg R. rosea extract for 1		
	month.		
The efficacy of Rhodiola	Ten men and women, aged 34-	Decreased scores in [67]	
rosea in generalized anxiety	55 years,	Hamilton	
disorder.	participated in the study. All	Anxiety Rating Scale and	
	participants had intake 340	Hamilton Depression	
	mg Rhodiola rosea extract per	Rating Scale.	
	day		
	for 10 weeks.		

The research findings reveal that Rhodiola Rosa possesses antioxidant and adaptogenic properties. The extract of Rhodiola Rosa not only proves highly beneficial in combating fatigue but also demonstrates great potential for individuals with heart conditions. Notably, the consumption of Rhodiola Rosa does not entail any significant side effects [58-67].

Another noteworthy plant is Schisandra Chinsing, recognized for its adaptogenic qualities and its ability to enhance physical endurance and alleviate bodily fatigue [68-69]. Studies indicate that the use of Schisandra Chinsing extract positively impacts the overall well-being of the body, particularly in mitigating fatigue. Furthermore, the consumption of Schisandra Chinsing extract does not pose any serious side effects [70-71]. Additionally, other studies affirm the positive therapeutic effects of these plants in addressing anxiety, stress, and mood disorders [72-73]. The systematic study conducted by Ishak et al. further establishes the favorable effects of these plants on physical and mental performance, as well as various psychological conditions experienced by individuals [74-75].

Animal studies conducted on these plants demonstrate that, in addition to their anxiety-reducing, stress-relieving, and fatigue-alleviating properties, they possess therapeutic effects, including antioxidant, anti-cancer, anti-diabetic, anti-depressant, neuroprotective, anti-inflammatory, and anti-addictive qualities. The results of various studies also confirm the safety of these plants, with rare and mild side effects, if any. However, caution is advised regarding high doses and long-term usage of medicinal forms and adaptogenic plants due to potential safety risks [76].

In conclusion, there is a growing trend in the use of adaptogens among the general public. Adaptogens have been utilized for medicinal purposes for centuries as natural substances that aid the body in coping with physical and psychological stress, anxiety, and fatigue, while enhancing endurance, strength, and overall performance. Consequently, adaptogens serve as powerful natural remedies for combating stress, anxiety, and fatigue. These natural adaptogens possess the ability to enhance the body's resistance to stress and adapt to various stressors, thereby improving physical endurance against fatigue. The inclusion of these plant extracts in human diets or medicinal products holds great potential for treating chronic fatigue, cognitive disorders, and boosting the immune

system. Overall, it can be concluded that adaptogenic plants offer favorable therapeutic effects, as demonstrated by individuals participating in various studies and interventions, particularly those suffering from mild anxiety who have benefited from herbal supplements. Furthermore, studies indicate that the use of adaptogenic plant supplements has had positive anti-anxiety and stress-reducing effects. Therefore, incorporating these medicinal plants as supplements to manage stress and anxiety can serve as a valuable alternative option [11].

Considering the fact that modern society is exposed to numerous stressors, anxiety-inducing factors, and excessive fatigue resulting from physical exertion, providing accessible means of utilizing treatment methods, including adaptogens, can significantly improve the mental and physical well-being of society. By reducing stress, anxiety, and fatigue, adaptogens can contribute to a healthier and more balanced society.

Research Limitations:

- 1. There was a scarcity of studies and clinical trials pertaining to the subject matter of this article. However, comprehensive research from diverse sources was conducted within the defined time frame to minimize this limitation.
- 2. Studies that involved the use of chemical sedative drugs in addition to adaptogenic plants were excluded from the research.
- 3. Language limitations were encountered, with articles in languages other than English and Farsi being excluded.

Application of Research:

Given the absence or minimal side effects of adaptogenic plants, their positive effects should be incorporated into people's diets. As a treatment method, they can be utilized as an alternative to chemical drugs in reducing stress, anxiety, and fatigue, thereby promoting better health and well-being within society.

Conflict of Interest:

The responsible author, on behalf of all the authors, affirms that ethical principles were upheld throughout the writing and publication of this article, ensuring the avoidance of plagiarism and data falsification. The authors have not received any financial benefits or compensation for their work. The responsible author further declares that this work has not been published elsewhere and has not been simultaneously submitted to other publications. Additionally, all rights to use the contents, tables, images, etc. have been transferred to the publisher.

Reference:

- 1. Panossian A. Understanding adaptogenic activity: specificity of the pharmacological action of adaptogens and other phytochemicals. Ann N Y Acad Sci 2017;1401:49e64. https://doi.org/10.1111/nyas.13399
- 2. Nair R, Sellaturay S, Sriprasad S. The history of ginseng in the management of erectile dysfunction in ancient China (3500-2600 BCE). Indian J Urol 2012;28:15e20. https://doi.org/10.4103/0970-1591.94946

- 3. Yun TK. Brief introduction of Panax ginseng CA Meyer. J Kor Med Sci 2001;16:S3. https://doi.org/10.3346/jkms.2001.16.S.S3
- 4. Rajabi N, Karimi jashni H. Evaluation of effect of tribulus terrestris extract on sex hormones in male rats after treatment with cyclophosphamide. J Jahrom Univ Med Sci 2014; 2(12): 15-22. https://doi.org/10.29252/jmj.12.2.1
- 5. Panossian A.G, Efferth, T, Shikov A.N., Pozharitskaya O.N, Kuchta K, Mukherjee P.K., Banerjee S, Heinrich M, Wu W, Guo D, et al. Evolution of the adaptogenic concept from traditional use to medical systems: Pharmacology of stress and aging related diseases. Med. Res. Rev. 2020; 41: 630–703. https://doi.org/10.1002/med.21743
- 6. Tabachnik B. Adaptogensdnatural protectors of the immune system, potentiating health and the crisis of the immune system. Springer; 1997: 143e7. https://doi.org/10.1007/978-1-4899-0059-3 13
- 7. S. Christiansen, What are adaptogens? Ayurvedic herbs claimed to promote anti-aging and anti-stress, Verywell Health [Internet]. Available from: https://www.verywellhealth.com/what- are- adaptogens- 4685073}toc- what- arethebenefits- of- adaptogens; 2022 . https://doi.org/10.1016/j.hsr.2023.100092
- 8. Shahinfar J, Zeraati H, Nasimi F, Shojaei S. [Effect of medicinal plants on anxiety]. Journal of Islamic and Iranian Traditional Medicine. 2017; 8(2):209-22. URL: http://jiitm.ir/article-1-859-en.html
- 9. Kalin NH. The critical relationship between anxiety and depression. The American Journal of Psychiatry. 2020; 177(5):365-7. https://doi.org/10.1176/appi.ajp.2020.20030305
- 10. World Health Organization. Mental health: Facing the challenges, building solutions [Internet]. 2005. Available from: https://www.euro.who.int/en/health-topics/noncommunicable-diseases/mental-health-facing-the-challenges,-building-solutions
- 11. Salve J, Pate S, Debnath K, et al. Adaptogenic and Anxiolytic Effects of Ashwagandha Root Extract in Healthy Adults: A Double-blind, Randomized, Placebo-controlled Clinical Study. Cureus, 2019; 11(12): e6466. DOI 10.7759/cureus.6466. https://doi.org/10.7759/cureus.6466
- 12. Amin GR, Bozorgi M, Khatamsaz M, Khalaj A, Zolfaghari B, Rahimi R, etal. [Gāvzabān (Persian)]. Journal of Islamic and Iranian Traditional Medicine. 2017; 8(1):139-45. http://jiitm.ir/article-1-851-fa.html
- 13. Page M.J, McKenzie J, Bossuyt P.M, Boutron I, Hoffmann T.C, Mulrow C.D, Shamseer L, Tetzlaff J.M, Akl E, Brennan S. et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 2021; 372: 71. https://doi.org/10.1136/bmj.n71
- 14. Saiiah Bargard M, Assadi SM, Amini H, Saiiah M, Akhondzadeh Sh, Kamalinejad M. [Efficacy of aqueous extract of Echium amoenum L. in the treatment of mild to moderate major depressive disorder: A randomized double blind clinical trial (Persian)]. Journal of Medicinal Plants. 2014;2(10):61-8. http://jmp.ir/article-1-749-en.html. Or dor/20.1001.1.2717204.2004.3.10.9.7

- 15. Komaki AR, Rasouli B, Shahidi S. Anxiolytic effect of Borago officinalis (Boraginaceae) extract in male rats. Avicenna Journal of Neuropsychophysiology. 2015; 2(1):e27189. https://doi.org/10.17795/AJNPP-27189
- 16. Masuod-Hamidi E, Khaksari M, Hojabri Kh. [The effects of aqueous extracts of Echium amoenum and Citrus aurantiflia on blood pressure and heart rate before and after phynelephrine injection in rat (Persian)]. Journal of Kerman University of Medical Sciences.

 2013;
 18(4): 349-57.

 https://jkmu.kmu.ac.ir/article 16556 59226728a40b6645a4692f53656f5f2c.pdf
- 17. Erfani N, Shahsavari A. [The effect of hypiran on anxiety among students in Karaj University's dormitories (Persian)]. Nursing Development in Health. 2013; 3(4-5):77-84. http://ndhj.lums.ac.ir/article-1-94-en.html
- 18. Rezaei A, Rezaei-Dorostkar K, Pashazadeh M, Ahmadizadeh C, Jafari B. [A comparative study of sedative and anxiolytic effects of the Hypericum perforatumin and diazepam on rats (Persian)]. Zahedan Journal of Research in Medical Sciences. 2012; 13(8):e93758. https://doi.org/10.1016/j.ijid.2008.05.426
- 19. Stanley PF, Wan LF, Abdul Karim R. A randomized prospective placebocontrolled study of the effects of lavender aromatherapy on preoperative anxiety in cataract surgery patients. Journal of PeriAnesthesia Nursing, 2020; March.https://doi.org/10.1016/j.jopan.2019.12.004
- 20. Kuchta K, de Nicola P, Schmidt M. Randomized, dose-controlled double-blind trial: Efficacy of an ethanolic kava (Piper methysticum rhizome) extract for the treatment of anxiety in elderly patients. Traditional & Kampo Medicine. 2018; 5(1):3-10. http://doi.org/10.1002/tkm2.1079
- 21. P. Panchal, N. Parvez, Phytochemical analysis of medicinal herb (Ocimum sanctum), Int. J. Nanomater. Nanotechnol. Nanomed. 2019; 5(2): 008-11. https://doi.org/10.17352/2455-3492.000029.
- 22. T.K. Maity, S.C. Mandal, B.P. Saha, M. Pal, Effect of Ocimum sanctum roots extract on swimming performance in mice, Phytother. Res, 2000; 14(2): 120–121, <a href="https://doi.org/10.1002/(sici)1099-1573(200003)14:2<120::aid-ptr557>3.0.co;2-0">https://doi.org/10.1002/(sici)1099-1573(200003)14:2<120::aid-ptr557>3.0.co;2-0
- 23. P. Kaur V.O., Makanjuola R., Arora, B. Singh, S. Arora, Immunopotentiating significance of conventionally used plant adaptogens as modulators in biochemical and molecular signalling pathways in cell mediated processes, Biomed. Pharmacother, 2017;95: 1815–1829, https://doi.org/10.1016/j.biopha.2017.09.081.
- 24. Y.Li J., Wu R., Shi N., Li Z., Xu M.S. Antioxidative effects of Rhodiola genus: phytochemistry and pharmacological mechanisms against the diseases, Curr. Top. Medicin. Chem, 2017; 17(15): 1692–1708, https://doi.org/10.2174/1568026617666161116141334.
- 25. Parisi A, Tranchita E, Duranti G, Ciminelli E, Quaranta F, Ceci F, Cerulli C., Borrione P., Sabatini S. Effects of chronic Rhodiola Rosea supplementation on sport performance and antioxidant capacity in trained male: preliminary results, J. Sports Med. Phys. Fitness, 2010; 50(1): 57. PMID: 20308973

- 26. Cropley M, Banks AP, Boyle J 'The Effects of Rhodiola rosea L.Extract on Anxiety, Stress, Cognition and Other Mood Symptoms'Phytother Res. 2015 Dec; 29(12): 1934–9. https://doi.org/10.1002/ptr.5486
- 27. Mao JJ, Xie SX, Zee J, Soeller I, Li QS, Rockwell K, Amsterdam JD 'Rhodiola rosea versus sertraline for major depressive disorder: A randomized placebo-controlled trial' Phytomedicine. 2015 Mar 15; 22(3): 394–9. https://doi.org/10.1016/j.phymed.2015.01.010
- 28. Talbott et al. Journal of the International Society of Sports Nutrition: Effect of Tongkat Ali on stress hormones and psychological mood state in moderately stressed subjects, 2013; 10: 28. https://doi.org/10.1186/1550-2783-10-28
- 29. Abdullaev FI. Cancer chemopreventive and tumoricidal properties of Saffron (Crocus sativus L). Exp Biol Med (Maywood). 2014; 227(1): 20-5. https://doi.org/10.1177/153537020222700104
- 30. Akhondzadeh S, Fallah Pour H, Afkham K, Jamshidi AH, Khalighi Cigaroudi F. Comparison of crocus sativus L.and imiperamine in the treatment of mild to moderate depression: A pilot double-blind randomized trial. BMC Complement Altern Med. 2014; 4: 12. https://doi.org/10.1186/1472-6882-4-12
- 31. Hosseinzadeh H, Karimi Gh and Niapoor M.Antidepressant effects of Crocus sativus stigma extracts and its constituents, crocin and safranal, in mice. J. Med. Plants. 2014; 3 (11): 48 58. http://dx.doi.org/10.17660/ActaHortic.2004.650.54
- 32. Chandrasekhar K, Kapoor J, Anishetty S: A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of ashwagandha root in reducing stress and anxiety in adults. Indian J Psychol Med. 2013; 34: 255-262 https://doi.org/10.4103/0253-7176.106022
- 33. Singh N, Nath R, Lata A, Singh SP, Kohli RP, Bhargava KP: Withania somnifera (Ashwagandha), a rejuvenating herbal drug which enhances survival during stress (an adaptogen). Int J Crude Drug Res. 2014; 20: 29-35. https://doi.org/10.3109/13880208209083282
- 34. Todorova V, Ivanov K, Ivanova S. Comparison between the Biological Active Compounds in Plants with Adaptogenic Properties (Rhaponticum carthamoides, Lepidium meyenii, Eleutherococcus senticosus and Panax ginseng). *Plants*. 2022; 11(1):64. https://doi.org/10.3390/plants11010064
- 35. Davydov M., Krikorian A. Eleutherococcus senticosus (Rupr. & Maxim.) maxim. (Araliaceae) as an adaptogen: A closer look. J.Ethnopharmacol, 2000; 72: 345–393. https://doi.org/10.1016/s0378-8741(00)00181-1
- 36. Hikino H, Takahashi M, Otake K, Konno C. Isolation and Hypoglycemic Activity of Eleutherans A, B, C, D, E, F, and G:Glycans of Eleutherococcus senticosus Roots. J. Nat. Prod. 1986; 49: 293–297. https://doi.org/10.1021/np50044a015
- 37. Asano K, Takahashi T, Miyashita M, Matsuzaka A, Muramatsu S, Kuboyama M, Kugo H, Mai J. Effect of eleutheroccocus senticosus extract on human physical working capacity. Planta Med. 1986; 52: 175–177. PMID: 3749339.
- 38. Reay J.L, Scholey A, Kennedy D. Panax ginseng (G115) improves aspects of working memory performance and subjective ratings of calmness in healthy young adults. Hum. sychopharmacol. Clin. Exp, 2010; 25: 462–471. https://doi.org/10.1002/hup.1138

39. Bhattacharjee I, Bandyopadhyay A. Effects of acute supplementation of panax ginseng on endurance performance in healthy adult males of Kolkata, India. Int. J. Clin. Exp. Physiol, 2020; 7: 63–68. PMID: 21321426; PMCID: PMC3100154.

- 40. Etemadifar M, Sayahi F, Abtahi S.H, Shemshaki H, Dorooshi G.A, Goodarzi M, Akbari M, Fereidan-Esfahani M. Ginseng in the treatment of fatigue in multiple sclerosis: A randomized, placebo-controlled, double-blind pilot study. Int. J. Neurosci. 2013; 123: 480–486. https://doi.org/10.3109/00207454.2013.764499
- 41. Perazzo F.F, Fonseca F.L., Souza G.H.B., Maistro E.L., Rodrigues M., Carvalho J.C. Double-blind clinical study of a multivitamin and polymineral complex associated with panax ginseng extract (Gerovital®). Open Complement. Med. J., 2010; 2: 100–104. https://doi.org/10.1021/np50044a015
- 42. Ziemba A.W. The effect of ginseng supplementation on psychomotor performance, indices of physical capacity and plasma concentration of some hormones in young well fit men. In Proceedings of the Ginseng Society Conference, Seoul, Korea, 1October 2002: 145–158. https://doi.org/10.1123/ijsn.9.4.371
- 43. Kim H.G., Cho J.H., Yoo S.R., Lee J.S., Han J.M., Lee N.H., Ahn Y.C., Son C.G. Antifatigue Effects of Panax ginseng CAMeyer: A randomised, double-blind, placebocontrolled trial. PLoS ONE, 2013; 8: 61271. https://doi.org/10.1371/journal.pone.0061271
- 44. Ping F.W.C., Keong C.C., Bandyopadhyay A. Effects of acute supplementation of Panax ginseng on endurance running in a hot & humid environment. Indian J. Med. Res. 2011; 133: 96–102. PMID: 25665208.
- 45. Todorova V., Ivanov K., Delattre C., Nalbantova V., Karcheva-Bahchevanska D., Ivanova S. Plant Adaptogens-History and Future Perspectives. Nutrients, 2021; 13(8): 2861. https://doi.org/10.3390/nu13082861
- 46. Cicero A., DeRosa G., Brillante R., Bernardi R., Nascetti S., Gaddi A. effects of siberian ginseng (eleutherococcus senticosus maxim.) on elderly quality of life: A randomized clinical trial. Arch. Gerontol. Geriatr. 2004; 38: 69–73. https://doi.org/10.1016/j.archger.2004.04.012
- 47. Ping F.W.C., Keong C.C., Bandyopadhyay A. Effects of acute supplementation of Panax ginseng on endurance running in a hot & humid environment. Indian J. Med. Res. 2011; 133: 96–102. PMID: 21321426 Or PMCID: PMC3100154.
- 48. Jacquet A., Grolleau A., Jove J., Lassalle R., Moore N. Burnout: Evaluation of the efficacy and tolerability of TARGET 1 for professional fatigue syndrome (burnout). J. Int. Med. Res. 2015; 43: 54–66. https://doi.org/10.1177/0300060514558324
- 49. Timofeev N.P. Leuzea Carthamoides DC: Application prospects as pharmpreparations and biologically active components. In Functional Foods for Chronic Diseases; Martirosyan, D.M., Ed.; Richardson: Texas, TX, USA, 2006: 105–120. https://leuzea_ru/leuzea_adaptogen.htm. ISBN 13: 978-0-9767535-2-0.[book]
- 50. Krasutsky A.G., Cheremisinov V.N. The use of Levzey's extract to increase the efficiency of the training process in fitness clubs students. In Proceedings of the Actual Problems of Biochemistry and Bioenergy of Sport of the XXI Century, Moscow, Russia, 2017; 10(26): 382–388. https://doi.org/10.3390%2Fnu13082861

- 51. Isenmann E., Ambrosio G., Joseph J.F., Mazzarino M., de la Torre X., Zimmer P., Kazlauskas R., Goebel C., Botrè F., Diel P., et al. Ecdysteroids as non-conventional anabolic agent: Performance enhancement by ecdysterone supplementation in humans. Arch. Toxicol. 2019; 93: 1807–1816. https://doi.org/10.1007/s00204-019-02490-x
- 52. Vanyuk A.I. Evaluation of the effectivnness of rehabilitation measures among female volleyball players 18-22 years old in the competitive period of the annual training cycle. Slobozhanskiy Sci. Sports Visnik. 2012; 5: 95–98. https://doi.org/10.7752/jpes.2020.s3281
- 53. Timofeev N.P., Koksharov A.V. Study of Leuzea from leaves: Results of 15 years of trials in athletics. New Unconv. Plants Prospect.Use 2016; 12: 502–505. PMID:2082083
- 54. Wilborn C.D., Taylor L.W., Campbell B.I., Kerksick C., Rasmussen C.J., Greenwood M., Kreider R.B. Effects of Methoxyisoflavone, ecdysterone, and sulfo-polysaccharide supplementation on training adaptations in resistance-trained males. J. Int. Soc.Sports Nutr. 2006; 3: 19–27 https://doi.org/10.1186/1550-2783-3-2-19
- 55. Ryan E.D., Gerstner G.R., Mota J.A., Trexler E.T., Giuliani H.K., Blue M.N.M., Hirsch K.R., Smith-Ryan A.E. The acute effects of a multi-ingredient herbal supplement on performance fatigability: A double-blind, randomized, and placebo-controlled trial. J.Diet. Suppl. 2020: 1–10. https://doi.org/10.1080/19390211.2020.1790709
- 56. Roumanille R., Vernus B., Brioche T., Descossy V., Van Ba C.T., Campredon S., Philippe A.G., Delobel P., Bertrand-Gaday C., Chopard A., et al. Acute and chronic effects of Rhaponticum carthamoides and Rhodiola rosea extracts supplementation coupled to resistance exercise on muscle protein synthesis and mechanical power in rats. J. Int. Soc. Sports Nutr. 2020; 17: 1–13. https://doi.org/10.1186/s12970-020-00390-5
- 57. Brown R.P., Gerbarg P.L., Ramazanov Z. Rhodiola rosea: A phytomedicinal overview. Herbal. Gram. 2002; 56: 40–52. https://doi.org/10.1080/02640414.2018.1538028
- 58. Ballmann C.G., Maze S.B., Wells A.C., Marshall M.R., Rogers R.R. Effects of short-term Rhodiola Rosea (golden root extract) supplementation on anaerobic exercise performance. J. Sports Sci. 2019; 37: 998–1003. https://doi.org/10.1080/02640414.2018.1538028
- 59. Jówko E., Sadowski J., Długoł ecka B., Gierczuk D., Opaszowski B., Cie'sli nski I. Effects of Rhodiola rosea supplementation on mental performance, physical capacity, and oxidative stress biomarkers in healthy men. J. Sport Health Sci. 2018; 7: 473–480. https://doi.org/10.1016/j.jshs.2016.05.005
- 60. Abidov M., Grachev S., Seifulla R.D., Ziegenfuss T.N. Extract of Rhodiola rosea radix reduces the level of c-reactive protein and creatinine kinase in the blood. Bull. Exp. Biol. Med. 2004; 138: 63–64. https://doi.org/10.1023/B:BEBM.0000046940.45382.53
- 61. Edwards D., Heufelder A, Zimmermann A. Therapeutic effects and safety of Rhodiola rosea extract WS®1375 in subjects with life-stress symptoms—Results of an open-label study. Phytother. Res. 2012; 26: 1220–1225. https://doi.org/10.1002/ptr.3712
- 62. Shevtsov V. Zholus B. Shervarly V. Vol'Skij V. Korovin Y. Khristich M. Roslyakova N. Wikman G. A randomized trial of two different doses of a SHR-5 Rhodiola rosea extract versus placebo and control of capacity for mental work. Phytomedicine 2003; 10: 95–105. https://doi.org/10.1078/094471103321659780

- 63. 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. Nord. J. Psychiatry 2007; 61: 343–348. https://doi.org/10.1080/08039480701643290.
- 64. Shanely R.A. Nieman D.C. Zwetsloot K.A. Knab A.M. Imagita H. Luo B. Davis B. Zubeldia J.M. Evaluation of Rhodiola rosea supplementation on skeletal muscle damage and inflammation in runners following a competitive marathon. Brain Behav. Immun. 2013; 39: 204–210. https://doi.org/10.1016/j.bbi.2013.09.005
- 65. Stejnborn A.S. Pilaczy 'nska-Szcze'sniak S. Basta P. Deskur-'Smielecka E. The influence of supplementation with Rhodiola rosea L. Extract on selected redox parameters in professional rowers. Int. J. Sport Nutr. Exerc. Metab. 2009; 19: 186–199. https://doi.org/10.1123/ijsnem.19.2.186
- 66. Parisi A. Tranchita E. Duranti G. Ciminelli E. Quaranta F, Ceci R. Sabatini, S. Effects of chronic Rhodiola Rosea supplementation on sport performance and antioxidant capacity in trained male: Preliminary results. J. Sports Med. Phys. Fit. 2010; 50: 57. PMID: 20308973
- 67. Bystritsky A. Kerwin L. Feusner J.D. A pilot study of Rhodiola rosea (Rhodax®) for generalized anxiety disorder (GAD). J.Altern. Complement. Med. 2008; 14: 175–180 https://doi.org/10.1089/acm.2007.7117
- 68. Hancke J. Burgos R. Ahumada F. Schisandra chinensis (Turcz.) Baill. Fitoterapia 1999; 70: 451–471. https://doi.org/10.1016/S0367-326X(99)00102-1
- 69. Kochetkov N. Khorlin A. Chizhov O. Sheichenko V. Schizandrin—Lignan of unusual structure. Tetrahedron Lett. 1961; 2: 730–734. https://doi.org/10.1016/S0040-4039(01)91684-3
- 70. Park J. Han S. Park H. Effect of Schisandra chinensis extract supplementation on quadriceps muscle strength and fatigue in adult women: A randomized, double-blind, placebo-controlled trial. Int. J. Environ. Res. Public Health 2020; 17: 2475. https://doi.org/10.3390/ijerph17072475
- 71. Zhao T. Mao G.-H. Zhang M. Li F. Zou Y. Zhou Y. Zheng W. Zheng D.-H. Yang L.Q. Wu X.-Y. Anti-diabetic effects of polysaccharides from ethanol-insoluble residue of Schisandra chinensis (Turcz.) baill on alloxan-induced diabetic mice. Chem. Res. Chin. Univ. 2012; 29: 99–102. https://doi.org/10.1007/s40242-012-2218-9
- 72. Dwyer AV. Whitten DL. Hawrelak J.A. 'Herbal medicines, other than St. John's Wort, in the treatment of depression: a systematic review.' Altern Med Rev. 2013 Mar; 16(1): 40–9. Review. PMID: 21438645
- 73. Sarris J. Panossian A. Schwitzer I. Stough C. Scholey A. Herbal medicine for depression, anxiety and insomnia: a review of psychopharmacology and clinical evidence. Eur Neuropsychopharmacol; 2011, https://doi.org/10.1016/j.euroneuro.2011.04.002
- 74. Ishaque S. Shamseer L. Bukutu C. Vohra S. Rhodiola rosea for physical and mental fatigue: a systematic review. BMC Complement Altern Med. 2013 May 29; 12: 70. https://doi.org/10.1186/1472-6882-12-70

- 75. Amsterdam JD. Panossian AG. Rhodiola rosea L. as a putative botanical antidepressant Phytomedicine. 2016 Jun 15; 23(7):770-83. https://doi.org/10.1016/j.phymed.2016.02.009.
- 76. Tao H. Wu X. Cao J. Peng Y. Wang A. Pei, J. Xiao J. Wang S. Wang Y. Rhodiola species: A comprehensive review of traditional use, phytochemistry, pharmacology, toxicity, and clinical study. Med Res Rev. 2019 Sep; 39(5):1779-1850. https://doi.org/10.1002/med.21564.