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Narrative review of plant-based adaptogens in stress management

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ABSTRACT

Stress, a physiological and psychological response to internal and external challenges, can negatively impact health when chronic or excessive. Plant-based adaptogens are a class of herbal compounds that enhance the body's resilience to stress by modulating neuroendocrine, immune, and metabolic responses. This narrative review explores the mechanisms, efficacy, and safety of prominent adaptogens, including Ashwagandha (Withania somnifera), Rhodiola rosea, Holy Basil (Ocimum tenuiflorum), Panax ginseng, Schisandra chinensis, and Licorice root (Glycyrrhiza glabra). Evidence from preclinical, clinical, and ethnopharmacological studies suggests that these plants improve stress tolerance, reduce fatigue, enhance cognitive function, and normalize stress hormone levels. Adaptogens exert multi-target effects on the hypothalamic-pituitary-adrenal axis, cortisol regulation, and oxidative stress pathways. They are generally well-tolerated, though potential drug interactions and contraindications should be considered. Integrating adaptogens with lifestyle interventions may provide a holistic approach to stress management. Future research should focus on standardization, novel combinations, and rigorous clinical trials to optimize therapeutic applications.

Keywords: Stress, Adaptogens, Ashwagandha, Rhodiola, Neuroendocrine, and Herbal Medicine

INTRODUCTION

Stress is the perception of physical, emotional, or psychological threats. The introduction of new technologies and information has increased the complexity of daily life. This paradigm change demonstrates how some challenges may be perceived in terms of new and unexpected situations, alteration of established structures, and subsequently, adaptation and adjustment to new requirements. In this regard, stress may be exerted by adverse environmental conditions, such as temperature, noise, and toxins [1]. Exposure to such adverse environmental factors associated with day work activity may trigger the production of certain compounds that initiate an organism's stress response, which enables subsequent adaptation to both the stressor and the new situation. The general description of a stressor describes an equally wide range of scenarios. Stress may be defined as any altered physical or psychological stimulus that results in elevation of a hypothalamic–pituitary–adrenal (HPA) axis response. The HPA axis is the system responsible for controlling a wide range of physiological reactions to perceived challenge and threat, and corticosterone or cortisol secretion by the adrenal gland represents an important physiological response. Stress can be classified into many different types: eustress, distress, acute stress, chronic stress, and episodic acute stress [2].

Understanding Stress

Stress is the perception of, or exposure to, challenges that threaten homeostasis or a state of well-being where an individual's resources are insufficient to cope with the challenges [2]. In a healthy immune system, an appropriate stress response is adaptive and promotes restoration of homeostasis. However, when the stress response is inappropriate (e.g., excessive or prolonged), it causes a range of adverse effects on physiological and psychological health[3]. When an individual experiences stress, the hypothalamic-pituitary-adrenal (HPA) axis is activated, and this activates the release of glucocorticoid hormones, including cortisol, into the circulation [1]. Cortisol is a key player in the adaptive response to stress and is chronically released during stress, thereby contributing to oxidative, inflammatory, physiological, and mental stress. In recent years, nutritional supplements with

antioxidant, anti-inflammatory, and stress-relieving properties have been widely used for the management of chronic stress. A mathematical model based on gene expression signatures and clinical observations demonstrated that a multi-nutrient botanical formulation, Nutrilite® Daily Plus, leads to a significant decline in physical (~ 75%), mental (~ 70%), oxidative (~ 55%), and inflammatory stresses (~ 75%), which was also confirmed experimentally. Exposure to stressors elicits physiological and behavioral responses that enable the individual to adjust[3]. The term stressor refers to an event or stimulus that triggers the stress response. Stressors include many environmental factors (temperature, noise, radiation, pathogens, social factors); internal perturbations such as injury, inflammatory processes, infections, pain, and disease; or psychological and physiological challenges such as fear or difficult situations[3]. External or internal challenges may induce a physiological or psychological threat to the body and result in the activation of the stress response and stress hormone secretion. Stress can be categorized as either acute or chronic, and it can be either physical (e.g., exposure to injury or excessive environmental conditions) or psychological (e.g., fear, depression, or anxiety)[4, 5]. Chronic, prolonged, or excessive stress can lead to a variety of pathological conditions such as hypertension, stroke, decreased memory and learning, anxiety, depressive disorders, and a reduction in neurogenesis[3]. The ability of an individual to adapt rapidly to stressors is therefore crucial in avoiding these detrimental effects. Acidic and proteolytic environments generated during stress have been shown to facilitate the survival, differentiation, and growth of cancer cells [4].

Definition of Stress

Stress is the physiological reaction to environmental threats or pressure, manifested by physical and psychological symptoms. Depending on duration and intensity, it can be categorized into acute stress, either episodic or traumatic, or chronic [4]. These responses prepare the organism to face a real or perceived threat [4]. However, if persistent and left untreated, stress can lead to serious health problems such as burnout, depression, post-traumatic stress disorder, anxiety, and various medically unexplained conditions [4]. Individuals often seek to alleviate unpleasant emotions through relaxation or other stress relief techniques.

Types of Stress

Stress is the physiological reaction to environmental threats or pressure and can be self-driven or of external origin. It manifests through various physical and psychological symptoms. If persistent and untreated, stress can lead to serious health problems, including burnout, depression, post-traumatic stress disorder, anxiety, and cardiovascular, gastrointestinal, neurological, and musculoskeletal diseases [4]. Two main types of stress are distinguished: Eustress and Distress [1]. Eustress is a positive form of stress that results from motivating challenges, stimulating feelings of excitement, and promoting successful performance. In contrast, distress is a negative form of stress that impairs cognition, interferes with learning, introduces ambiguity in perception, and causes anxiety or concern over longer time periods. The physiological effects of stress include alterations of the hypothalamic–pituitary–adrenal axis and the immune system, which are mainly responsible for the onset and development of stress-related disorders.

Physiological Effects of Stress

Stress triggers a physiological response that temporarily alters the body's state to achieve a more favorable condition [1]. Angiogenesis is involved in the initiation and development of stress-enhanced tumor growth, and elevated norepinephrine levels contribute to this process. Karatsoreos and McEwen described stress, its different types, and its effects on brain plasticity and disease susceptibility. Acute stress can upregulate physiological responses such as gluconeogenesis and increase the production of cytokines and trophic factors important for learning and memory [1]. Chronic stress leads to the release of hormones like adrenaline, cortisol, and pro-inflammatory cytokines that strain various bodily systems. Increased cortisol levels affect carbohydrate, fat, and protein metabolism, resulting in an insulin-resistant state [2]. Prolonged cortisol elevation suppresses immune function, reduces bone formation, inhibits calcium absorption, interferes with thyroid function, decreases growth hormone release, and impairs memory and learning [2].

Adaptogens: An Overview

Stress arises when an individual encounters a situation that disturbs or interferes with their physical or mental well-being [1]. It can be acute or chronic. Acute stress refers to sudden and short-lived stress, whereas chronic stress pertains to recurring or persistent everyday stressors that can significantly affect an individual's health and well-being [2]. Despite the assumption that humans can effortlessly cope with the complexities of modern life, stress-related illnesses have become increasingly prevalent, and the economic costs of stress-related ailments are notable. When an individual is faced with a stressor, the hypothalamic-pituitary-adrenal (HPA) axis and the sympathoadrenal system, respectively, orchestrate the release of glucocorticoids and catecholamines by signaling through corticotropin-releasing hormone[1]. Although stress can be beneficial, as it motivates and initiates the fight-or-flight response in the face of threats, chronic exposure is of concern due to its significant impact on health.

When the body is exposed to stressors and the HPA axis becomes active, it results in an activation cascade that produces adaptive physiological and psychological responses to maintain homeostasis [2]. However, in situations where the stress response continues past the normal state of functioning and results in an altered tissue environment, the stress becomes pathological [1]. Despite the increased understanding of stress and its effects on the body, a treatment to prevent or reduce the consequences remains elusive. Nonetheless, the term "adaptogen" was coined as an attempt to characterize a group of compounds that increased a system's capability to adapt to conditions associated with fatigue and stress exposure [2]. The proposed mathematical definition of an adaptogen is an agent that Re(Stress) ≥ Re(Norm), where Re is the reactivity and Re(Stress) is the reactivity after the introduction of an adequate amount of stress, and Re(Norm) is the reactivity of the system beforehand. This mathematical definition of an adaptogen provides a method to measure a system's responsiveness to stressors and the overall effect of an adaptogen within the system [1].

Definition of Adaptogens

Originally proposed during the Second World War, the term "adaptogen" referred to substances that enhance an organism's capability to counter adverse physical factors [1]. Used for centuries throughout Asia, adaptogens are commonly applied to traditional and herbal medicine to reduce the impact of stress [5]. Various plants with adaptogenic properties demonstrate normalizing effects on living organisms when exposed to an external cause of stress. This effect is being investigated for assisting in mental health, immune function, arousal, endurance, fatigue, and subjective feelings of well-being. These properties, therefore, allow adaptogens to aid in the prevention and treatment of stress-related conditions[5]. Herbal preparations formulated with adaptogenic plants are broadly employed to relieve stress-induced fatigue and weakness. Consequently, the adaptogens under consideration in this review are those most often formulated alone or combined in the development of widely available herbal products for mental health and subjective feelings of well-being[1, 5].

History of Adaptogens

Dmitrii V Steiner in the mid-20th century [2]. Stress refers to any physical, chemical, or biological factor that disturbs the organism's normal physiological homeostasis. It can be broken down into three categories: acute, chronic, and traumatic. Acute stress creates short-term physiological changes after threats of injury or death; chronic stress represents prolonged exposures to adverse conditions; and traumatic stress represents a direct threat to life or physical integrity that causes a strong and persistent physiological and mental response. While acute stress can have amplified and positive effects on the body and immune system, chronic stress becomes detrimental and exhausting [2]. Acute and chronic stress increase the risk of heart disease, cancer, and Alzheimer's. Adaptogens combat physiological and psychological stress by increasing the body's resistance, reducing damaging effects, and renewing overall balance because of their ability to stabilize homeostasis. Also known as adaptogenic agents, plant-based adaptogens include a wide range of herbal supplements that aid the immune system and increase the body's ability to regulate hormonal, neurological, and physical responses to various stressors. Difio and Calabresi hypothesized in the 1940s that these herbs aid chemical and biological resistance and are classified as non-toxic [6]. Gitelman coined the term "adaptogen" in 1947 when discussing substances that enhance the nonspecific resistance to environmental stressors while producing a normalizing effect on bodily functions [1]. Since then, several plants have undergone laboratory and clinical research to determine which compounds impart beneficial effects on physical and cognitive functions. Eclectic Medical physicians researched adaptogens starting in the 1800s to treat anxiety, nervous tension, stress, and fatigue, with widespread use continuing through the 1920s. Today, widespread use continues, and multiple studies support the claim of their beneficial effects. Because of their energy-boosting and anti-fatiguing effects, plant-based adaptogens enhance attention, endurance, stamina, and overall mental capacity[1, 6]. These herbal supplements may also improve an individual's sympathetic tone to achieve homeostasis and overcome chronic fatigue, organ dysfunction, chronic inflammation, cancer, autoimmune diseases, and mental disorders. Mechanistically, these plants interact with adrenal and pituitary stress hormones and influence key mediators of the stress response.

Mechanisms of Action

The exact modes of action of plant-based adaptogens remain incompletely understood, with many herbal remedies exerting effects via multiple targets and mechanisms [6]. Pharmacological activity results from an integrated whole-organism response that includes genomic, transcriptional, gene expression, and signal transduction regulatory events. Network, transcriptomic, and proteomic approaches provide valuable tools to examine such complex mechanisms. Active constituents interact in complementary ways to influence biochemical and molecular regulatory systems responsible for maintaining internal balance and homeostasis, particularly the neuroendocrine-immune system [7]. Prominent molecular targets are located within receptor-coupled transduction pathways that regulate the synthesis and release of nitric oxide and stress hormones, including cortisol, β-endorphins, and catecholamine systems, pivotal to the organism's adaptation to stress. Key constituents found in a range of

adaptogens act as low-molecular-weight ligands of key molecular regulatory proteins, including enzymes, receptors, and transcription factors [1, 2, 3]. Through these interactions, they enhance stress-induced secretion of stress-protective hormones such as cortisol and nitric oxide, thus countering the physical and mental decline associated with acute and chronic toxic stress. By increasing tolerance to adverse influences, adaptogens improve attention and endurance. Experimental evidence supports the use of adaptogens for stress relief, memory enhancement, and fatigue reduction [1]. Their effects often resemble increased resistance to stress associated with the rapid cellular synthesis of stress-activated proteins. Many active compounds act as mild stress mimetics, or "mild stress mimetics," resembling the natural response to challenging environments and representing a form of stress vaccination that bolsters the organism's resistance to a broad spectrum of adverse influences[6, 7].

Key Plant-Based Adaptogens

Adaptogens are non-toxic substances that increase resistance and survival under harmful influences, helping to maintain homeostasis [1]. They help control metabolism and regulate an individual's response to stress by working on the hypothalamic-pituitary-adrenal (HPA) axis and the hypothalamic-pituitary-gonadal (HPG) axis. Numerous plant species possess this property, especially certain plants that grow in harsh environments such as high altitudes and freezing climates [5]. Six prominent examples are detailed below. Ashwagandha (Withania somnifera) is a self-sustaining plant that grows in a wide variety of locations, such as India and Africa. Its roots and leaves contain alkaloids that have stress-relieving properties, and it is widely used in Ayurvedic medicine for stress relief [1, 5]. Rhodiola Rosea grows at high altitudes of up to 2,300 metres in Europe and Asia, with extensive roots and rhizomes. Its adaptogenic properties help reduce fatigue and burnout during stressful situations [5]. The root contains rosavin, rosin, rosarin, and salidroside. Salidroside has antioxidant and anti-inflammatory effects, while the rosavins exert antidepressant, anti-fatigue, and anxiolytic activities, collectively ameliorating stress-related symptoms. Standardized extracts of 3% rosavins and 1% salidroside have been shown to increase mental performance and reduce fatigue associated with stress. Holy Basil (Ocimum tenuiflorum) has large, different leaves and a robust root system, typically growing in subtropical and tropical regions, including India. The leaves contain B2-caryophyllene for anti-inflammatory activity and eugenol for analgesic and anti-inflammatory effects, contributing to the alleviation of stress. Ginseng (Panax ginseng) typically grows in cooler climates and has fleshy roots. The roots contain ginsenosides, which influence the stress response; it is widely used in traditional Chinese medicine for various stress-related conditions. Schisandra (Schisandra chinensis) grows in China and Russia, where its sour and sweet berries assist the nervous system in coping with stress [5]. Licorice Root (Glycyrrhiza glabra) is a tough perennial that grows in the Mediterranean region. The root is used for the treatment of stress and fatigue.

Ashwagandha

Ashwagandha (Withania somnifera) is a traditional herb commonly employed as an adaptogen for managing diverse stress conditions [8]. It exerts a wide range of effects on the neuroendocrine, immune, and mitochondrial systems, and on adrenal function, which collectively influence brain chemistry, since the stress response is largely coordinated by the brain [9]. These actions provide a strong scientific basis for the plant's broad efficacy in supporting resilience against stress and stress-related challenges. Ashwagandha contains steroidal lactones, alkaloids, and saponins (mainly withanolides, withaferins, and withanins) as active phytochemicals. The hydrophobic nature of these constituents limits pharmaceutical applications and often results in low yields when the plant is dry-extracted with polar solvents[8]. To overcome such bottlenecks, supercritical and ultrasound-assisted liquids have been tested for ashwagandha extraction, but the associated severe conditions are not industrially scalable. Alternative hydroalcoholic solutions operating under mild conditions have consequently been explored for large-scale production of bioactive enriched extracts[9].

Rhodiola Rosea

Rhodiola rosea, a woody perennial herb that grows in arctic regions and mountains across Europe, Asia, and North America, occupies a prominent position among plant-based adaptogens for managing stress [10]. It has an established history and extensive evidence base supporting its application as a plant adaptogen that enhances the body's capacity to resist a variety of stressors by normalizing bodily functions. Traditional medical systems of Nordic countries, Eastern Europe, and Asia have employed Rhodiola preparations and extracts to enhance mental and physical performance, reduce fatigue and depression, and increase productivity; the herb has also been attributed with antioxidant and anti-inflammatory effects [8, 9]. During stress, physiological systems mobilize resources to adapt to the challenge, but persistent or severe stress responses can compromise neuroendocrine, immune, cardiovascular, and reproductive functions, resulting in decreased capacity, anxiety, depression, fatigue, burnout, and other symptoms. Well-designed preclinical studies confirm stress-reducing properties of Rhodiola rosea root extracts, and clinical investigations indicate they relieve stress-related symptoms such as fatigue, weakness, and impaired cognitive function [4]. Extensive research and a long history of traditional use suggest

that Rhodiola extracts are efficacious in alleviating many symptoms associated with stress-induced conditions and stress-related disorders.

Holy Basil

Holy Basil (Ocimum tenuiflorum, synonym O. sanctum) naturally grows throughout the Indian subcontinent [11]. It occupies a prominent position within Ayurvedic tradition because of its diverse health-supportive properties, some of which have been corroborated experimentally. Resilience to a range of chemical, physical, metabolic, and psychological stresses constitutes another of its long-standing and relevant claims. To elucidate its adaptogenic potential, a recent investigation has assessed the effects of aqueous and ethanolic leaf extracts on tobacco (Nicotiana tabacum) explants cultivated under in vitro morphogenesis-inducing conditions [11]. Treatment of leaf explants with these extracts nearly doubles the number of regenerating shoots and enables the formation of somatic embryo-like structures[11]. Accumulations of tryptamine and N-acetyl-serotonin accompany a notable reduction in browning, suggesting that alterations in indoleamine dynamics contribute to the induction of shoot organogenesis and stress tolerance. Indeed, the pivotal roles of melatonin and 2-hydroxymelatonin as antioxidants for stress adaptation emerge from comparative measurements of indoleamine compounds produced by intact and cut tobacco leaves. With its capacity to induce in vitro regeneration, Hindu sacred basil represents a candidate adaptogenic herb for new lines of research focused on plant stress biology[11].

Ginseng

Ginseng has been used as an adaptogen to treat illness, both as a tonic and as a rejuvenator [12]. Modern life involves constant exposure to stress, which can cause detrimental biological responses. Chronic stress can promote anxiety, depression, and panic disorders [12]. Although the adaptogen concept has yet to be scientifically substantiated, ginseng is among the most effective and widely used herbs to prevent and treat stress-associated symptoms. In addition, ginseng shows superior regulation of stress compared with other adaptogens. The efficacy of ginseng as an antistress agent has been demonstrated unequivocally through behavioral stress tests and in vivo biochemical and physiological studies [13].

Schisandra

Schisandra Chinensis is an adaptogenic plant that originated in northern China and is commonly found in the northern part of Russia. It has a long history of use in traditional medicine. Schisandra berries contain phytochemicals that demonstrate physiological actions, such as helping the lungs resist dryness and reducing coughing and wheezing [1, 10]. Current studies show that schizandrin, one of the biological ingredients of Schisandra, protects the liver by helping to remove lipid toxins. Schizandrin is also a powerful antioxidant that protects the brain cells from the toxicity of free radicals, and it supports both the circulatory and coronary systems. For thousands of years, humans have sought plants capable of resisting the impact of stress on the mind and body. Schisandra is an ancient plant that grows in the forested areas of northeast China, Korea, and Russia, and it can adapt to extreme climate changes [11]. It was employed as a protective remedy for the body during the winter. In recent centuries, Schisandra has also been used to treat bronchitis, as an anti-smog agent, and as an energy booster for tired athletes. The berries contain a high concentration of vitamin C and high levels of lignans, antioxidants known to protect cells from the dangerous effects of free radicals. They also possess particular adaptogenic substances that promote vitality and mental functions and can help maintain focus and reduce stress[1, 15].

Licorice Root

Glycyrrhiza glabra, commonly known as licorice or sweetwood, is a leguminous perennial shrub native to Asia and the Mediterranean[2]. Its root yields a sweet extract used by the food and pharmaceutical industries in products such as chewing gums, sweets, and palatable tablet coatings [6]. Licorice root preparations are employed to treat stress-induced conditions, including gastritis, gastric ulcers, chronic fatigue syndrome, Addison's disease, and allergic and inflammatory states. The phytochemistry of licorice roots comprises flavonoids, triterpenoids, phenolic acids, amino acids, sugars, starches, mineral salts, choline, and asparagine, with glycyrrhizinoside (glycyrrhizic acid) identified as the main active constituent possessing antistress activity[7]. Mechanistically, licorice root extracts mitigate stress effects by inhibiting the cortisol-degrading enzyme 11-β-hydroxysteroid dehydrogenase type 2 (11-β-HSD2) in kidney cells. Such inhibition may potentiate the antihyperglycemic effect of cortisol and reduce hyperglycemia-induced oxidative stress in streptozotocin diabetic rats [1, 6, 7].

Effectiveness of Adaptogens in Stress Management

Clinical studies indicate that adaptogenic plants can be effective in stress management. Ashwagandha, Rhodiola, and Bacopa, each consumed at standardized dosages, may alleviate physical and psychological symptoms of chronic stress [1, 5]. Due to their normalizing effects, combinations of adaptogens might enhance the reduction of such symptoms beyond that achieved by single agents. Adaptogens combined with other herbs or dietary supplements could also exert synergistic stress-relief benefits [1]. Comparative research reveals that specific herbs are more

efficacious than others for particular stress responses and cognitive functions. For instance, Rhodiola and Siberian ginseng address mental fatigue and enhance physical endurance, whereas Schisandra and Ashwagandha target mental performance and concentration. Across diverse cultural contexts, user testimonials consistently affirm the effectiveness of plants such as Ashwagandha, Rhodiola, Holy Basil, Panax Ginseng, Schisandra, and Liquorice in managing stress and promoting mental well-being [5].

Clinical Studies

Numerous clinical studies indicate that withanolide-containing herbal extracts can safely treat stress-related symptoms, enhance well-being, and expedite recovery following prolonged stress [13]. Adaptogenic plants such as W. somnifera (L.) Dunal and R. rosea L. are the most comprehensively investigated species of the adaptogens discussed here [14]. Comparing Saposhnikovia divaricata (Turx.) Schischk. Root extract from the sacred basil leaf extract, Ocimum tenuiflorum L., demonstrated that the root extract of the former might offer slightly more pronounced adaptogenic effects in managing general stress. In a randomized, double-blind, placebo-controlled study, the adaptogen Ashwagandha (Withania somnifera) exhibited substantial pharmacological promise 8. Ashwagandha significantly reduced anxiety in generalized anxiety disorder after oral administration, lowered stress biomarkers such as cortisol, pulse rate, and blood pressure, and increased levels of DHEA-S and hemoglobin [14]. Additional research confirmed its anti-stress potential in stressed populations and identified minimal adverse effects. Given Ashwagandha's established influence on stress and anxiety, the study evaluated the medium-term antistress effects and safety of a standardized root extract (Shoden) over a 60-day period in healthy adults experiencing mild stress. Changes in stress-related hormones, including cortisol, DHEA-S, and testosterone, were monitored, with the expectation that the extract would decrease stress markers and elevate testosterone relative to placebo [13].

Comparative Analysis

ADAPT-232 (Chisan®) comprises aqueous extracts from Rhodiola rosea roots (dry extract ratio 4:1, 3% rosavin, 1% salidroside) and the fruits of Schisandra chinensis (7:1, 9% schisandrin) in a defined ratio. Both plants exhibit psychostimulatory effects at low to moderate doses but become sedative at high doses[1]. They stimulate the contractility of isolated smooth muscle tissue and possess anti-inflammatory capabilities. Other constituents, such as essential oils, also contribute to the modulating effects of ADAPT-232 [11].

User Testimonials

The effectiveness of certain adaptogens is also apparent from customer reports. Some who have experienced fatigue and declined meditative concentration due to stress and reintroduction of work, showed a reduction in their stress, as measured through a relaxing effect after a few days of supplementation [3]. Because of adaptogens' stress-mitigating effect, they can relieve subjective stress and physical fatigue. The mechanism of such stress relief is probably based on the facilitation of coping with stressors mediated through the hypothalamic-pituitary-adrenal system and regulation of key mediators of the stress response[13]. The term adaptogen was created in 1947 by N. V. Lazarev to describe substances that enhance the "state of nonspecific resistance" in stress. Physiological and adaptogenic effects may be linked to chemical constituents associated with stress hormone regulation; however, the full mechanism of action is likely the result of a multifunctional system armed to promote homeostasis via neuroendocrine and molecular mediators [12]. Due to the challenging nature of adapting to various stressful conditions in the modern environment, interest in adaptogens as alternative remedies appears timely. Scientific investigations indicate broad-spectrum activity, including anabolic, antitoxic, and antihypoxic effects, with the potential to promote increased attention and endurance under stress [3].

Safety and Side Effects

Adaptogens have a long history of generally safe use. Studies provide further evidence of their safety and tolerability for routine consumption in stress prevention and recovery [14]. Although nontoxic and well-tolerated, the multiple bioactive compounds in adaptogenic plants may result in pharmacologically relevant interactions with other drugs, potentially intensifying or offsetting adverse effects, particularly when used alongside prescribed medications [15]. For example, in patients with mental disorders who often take multiple psychotropics, adaptogens may interact with antidepressant drugs, necessitating clinical monitoring to manage possible adverse events.

General Safety Profile

Plant-based adaptogens are proposed to be safe for long-term use and have generally minor or transient side effects [14]. In high doses, they may cause symptoms such as restlessness, excitation, insomnia, or, conversely, an overly calm state resulting in depressed activity and drowsiness [6]. Due to their pronounced effects on hormonal and immune systems, adaptogens are not recommended during pregnancy, lactation, or in individuals with hormone-sensitive or autoimmune diseases [7]. Certain adaptogens exhibit stimulatory effects on the central

nervous system, which could exacerbate anxiety or agitation in some users. Concerns have also been raised about potential interactions with other medications, including hormonal contraceptives, sedatives, and stimulant drugs.

Possible Side Effects

Plant-based adaptogens can induce occasional side effects such as headaches, dry mouth, and sleep disturbances. Other less common adverse effects include gastrointestinal discomfort, allergic reactions, and restlessness. Furthermore, these herbs may interact with prescription drugs, including blood thinners and medications for diabetes[2]. Consequently, individuals who are pregnant, breastfeeding, or undergoing medical treatment should consult a healthcare provider before commencing adaptogen use. Despite these considerations, adaptogens have generally demonstrated a favorable safety profile when administered at recommended doses [2].

Contraindications

Several plant-based adaptogens are considered safe for most people when consumed orally in recommended doses. Nevertheless, some reported cases indicate there may be certain contraindications for specific individuals. Ginseng is not recommended for people with caffeine sensitivity due to potential overstimulation effects. Licorice root may be inappropriate for individuals with cardiovascular problems or high blood pressure, given its potential to elevate blood pressure[15]. Ashwagandha is best avoided during pregnancy due to possible uterine contractions [15]. Many adaptogens can cause interactions with prescription drugs, especially psychotropic medications. Concomitant use with antidepressants requires careful monitoring to prevent adverse events. Known interactions include cinnamaldehyde content in cinnamon increasing the bioavailability of certain prescribed drugs and inhibition of cytochrome P450 enzymes and p-glycoprotein by ginseng, altering the metabolism of antidepressants, leading to elevated plasma concentrations [15].

Integrating Adaptogens into Daily Life

Plant-based adaptogens are available in various forms for daily consumption, including capsules, powders, teas, and liquid extracts. Dosage depends on factors such as specific adaptogens, concentration, individual tolerance, and health conditions[1]. Adhering to manufacturer recommendations and consulting healthcare providers can help establish appropriate intake levels. When combined with other stress-relief approaches like meditation, exercise, and diet, adaptogens may enhance overall effectiveness in stress management [1].

Forms of Adaptogens

Adaptogens are commonly available in powder, capsule, tincture, tea, and other formats, allowing for versatile integration into daily routines [5]. Typical dosages range from 100 to 450 mg per day, though amounts can vary based on specific plant extracts, formulations, and individual needs. Both meat eaters and vegans find these options adaptable to their dietary preferences. Such diversity in forms and dosages facilitates the incorporation of adaptogens into supplemental and nutritional strategies aimed at supporting resilience to daily stressors. The selection of a suitable format and dosage depends on personal preference and specific health objectives [1, 5].

Dosage Recommendations

Various preparations contain adaptogenic plants, including standardized liquid extracts, powdered extracts (supercritical, hydro-alcoholic, or aqueous), full-spectrum extracts, and plant powders. These can be consumed as single herbs or in combinations as multi-constituent formulations [6]. Adaptogens can be consumed daily for maintenance or as a short-term therapeutic aid. They are most effective when taken in cyclical periods of 4–8 weeks: 3–4 weeks for daily health maintenance, followed by 1–2 weeks off to prevent tolerance build-up and support the body's natural resilience. This approach is supported by recent findings on the multi-targeted mechanisms of adaptogens at the molecular level [6]. Nonetheless, individualised recommendations remain essential, and some adaptogens do not require cycling [14]. Dosage guidelines for several adaptogens are summarised in Table 7.2. Many adaptogens have traditionally been combined in tonic herbal formulas (polyherbalism) to enhance efficacy, reduce side effects, and address drug resistance.

Combining Adaptogens with Other Therapies

The combination of adaptogens with other therapies offers a multifaceted approach to managing stress and related disorders. Integrating multiple strategies that include nutraceuticals and pharmaceuticals can be synergistic and ensure that several pathways are simultaneously targeted. Adaptogens possess unique efficacy and safety profiles, contributing to stress relief without inducing sedation, tolerance, or addiction [15]. Concerns about potential interactions between adaptogens and psychotropic medications are justified because many patients experiment with combinations independently[15]. Nevertheless, the majority of studies conclude that such interactions are unlikely. Adaptogens differ from pharmaceuticals in their multi-target effects conferred by several constituents, rather than a single active principle. Their ability to modulate the release of stress hormones and restore immunity promotes resistance in stress-vulnerable populations [15].

Future Directions in Research

Emerging plant adaptogens may offer the promise of new preventative and therapeutic applications. For instance, the versatility and diverse mechanisms of action of botanical extracts suggest they may be used to prevent or treat a number of stress-related clinical and subclinical conditions, including metabolic syndrome, neurodegeneration, and chronic fatigue [14]. Adaptogens like Gotu Kola, Moringa, and Fo Ti could provide additional options [3]. Further research should confirm the efficacy and safety of medicinal plants used traditionally in stress-related disorders and explore novel research areas, including new therapeutics and adaptogenic combinations, to support the continued value of this class of products in phytomedicine [6].

Emerging Adaptogens

Plant adaptogens are natural substances, mostly herbal, proposed to enhance the body's nonspecific resistance to stress, prompting interest in their application for modern stress management [5]. As defined by Panossian et al. [6], adaptogens are substances that increase the state of nonspecific resistance and the ability to adapt, without altering parameters in the absence of stress. They are thought to stimulate the hypothalamic-pituitary-adrenal axis and the sympathoadrenal system and to regulate hormone levels, thereby increasing resistance to physical stress. Adaptogenic plants are primarily used to augment mental and physical work capacity during fatigue and in convalescence following illness or injury [14]. Contemporary studies show that Panax ginseng (Araliaceae), Eleutherococcus senticosus (Araliaceae), Rhodiola rosea (Crassulaceae), and Schisandra chinensis (Schisandraceae) exert stimulating effects on the central nervous system, increase performance under fatigue and mental exhaustion, and enhance the general state and mood. In particular, supplementation with Panax ginseng for over a week has been demonstrated to improve physical working capacity, whereas Rhodiola rosea may produce stimulatory effects after a single dose[15].

Potential Areas of Study

The field of adaptogenic natural products continues to grow, with an increasing number of natural compounds and product types appearing on the market [3]. While safety and the range of therapeutic activities are important considerations, research and commercial interests have mainly focused on several well-known, long-established adaptogenic plants. This section, therefore, highlights plants for which some scientific evidence regarding anti-stress activity exists but which remain under-investigated. Herb formulations and isolated components requiring further adaptation research are also briefly discussed. Hypericum perforatum, a well-known traditional anti-depressant with anxiolytic properties, possesses stress-protective and anti-stress effects in a variety of stress models [15]. The main function of its distinct secondary metabolites, predominantly hypericin (a naphthodianthrone), hyperforin (a phloroglucinol derivative), and several xanthones, remains unclear. The dual inhibition of Monoamine oxidase and the Monoamine reuptake system leads to increased levels of dopamine, noradrenaline, adrenaline, and serotonin in the synaptic cleft [3]. These monoamines function in the central nervous system as stress messengers, which indicate a probable mechanism for the anti-stress activity of H. perforatum. Polygonum minus, commonly known as kesum and found predominantly in West Malaysia, lacks pharmacological activity profiles in the open literature. To date, however, preliminary evidence suggests that this herb may have potential anti-stress activity. Further research is warranted on bioactive compounds derived from Siberian ginseng (Eleutherococcus senticosus), various Angelica species, and several Chinese adaptogens similar to ginseng (e.g., codonopsis and asparagus), which all require comprehensive investigation in strictly controlled human studies conducted independently of the commercial interests of herbal medicine suppliers [6]. Candidate plants of broader ethnopharmacological significance include coleus (Plectranthus barbatus) and acorus (Acorus calamus and Acorus gramineus), both of which possess a variety of promising pharmacological activities [3, 16].

CONCLUSION

Plant-based adaptogens offer a promising, evidence-supported approach to managing stress and its physiological and psychological consequences. Compounds from Ashwagandha, Rhodiola, Holy Basil, Ginseng, Schisandra, and Licorice root demonstrate multi-faceted mechanisms that enhance resilience, improve cognitive and physical performance, and modulate stress-related hormonal pathways. Clinical studies and user reports support their efficacy, particularly in reducing chronic stress, fatigue, and anxiety, with generally favorable safety profiles. While widely used in traditional medicine and increasingly in modern herbal practice, further research is warranted to standardize dosages, explore novel adaptogenic combinations, and confirm long-term safety and efficacy across diverse populations. Integrating adaptogens with lifestyle measures such as exercise, meditation, and balanced nutrition may optimize their stress-relieving potential, making them a valuable tool in comprehensive stress management strategies.

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