

The Role of Adaptogens in Eastern Medicine for Alleviating Stress: A Brief Review

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ABSTRACT

Authors' Contributions

1 Conception & Study design, Data Collection & Processing.

2 Data Analysis and/or Interpretation, Critical Review.

3,4,5 Drafting of Manuscript, Critical Review. 6, 7 Drafting of Manuscript.

Article info.

Received: April 25, 2024

Accepted: June 15, 2024

Funding Source: Nil

Conflict of Interest: Nil

Cite this article: Zahidi M, Naeem S, Khan SS, Tahir A, Mehmood M, Ullah G. The role of adaptogens in Eastern medicine for alleviating stress: a brief review. RADS J Pharm Allied Health Sci. 2024;2(2):98-108.

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Background: Chronic stress is a major contributor to various physical and mental health disorders, including anxiety, depression, and cardiovascular diseases. Traditional Eastern medicines offer a holistic approach to managing stress, incorporating natural substances known as adaptogens. These compounds have been recognized for their potential to enhance the body's resilience to stress.

Methodology: The systematic literature search involved review from published trials of *Rhodiola rosea*, *Panax ginseng*, and *Withania somnifera*. Original human and animal intervention and observational studies based on hypothalamic-pituitary-adrenal (HPA axis), cortisol levels, and stress-related biomarkers of adaptogens and their effects during clinical trials, in vivo studies, and Meta – analyses were included.

Results: Adaptogens consistently demonstrated their ability to reduce cortisol levels, improve cognitive function, and alleviate symptoms of anxiety and depression. Notably, *Rhodiola rosea* reduced fatigue and improved mental clarity, while *Withania somnifera* showed significant reductions in anxiety and stress-induced inflammation. The safety profiles of these adaptogens were favorable, with minimal adverse effects reported.

Conclusion: Adaptogens offer a promising, low-risk approach to stress management by modulating the body's stress response and improving mental and physical health. While current evidence supports their efficacy, further research is needed to clarify optimal dosing, long term safety, and mechanism of action in clinical settings. Integrating adaptogens into modern health care could enhance holistic approaches to managing chronic stress.

Keywords: Adaptogens, Stress, Eastern Medicine System, *Rhodiola rosea*, *Panax ginseng*, and *Withania somnifera*.

INTRODUCTION

Emergence of Adaptogens in Eastern Medicine

The stress-related disorder has emerged as a major public health concern around the world, again affecting

millions. Current Post traumatic stress disorder (PTSD) affects 7.7 million adults (3.5%) in America per year, and stress is involved in the development of 75% of diseases from psychiatric disorders to immunosuppressive, diabetes mellitus and

hypertension [1]. Current treatments for stress-related disorders primarily include benzodiazepines, selective serotonin reuptake inhibitors (SSRIs), and serotonin-norepinephrine reuptake inhibitors (SNRIs) [2]. While effective, these pharmacological treatments have limitations, especially in addressing the long-term impacts of chronic stress on immunity, in cognition, digestion, and cardiovascular health. Consequently, there is an urgent need for novel therapeutic approaches that mitigate stress without the adverse effects associated with long-term medication use.

Over the past decade, botanical therapeutics called adaptogens elicited a lot of interest for their effects on the prevention of depression and stress. Adaptogens are substances modeled after certain herbs or plant-derive products that assist the body to deal with stress and improve the tone of the body's functions throughout different physiological systems [3]. First introduced by Soviet scientist N. Lazarev in the 1940s, adaptogens were characterized by their ability to boost the body's resistance to a wide array of stressors, from environmental toxins to physical and emotional challenges [4]. Over decades, the concept has evolved, with contemporary definitions emphasizing their functions as bio regulators that counteract stress, support homeostasis, and promote an enhanced, balanced response to external stressors [5].

Defining Adaptogens and their Key Criteria

Adaptogens are defined by specific characteristics that set them apart from other botanical agents. To qualify as an adaptogen, a plant compound must meet three criteria as mentioned below [6].

- **Non-specific Action:** Adaptogens should support the body in withstanding various stressors, whether chemical, biological, or physical. This non-specific response to a wide range of stressors is essential, as it enables the body to manage challenging conditions without targeting a single physiological pathways.
- **Preservation of Homeostasis:** Adaptogens must help maintain internal stability by balancing physiological processes, supporting the body's equilibrium without over activation or overstimulation.
- **Non-disruption of Normal Body Functions:** They should exert their beneficial effects without impairing the body's natural functions or causing adverse reactions

These principles, formulated in the mid-20th century, have evolved over decades of research. In the 1990s, a team of researchers refined the adaptogen concept, describing them as "*natural bio regulators that enhance the body's capacity to adapt to environment changes, thereby mitigating the negative effects of stress.*" By limiting the stress response at the alarm phase, adaptogens help delay or even prevent the onset of the exhaustion phase, a critical component of the general adaptation syndrome (GAS) [7].

In practical applications, adaptogens have demonstrated uses beyond simple stress reduction. They are commonly used to induce a balanced state of health and are frequently taken to alleviate specific age-related diseases, such as cognitive decline, fatigue, general weakness, and other stress-related symptoms. For example, adaptogens are used to address conditions like memory impairments, concentration difficulties, and sexual impotence, highlighting their potential benefits across a broad spectrum of health concerns [8, 9].

Traditional and Contemporary Use of Adaptogens

The prophylactic use of adaptogens has been especially prevalent in Eastern Asian countries, including Japan, Korea, India, and China, where these compounds have long been integrated into traditional medicine. In these regions, adaptogens are utilized not only to alleviate symptoms but also as a components of a holistic approach to promote physical and mental well-being [10]. For instance, adaptogenic herbs such as *Withania somnifera* (Ashwagandha) and *Panax ginseng* are staples in traditional Asian medicine for their reported ability to support endurance, resilience, and overall health [11].

In 1998, the United States Food and Drug Administration (FDA) recognized adaptogens as "a type of metabolic regulator with demonstrated efficacy in helping the body adapt to changing environmental conditions and protecting against external threats [12]." This modern definitions aligns with contemporary research findings, which have shown that adaptogens interact with multiple molecular systems, from cellular signaling pathways to broader regulatory mechanism of the body. Despite the ambiguity surrounding the specific mechanisms of individual adaptogens, research supports their potential to elicit biochemical responses that contribute to resilience against stress [8, 13].

Current Understanding in Adaptogen Research

Although adaptogens have a long history of use, ongoing research continues to explore their broader applications and effects on human health. Studies on their molecular mechanisms indicate that adaptogens may influence biochemical changes in healthy individuals, such as the regulation of stress hormones and enhancement of cellular defense systems. However, due to their broad and sometimes vague classification, there are ongoing efforts to clarify which plant compounds truly meet the adaptogenic criteria and how these compounds work on a cellular level.

Table 1 provides an overview of the most common adaptogenic plants worldwide, along with their botanical family and commonly used parts. Notably, the Araliaceae family is well-represented, with roots frequently used for medicinal purposes. *Panax ginseng*, or Korean ginseng, serves as a classic example of an adaptogen, with its roots applied to various health uses across traditional and modern medicine.

Role of Adaptogen in Elevating Stress

In 1950, Hans Selye introduced the concept of stress in physiological and biological research, sparking significant academic interest and debate. Stress was initially understood as the body's natural response to any adverse stimulus. While stress is an inherent part of life, managing chronic stress is crucial, as its

prolonged presence can lead to various health issues, including heart disease, memory impairment, anxiety, chronic fatigue syndrome, and depression [25].

Research suggests that the hypothalamic-pituitary-adrenal (HPA) axis plays a central role in the body's stress response. When faced with a stressor, the hypothalamus releases corticotrophin-releasing hormone (CRH), which prompts the anterior pituitary gland to produce adrenocorticotrophic hormone (ACTH). ACTH then stimulates the adrenal cortex to secrete cortisol, a primary stress hormone responsible for various physiological effects. Cortisol levels are regulated by a negative feedback loop, where normal cortisol levels inhibit CRH and ACTH production, maintaining a natural diurnal cycle. However, continuous or recurrent stress can lead to HPA axis dysregulation, altering normal cortisol secretion patterns and affecting organ function. This result in an "allostatic load", or the cumulative physiological strain from prolonged stress exposure, which may lead to receptor desensitization, tissue damage, and immune suppression, as illustrated in Figure 1 [13, 26, 27]. Adaptogens, natural compounds derived from plants, play an essential role in enhancing the body's resilience to stress by modulating the HPA axis. These agents help to stabilize cortisol levels, reduce the effects of allostatic load, and improve stress tolerance, providing a complementary approach to stress management [13].

Table 1. Common Adaptogen Plants, Their Families, and Utilized Parts.

S. No	Plant Name	Family	Part Use	Common Name	Reference
1	<i>Ocimum sanctum</i> L.	Lamiaceae	Whole plant	Tulsi	[14]
2	<i>Schisandra chinensis</i>	Schisandraceae	Fruit	Chinese mafenolia vine	[15]
3	<i>Withania somnifera</i> L. Dunal	Solanaceae	Root	Indian ginseng	[16]
4	<i>Eleutherococcus senticosus</i>	Araliaceae	Root	Siberian ginseng	[17]
5	<i>Rhodiola rosea</i> L.	Crassulaceae	Root	Golden root	[18]
6	<i>Panax ginseng</i>	Araliaceae	Root	Korean ginseng	[19]
7	<i>Panax quinquefolius</i> L.	Araliaceae	Root	American ginseng	[20]
8	<i>Bryonia alba</i> L.	Cucurbitaceae	Root	Ioshtak	[21]
9	<i>Glycyrrhiza glabra</i>	Leguminosae	Root	Licorice	[22]
10	<i>Asparagus racemosus</i> Willd.	Liliaceae	Roots	Satavari	[23]
11	<i>Tinospora cordifolia</i> Willd.	Menispermaceae	Whole plant	Guduchi	[23]
12	<i>Curcuma longa</i> L.	Zingiberaceae	Roots	Turmeric	[24]

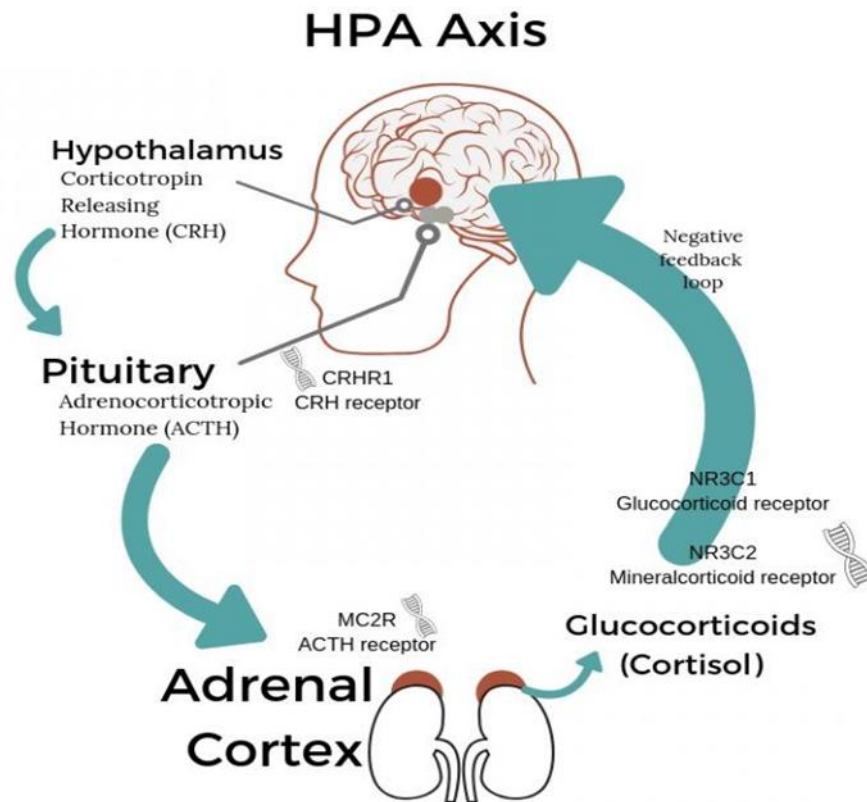


Figure 1. HPA Axis and Stress Response [28].

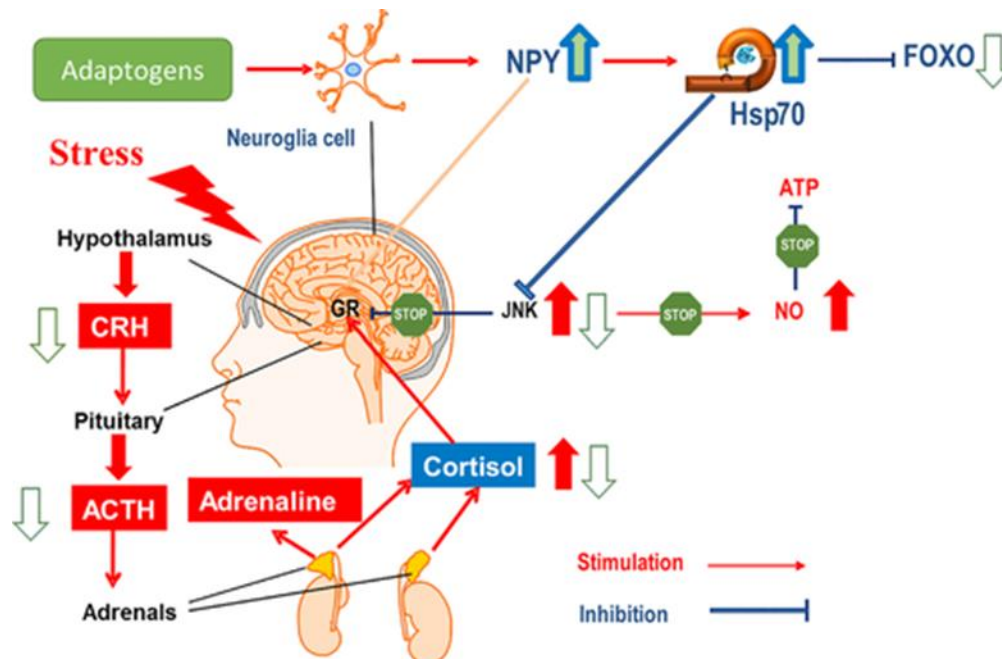


Figure 2. Hypothetical Mechanism of Adaptogen Elevating Stress [33].

Adaptogens are natural substances that support the body in resisting stress by extending the resistance

phase and strengthening non-specific defense mechanism. By enhancing the body's resilience to

stress, adaptogens contribute to achieving a state of heterostasis, or a higher, adaptive equilibrium instead of leading to exhaustion. The stronger the heterostasis, the better the adaptation to stress [9].

In both human and animals studies, adaptogens have demonstrated anti-fatigue and endurance-enhancing effects, partly mediated by stress mediators by stress hormones like cortisol and neuropeptide Y (NPY) [29]. Single dose animal studies show that adaptogens can transiently elevate cortisol and anti-diuretic hormone (ADH) levels, preparing the body for immediate stress. However, with consistent sub-chronic administration, adaptogens tend to normalize these hormones, generally reducing stress [30].

Research indicates that adaptogens exert their effects through several key molecular mechanisms. They modulate the activity of stress mediators such as nitric oxide (NO), stress-activated protein kinases, and heat shock proteins (e.g., HSP70 and HSP25), which are critical in cellular protection and repair processes as seen in Figure 2 [31]. Additionally, they influence transcription factors like Fork head Box O (FOXO) that is DAF-16 gene, which play a role in stress resistance and longevity. These mechanisms support the body's adaptive stress response and may help prevent stress-related conditions, aging, and disease [32].

Figure 2 illustrates the potential mechanism of adaptogens in modulating the stress response system. During stress, the brain releases corticotrophin-releasing hormone (CRH) and the pituitary gland secretes adrenocorticotrophic hormone (ACTH), which triggers the release of neuropeptide Y (NPY) and adrenal hormones to manage the stress response. Cortisol, released from the adrenal cortex, binds to glucocorticoid receptors (GR) in the brain as part of a feedback loop that regulates further hormone release, helping return elevated cortisol levels in the blood stream to normal [33, 34].

While moderate, short-term (eustress) is beneficial for daily functioning, chronic stress can contribute to various health conditions. For instance, chronic stress is associated with increased levels of reactive oxygen species (ROS), like nitric oxide, linked to symptoms of depression. Stress-activated protein c-Jun N-terminal kinase (JNK) has been found to inhibit GR, disrupting this feedback loop, which can lead to persistently high cortisol levels in individuals with depression. Elevated cortisol is associated with symptoms like fatigue, poor concentration, memory impairment [33, 35].

Adaptogens play a role in alleviating this process by enhancing the production of heat shock protein HSP70, which has been shown to inhibit JNK. This reduces JNK and cortisol levels under stress, preventing increased nitric oxide and preserving Adenosine Triphosphate (ATP) synthesis [9].

Active Compounds Present in Adaptogens Responsible for Physiological and Pharmacological Mechanism

Plant adaptogens contain a complex array of biologically active phytochemicals that contribute to their diverse effects on health. These phytochemicals are typically classified as either advanced phenolic compounds or tetracyclic triterpenoids/steroids. Phenolic compounds are commonly found in adaptogens such as *Rhodiola rosea*, *Schisandra chinensis*, *Eleutherococcus senticosus*, and *Withania somnifera* (Ashwagandha). These phenolics, which resemble catecholamines in structure, may influence central nervous system (CNS) activity [13].

In contrast, tetracyclic triterpenes, prevalent in *Panax ginseng*, *Bryonia alba*, and *Eleutherococcus senticosus*, share a structural similarity with corticosteroids, suggesting their role in enhancing stress resilience. Studies indicate that triterpenoid-rich adaptogens exhibit stress-protective effects, especially when administered consistently over periods of one to four weeks [31].

Figure 3 shows the phenolic compounds include phenylpropanoids and phenylethane derivatives like salidroside (rhodioloside), rosavin, syringin, triandrin, and tyrosol.

Figure 4 illustrates triterpene-based compounds, including phytosterols commonly found in *Rhaponticum carthamoides*, phytoecdysteroids, and ginsenosides, as well as phytosterols-glycosides (e.g., eleutheroside A, SG, sitoindosides, and daucosterol). These compounds collectively contribute to adaptogens' ability to modulate stress responses and support overall physiological balance.

Tyrosol, abundant in *Rhodiola* species, *Camellia sinensis* (green tea), *Olea europaea* (olive), and various adaptogens, is well recognized for its ability to mitigate oxidative stress. It plays a dual role by reducing oxidative damage and enhancing the activity of antioxidant defense enzymes, an effect observable at the cellular level side, widely found in *Rhodiola rosea* L., a traditional herbal medicine, has shown

potent neuroprotective properties, Research indicates that its mechanism involve anti-inflammatory, anti-apoptotic, and anti-oxidant actions, achieved through modulation of several critical signaling pathways and

key molecules such as Nuclear Factor kappa-light chain enhancer of activated B cells (NF- κ B), Tumor Necrosis Factor α (TNF- α), and Phosphoinositide 3-kinase (PI3K/A) [9, 41, 42].

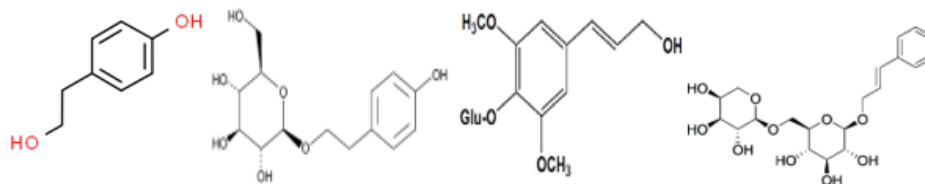


Figure 3. Phenolic compounds tyrosol, salidroside, syringin, and rosavin from left to right [36-38].

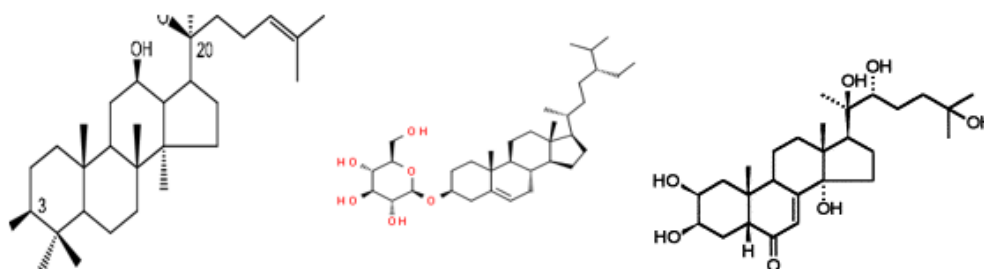


Figure 4. Triterpene compounds ginsenosides, daucosterol, and phytoecdysteroids from left to right [39, 40].

Syrinoside prevalent in *Eleutherococcus senticosus*, *Schisandra chinensis*, *Rhodiola rosea*, and other adaptogens, has notable neuroprotective effects. Studies reveal that syringin can suppress the production of pro-inflammatory factors, including NF- κ B, Interleukin 1- β (IL-1 β), IL-6, TNF- α and Myeloperoxidase (MPO). It also increases phosphorylation and cytoplasmic retention of FOXO3a, preventing NF- κ B from translocating to the nucleus, thereby enhancing neuroprotection, and potentially guarding against neurodegenerative disease [43].

Plants like *R. rosea* and *R. sachalinensis* rich in rosavin, a compound that may improve and cognitive function by reducing neurotoxicity and cellular damage, making it a promising candidate for treating neurodegenerative conditions [44].

Among triterpenes, ginsenosides are highly valued and abundantly found in *Panax ginseng*, *Panax quinquefolius*, and other *Panax* species. Used as a traditional remedy for centuries, these active compounds-known as ginseng saponins-possess anti-oxidants, anti-apoptotic, immunostimulant, and anti-

inflammatory properties, such characteristics suggest that ginsenosides may help protect against neurodegenerative disease and delay neuronal aging [45].

Additionally, multiple systemic reviews and meta-analyses indicate that adaptogens are rich in beneficial compounds such as lignans (e.g., sesamin in *Schisandra chinensis*) and saponins (e.g., daucosterol). These adaptogenic constituents, along with coumarins, have been shown to significantly improve learning and memory, protect neurons, reduce A β -induced ROS generation in the hippocampus, and enhance the expression of synaptophysin in the hippocampal neurons [6, 46].

Key Adaptogens in Eastern Medicine

Eastern medicine acknowledges the interconnectedness of the body and its environment, and adaptogens are seen as a means to restore harmony and promote optimal health. As interest in natural remedies grows, adaptogens continue to gain recognition for their potential therapeutic benefits in Eastern medicine. Derived from various plants and herbs, adaptogens are recognized for their unique

potential to assist the body to adapt and respond to stressors. Some of the commonly used adaptogens in eastern medicine systems such as Ayurveda and Traditional Chinese Medicine (TCM) are discussed below [47].

Ocimum sanctum

Ocimum sanctum, also called 'Tulsi' is a holy plant in Hindus and associated with ancient Ayurveda. Traditional usage is supported due to various characteristics including antiseptic, anti-allergic, and anti-cancer actions, as well as revitalizing, tonic, and renewing qualities that would promote longevity and a healthy existence. The plant is accurately categorized as an adaptogen because of its immuno-modulating, anti-stress, hepatoprotective, chemo preventive, and anti-inflammatory properties [48].

Withania somnifera

Withania somnifera, sometimes called as 'ashwagandha', is highly valued in the Indian Ayurvedic medical system. It is utilized as a nervine tonic in particular and for a variety of illness processes. In light of these facts, several scientific investigations were conducted, and its adaptogenic and anti-stress properties were thoroughly examined and proved beneficial for neurological illnesses [49].

Rhodiola rosea

Rhodiola rosea is a well-known plant in both Traditional Chinese Medicine and Siberian medicine. It is known for stimulating the neurological system, reduce depression, improve job performance, get rid of weariness, and avoid high altitude sickness in Eastern Europe and Asia. Russian researchers have classified *Rhodiola rosea* as an adaptogen because of its documented capacity to boost resistance against a range of chemical, biological, and physical stresses [18].

***Schisandra chinensis* (Turcz.) Bail.**

One plant that is frequently mentioned as an example of a medicinal herb used in contemporary Chinese medicine is *Schisandra chinensis* (Turcz.) Bail. The plant has included in the State Register of Drugs and recent editions of the USSR's National Pharmacopoeia. It is known to enhance physical performance and provide a protective impact against a wide range of hazardous conditions, such as heat exhaustion, skin burn, cooling, frostbite, immobilization, swimming while under confined in a

low air pressure environment, aseptic inflammation, irradiation, and heavy metal poisoning [15].

METHODOLOGY

Data Resources

The systematic literature search was conducted using data bases such as PubMed, Cochrane Library, Scopus, Web of Sciences, and Google Scholar.

Search Strategy

We utilized key words including Adaptogens, Chronic Stress, *Rhodiola rosea*, *Panax ginseng*, *Withania somnifera*, and HPA-axis, Cortisol, and stress biomarkers.

RESULT DISCUSSION

Stress is an inevitable part of people's lives, and often can cause dysregulation of the HPA axis, if chronic. In modern studies on adaptogenic herbs it has been revealed that those substances are able to dampen stress reactions by regulating cortisol concentrations and enhancing the psychological condition. The current paper is a systematic review investigating the findings of nine adaptogenic herbs on cortisol and ACTH, which are released by mentally stressed healthy adults.

The research conducted up to date clearly shows richness and diverseness of the adaptogen towards the stress response system, especially the HPA axis. This has given a boost to the necessity of cortisol stabilization due to the numerous health risks that chronic dysregulation of this system causes. The results show the practical applicability of the theoretical approach, which identifies that adaptogenic herbs can play a role in altering biomarkers of stress. In a meta-analysis of the effects of *Withania somnifera*, Tóth-Mészáros et al. (2023) reported a significant decrease in serum cortisol levels and highly significant reductions in the Perceived Stress Scale (PSS) scores in the treatment group compared to placebo [50]. The findings are in harmony with the previous research of Lopresti et al. (2019) who discovered reduction in anxiety by Ashwagandha supplementations shown by decreased Hamilton Anxiety Rating Scale (HAM-A) scores and Depression, Anxiety, and Stress Scale -21 (DASS-21). Consequently, Ashwagandha as other adaptogens proved to be capable of regulating stress responses through modulation of the HPA axis [51].

However, the implications of the present study need to be cognizant of the existing research limitations. Studies are not uniform in their design, dosing regimens and the measures used to assess patients; this makes the development of benchmarks difficult. Furthermore, although the effects of adaptogens are not questioned, there remains some concern with the interaction of these substances with conventional pharmacologic treatments in addition to patient tolerance. The use of adaptogens in the treatment plans requires a combination of understanding the given patient's medical history, a list of medications taken, and particular stress-related concerns.

In conclusion it can be said that most of the data about using adaptogens for preventing or treating stress are quite convincing and conclusive; however, more research needs to be done in this field. Further research should be directed to finding out more of the correct functioning of these natural products, proper dosage for use and the effect of long-term uses on the human system. Including adaptogens in clinical practice enables healthcare to improve the approaches to address challenged by the reach effects of chronic stress. Including adaptogens into modern approaches to treating clients with the signs of stress-related disorders appears to be effective as a complementary approach to attaining better mental and physical conditions.

CONCLUSION

Adaptogens are agents that improve the nonspecific response to stress and promote recovery from the damaging effects of stress. Their prophylactic use by healthy subjects to reduce the negative effects of stress and for prevention of age-related diseases is justified. Further studies are warranted if we are to understand the range of interactions between adaptogens and stress response pathways (both intracellular and extracellular) in terms of the metabolic regulation of homeostasis in stress- and age-associated disease. Further, any strict specificity of pharmacological action when using phytochemicals remains questionable.

FUNDING

This study received no funding.

CONFLICT OF INTEREST

All the authors do not have any conflict of interest.

ACKNOWLEDGMENT

The authors would like to express gratitude for the support offered by the University of Karachi (UOK), Department of Pharmacology.

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