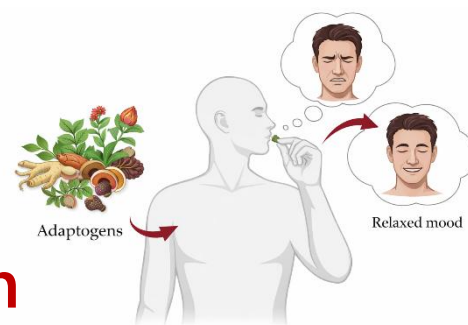


CHAPTER 20



Adaptogens and Their Role in Stress and Anxiety Management

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ABSTRACT: Stress has become a substantial part of modern life; however, persistent psychological stress can disrupt the mental and physiological equilibrium of the body, leading to neuroendocrine imbalance, metabolic dysregulation and oxidative stress. Adaptogens are natural plant-derived compounds that enhance cellular adaptability to external stressors by modulating the hypothalamic–pituitary–adrenal (HPA) axis, and by exerting regulatory effects on neuroendocrine, immune, and cardiovascular systems. Adaptogens are classified on the basis of their primary targets into monoamine neurotransmitters of the sympathoadrenal system (SAS) and steroid hormones of the HPA axis. This chapter encompasses the mechanism of action of adaptogens as the modulators of stress response and homeostatic balance, and their interaction with the network of neuroendocrine–immune complex mediators that regulate various pharmacological systems. Adaptogens possess the ability to trigger cellular and systemic adaptive stress-response mechanisms, which consequently strengthen resilience against environmental, emotional, and metabolic overload. Here, the most effective botanical adaptogens are discussed that provide a rationale for their potential use in individuals experiencing chronic stress, fatigue, mental burnout, anxiety, depression, cognitive decline, and sleep disturbances. Moreover this, chapter provides insights into potential future research on the therapeutic applications of adaptogens in preventing and rehabilitating physiological and psychological impairments following chronic stress, neurodegeneration, metabolic dysfunction, and immune dysregulation.

Adaptogens are phytochemicals which are stress relieving and are known for their pharmacological activity, supporting the body's adaptability and resilience to stress while maintaining metabolic homeostasis (Panossian et al., 2025). Adaptogens can nonspecifically enhance the mental as well as physical performance of the body under any external stress factor and exhibit neuroprotective, anxiolytic, nootropic, anti-fatigue, antidepressant, antioxidant and antiaging activity. Mental health issues have become one of the most pressing global challenges, impacting about 14% of individuals across the world (WHO, 2022). Serotonin-norepinephrine reuptake inhibitors are frontline antidepressants; however, their prolonged

consumption has constrained their therapeutic efficacy due to side effects, impair cognition, disrupt gastrointestinal balance and cardiovascular function. Consequently, mental distress treatment requires an approach with long term safe profile medication use.

The concept of using plant-based products to enhance stamina and resilience dates back several decades, notably when they were administered to pilots and submarine crew during World War II to enhance cognitive function and physical performance (Drake et al., 1942). These agents were later coined as “adaptogens” as innocuous agents which nonspecifically elevate resilience against physical, chemical, biological and psychological

noxious stresses. In pharmacotherapy, the adaptogens were defined and classified as herbal components that enhance attention, physical endurance, improve cognitive function and are effective in neuro-endocrine and immune system disorders and anomalies (Panossian & Wikman, 2010). The adaptogens don't follow the concept of one drug for one disease due to their multifaceted pharmacological profile. The bioactive compounds of adaptogens influence different molecular targets therefore, their pharmacological effects and stress alleviation can be synergistically harnessed (Todorova et al., 2021).

Thus, adaptogen is a promising and non-toxic approach to stress management by modulating neuroendocrine responses and balancing stress-related mediators. Adaptogens have long been an integral part of traditional medicine systems such as Chinese (e.g., Ginseng, Rhodiola, Schisandra, Astragalus), African (e.g., Sutherlandia, Rooibos, Hypoxis), and Ayurvedic medicine (e.g., Turmeric, Tulsi, Ashwagandha, Shatavari) (Fatima et al., 2024). These herbal adaptogens have been used to enhance attention and cognitive function during fatigue, as well as to improve physical stamina, manage stress-related disorders, and treat sexual dysfunction. Molecular and pharmacological studies have demonstrated that adaptogens worked mechanistically to modulate the stress related hypothalamic-pituitary-adrenal (HPA) axis, which in response regulates the secretion of cortisol and other stress related hormones such as catecholamines and adrenocorticotrophic hormone (ACTH) (Llopis et al., 2025).

Stress is a complex physiological and psychological response to the environmental or internal stressors. Stress has become a prevalent and persistent concern of life amid today's fast-paced, technology dominant lifestyle (Slavich, 2016). The stress level is influenced by multiple factors such as chronic illness, examination stress, strained relationships, financial instability and social anxiety. Stress needs to be treated beforehand as chronic stress can lead to various stress related disorders including hypertension, cardiac ailments, post-traumatic stress disorder, major depressive disorder, chronic fatigue syndrome (Swathi et al., 2023). According to the World Health Organization (WHO), one in every eight individuals experiences

some form of mental distress. With its rate rising exponentially each year, stress has become one of the most prevalent public health concerns, contributing significantly to the increased use of psychotropic medications, especially anxiolytics. While these pharmacological treatments may provide symptom relief, they are often associated with side effects, and in many cases, patients fail to achieve full remission even with psychotherapy (Liu et al., 2025). The inevitable role of stress as a mediator in both mental and physical disorders necessitates the exploration of more effective, non-toxic, and potent treatment options to yield substantial societal benefits. This chapter examines the adaptogens as a natural, nontoxic and effective strategy for stress and anxiety management.

OVERVIEW OF STRESS AND ANXIETY MECHANISMS

Stress is a neuroendocrine-mediated, multi-step cascade, triggered by the activation of the HPA axis and the sympathetic nervous system (SNS) that cause systemic physiological and behavioral responses. Stressful stimuli or environmental threats are perceived by the hypothalamus, which plays a multifaceted role by activating the autonomic nervous system (ANS), responsible for regulating visceral functions, stimulating the hypothalamic-pituitary-adrenal (HPA) axis, and promoting the release of arginine vasopressin (AVP), also known as antidiuretic hormone (ADH) (Herman et al., 2016). The hypothalamus also releases corticotropin releasing hormone (CRH) via the paraventricular nucleus (PVN), which acts on the anterior pituitary gland. In response, the anterior pituitary secretes adrenocorticotrophic hormone (ACTH), which then stimulates the adrenal cortex to produce glucocorticoids. Concurrently, the adrenal medulla activates the catecholaminergic system by releasing the primary catecholamines, epinephrine and norepinephrine (noradrenaline). These hormones mediate the classic 'fight-or-flight' response, inducing physiological changes such as increased heart rate, arterial vasodilation, bronchodilation, pupil dilation, and suppression of gastrointestinal activity. Collectively, these responses enhance the body's ability to cope with acute stressors.

MECHANISMS OF ACTION

The adaptogens control stress-related biological processes through their effects on the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system and molecular chaperone expression (such as Hsp70) and oxidative stress pathways and inflammatory signaling and neurotransmitter regulation (Panossian et al., 2025). Adaptogens affect the HPA axis and central nervous system (CNS) to create multiple biological effects through their ability to control stress hormone secretion and gene expression at multiple levels. The body activates multiple signaling systems inside cells and outside cells during each stage of the stress response which goes beyond a single biological pathway. Adaptogens work to regulate neurotransmitter activity while reducing oxidative damage and promoting neuroplasticity (Liao et al., 2018).

Under stressful conditions the hypothalamus begins hormone stimulation by releasing corticotropin-releasing hormone (CRH) which activates the pituitary gland to produce adrenocorticotrophic hormone (ACTH) that then causes the adrenal gland to produce cortisol (Mbiydzennyuy et al., 2024). The body prepares for stress through cortisol which raises blood sugar levels and speeds up metabolism and blood pressure and alertness but at the same time decreases immune system function by blocking cytokine production, T-cell growth and antibody manufacturing. The body reduces CRH and ACTH production through negative feedback when cortisol levels become elevated which leads to cortisol levels dropping back to normal after stress subsides (Faye et al., 2018). The autonomic nervous system together with the HPA axis functions as the main systems which handle stress to help organisms deal with daily challenges and threats in life. Adaptogens work through their main mechanism to control cortisol production. The HPA axis produces excessive cortisol during chronic stress which damages the nervous system. Adaptogens work to maintain normal cortisol levels which helps reduce stress-related symptoms including anxiety, fatigue, depression, sleep problems and cognitive deterioration (Hovhannisyan et al., 2015).

The compounds in adaptogens have been proved to impact neurotransmitters such as serotonin,

dopamine, norepinephrine, and GABA, which promote mood enhancement and resilience to stress (Chiavaroli et al., 2024). In humans, depression and stress have been reported to blunt reward sensitivity, which is correlated with anhedonia, lack of motivation, and feeling of despair (Pani et al., 2000). The reward anticipation is associated with the mesolimbic dopaminergic system; thus, its modulation is essential to cope with these aversive events. The adaptogens have bioactive compounds including flavonoids, saponins, phenolics, and alkaloids which modulate the dopaminergic reward system which is essential in the pathophysiology of stress-related behavior (Balkrishna et al., 2025).

The impact of adaptogens on oxidative stress is also a crucial aspect as free radicals (ROS) are known to damage nervous system which causes cognitive decline and neurodegenerative disease. Adaptogens including *Panax ginseng*, *Rhodiola rosea*, *Schisandra chinensis*, and *Eleutherococcus senticosus* possess flavonoids, saponins, phenolic compounds, and alkaloids, which lower oxidative neural damage (Faye et al., 2018). Adaptogens improve the expression level of neurotrophic factors enhancing the ability of brain to adapt and regenerate. Table 1 demonstrates different adaptogens, their target pathways and clinical benefits.

KEY PLANT-BASED ADAPTOGENS IN STRESS AND ANXIETY MANAGEMENT

Ashwagandha (*Withania somnifera*)

Ashwagandha (*Withania somnifera*) is an evergreen shrub from Solanaceae family, commonly found across subtropical regions of Asia, Africa, the Middle East, and parts of North America (Banadka et al., 2025). Ashwagandha, commonly referred to as winter cherry or Indian ginseng, has long been a vital and revered element of Ayurvedic, Unani and Chinese medicine, known for boosting vitality and promoting general well-being. The roots of Ashwagandha are widely recommended for their pharmacological activities, having been traditionally used as a tonic, narcotic (Jain et al., 2024), diuretic, anthelmintic, anti-inflammatory, adaptogenic, anxiolytic, and immunomodulatory agent due to the presence of bioactive compounds such as withanolides and alkaloids.

Table 1. Adaptogens and their clinical benefits

Adaptogen	Target Pathway(s)	Primary Effect(s)	Clinical Benefit(s)	References
<i>Panax ginseng</i> (Korean/Asian ginseng)	HPA-axis modulation; antioxidant (Nrf2); NO/endothelial signaling	Normalizes cortisol; antioxidant, anti- inflammatory, improves vascular tone	Reduced stress markers, improved fatigue, cognitive function, and well- being	Baek et al., 2019; Lee & Rhee, 2017
<i>Rhodiola rosea</i>	HPA-axis modulation; monoamine neurotransmission (serotonin/dopamine); mitochondrial metabolism	Reduces acute cortisol spikes; modulates monoamines; supports energy metabolism	Decreased fatigue, improved mental performance, attention, and resilience to stress	Stojcheva & Quintela, 2022; Anghelescu et al., 2018
<i>Schisandra chinensis</i>	Nrf2/antioxidant pathways; HPA-axis; stress protein regulation	Antioxidant, mitochondrial protection, stress protein induction	Mental endurance, reduced fatigue, neuroprotection	Chencen et al., 2024
<i>Eleutherococcus senticosus</i> (Siberian ginseng)	HPA-axis; immune regulation	Enhances endurance, modulates immunity	Improved stamina, reduced fatigue, immune support (evidence mixed)	Gerontakos et al., 2021
<i>Withania somnifera</i> (Ashwagandha)	HPA-axis (cortisol lowering); GABAergic & monoaminergic modulation; antioxidant	Reduces cortisol; anxiolytic and neuroprotective	Lower stress and anxiety; improved sleep and cognition (multiple RCTs)	Majeed et al., 2023; Pandit et al., 2024
<i>Bacopa monnieri</i> (Brahmi)	Monoaminergic modulation; BDNF signaling; antioxidant	Cognitive enhancement; cortisol reduction	Improved memory, attention, reduced anxiety and fatigue	Sivasangari & Rajan, 2020
<i>Ocimum sanctum</i> (Holy basil/Tulsi)	HPA-axis modulation; antioxidant/anti-inflammatory	Reduces cortisol; metabolic regulation	Stress reduction, improved mood, better attention and immunity	Muszalska & Wiecanowski, 2024; Yadav et al., 2024
<i>Cordyceps</i> spp.	Mitochondrial metabolism; antioxidant; immune signaling	Improves energy production, antioxidant, immunomodulatory	Better exercise tolerance, reduced fatigue, immune support	Chen et al., 2024a; 2024b
General mechanisms (cross-cutting)	HPA-axis (CRH/ACTH/cortisol); Nrf2 antioxidant; neurotransmitters (serotonin, dopamine, GABA); mitochondrial support	Cortisol normalization, oxidative stress reduction, neurotransmitter balance	Reduced stress, fatigue, anxiety, improved cognition and resilience	Tsigos et al., 2020

Pharmacological research on Ashwagandha extracts from different plant sections has shown its diverse therapeutic properties which protect against stress and inflammation and oxidative damage and blood-related disorders and memory loss and neurodegenerative conditions (De Oliveira et al., 2024). The adaptogenic properties of Ashwagandha root extract have been demonstrated in obese individuals, showing efficacy in reducing stress, improving eating behavior, enhancing mental well-being, and supporting endocrinological balance (Choudhary et al 2017). The substance operates as an adaptogen through its ability to boost physical

stamina and mental performance and immune function while reducing stress-related effects including gastric ulcers, fatigue, anxiety and sleep problems. Biological experiments have validated its traditional Ayurvedic use as a tonic, vitalizer, and rejuvenator by demonstrating efficacy in managing stress-induced ailments such as arteriosclerosis, premature aging, diabetes, hypertension, arthritis, anxiety, and impaired immunity (Zhang et al., 2022).

Golden Root (*Rhodiola rosea*)

Golden root (*Rhodiola roseai*) is a high-altitude dwelling perennial herb known for its putative

antistress and anti-depressive actions. The plant belongs to the Crassulaceae family and it grows naturally in Eastern Europe and Asia (Polumackanycz et al., 2022). *Rhodiola* serves as a highly sought-after medicinal plant which European, Tibetan and Chinese traditional healing systems have utilized for their benefits. The plant serves as a traditional treatment for altitude sickness because it helps lower oxygen consumption while easing symptoms like tiredness and headaches and breathing difficulties (Williams et al., 2021). *R. rosea* have exhibited purported adaptogenic properties during different biological and physiological experiments by eliciting non-specific stress resistance response. The herb functions as a popular treatment for anxiety and stress relief while researchers have identified its ability to enhance memory and combat depression through its physical and mental performance improvements (Zhumagul et al., 2023).

Ethnobotanical research shows that *R. rosea* serves as a common traditional medicine for folk communities who live at high altitudes because it helps them fight fatigue and depression while improving anemia and work performance during stressful environmental conditions at high elevations (Stojcheva & Quintela, 2022). Early Swedish pharmacopeias listed this herb as a medicinal plant which Vikings used to build their strength and endurance for physical activities. *R. rosea* exhibits analgesic, antihemorrhagic, anti-inflammatory and stimulation properties. The chemical makeup of *R. rosea* extract contains phenols, rosarin, rosavin, rosin, salidroside, tyrosol and flavonoids which create these characteristics (Bhardwaj et al., 2018).

Clinical trials have demonstrated the anti-depressive effects of *R. rosea*; in a placebo-controlled study involving patients with depression, its extract showed improvements in insomnia, emotional stability, and self-esteem (Kim et al., 2021). The plant extract has also demonstrated anti-stress activity by mitigating stress-induced parameters, including reductions in β -endorphin, adrenocorticotrophic hormone (ACTH), cortisol, insulin, thyroxine (T4), and triiodothyronine (T3) levels. Molecular studies on its mechanism have documented the effects of *R. rosea* on the CNS, which are attributed to the modulation of monoamines (Alam et al., 2023). The *R. rosea* acts

as a μ - and κ -opioid receptor agonist whose attachment enhanced the expression of 5-hydroxytryptamine (5-HT) and serotonin receptor which in turn increases the β -endorphin release that is responsible for its signature attributes like anxiolytic, antiarrhythmic, and hypotensive actions (Zhumagul et al., 2023).

Asian Ginseng

Panax ginseng or Korean ginseng is a slow growing perennial plant from Araliaceae family inhabited to Korea, China and Japan. The plant serves traditional medicine needs through its adaptogenic properties which enhance sexual, physical performance, combat fatigue and treat exhaustion symptoms (Lu et al., 2021). *Panax ginseng* serves multiple medical purposes because of its various pharmacological properties which include immune system regulation, antioxidant effects, anti-inflammatory actions, brain protection, diabetes management, cancer defense, cardiac health. The bioactive compounds found in *P. ginseng* extract were identified through ethnopharmacological research which revealed ginsenosides, polysaccharides, polyacetylenes, phenolic compounds, peptides and alkaloids (Lu et al., 2021). *P. ginseng* shows two opposite effects on blood pressure through its biphasic response that starts with a short-term decrease followed by a sustained increase after extract administration. Research shows that blood pressure regulation occurs when people consume ginsenosides at doses which exceed standard levels (Irfan et al., 2020).

Macrophages are the innate immunity cells responsible for the phagocytosis of pathogens and apoptotic cells thus help the cell in autonomous self-renewal. Ginseng extract has been investigated for its immunomodulatory effects on macrophages. Studies have reported that ginsenosides activate murine macrophages (RAW 264.7 cells) by inducing nitric oxide production, which plays a critical role in pathogen elimination. The extract also upregulates inflammatory cytokines, granulocyte-macrophage colony-stimulating factors (GM-CSF), and chemokines (Byun et al., 2021).

Schisandra chinensis

Schisandra chinensis is deciduous woody vine, native to the North China, Russia, Korea and Japan. It thrives in humid climate and well-drained soil. *S.*

Table 2. Plant based adaptogens and their effects on HPA axis, neurotransmitters and oxidative

Adaptogen	Effect on HPA Axis	Effect on Neurotransmitters	Effect on Oxidative Stress
Ashwagandha	Downregulates HPA axis activity; reduces cortisol levels.	Enhances GABAergic signaling; modulates serotonin and dopamine levels, contributing to anxiolytic effects.	Increases antioxidant enzymes (SOD, catalase); reduces lipid peroxidation and ROS.
<i>Rhodiola rosea</i>	Balances HPA axis; normalizes cortisol response to acute and chronic stress.	Increases serotonin, dopamine, and norepinephrine levels in the brain.	Scavenges free radicals; upregulates antioxidant defenses and reduces oxidative damage.
<i>Panax Ginseng</i>	Modulates HPA axis response; normalizes ACTH and cortisol secretion.	Enhances acetylcholine, dopamine, and serotonin levels; neuroprotective and memory-enhancing effects.	Promotes antioxidant activity via ginsenosides; reduces oxidative stress and improves resilience.

chinensis have been used in the Traditional Chinese medicine (TCM) for gastrointestinal tract illness, tonic to support vital energy (Qi), sleep disorder, depression, and cognitive decline, respiratory ailments, fatigue, and liver diseases (Bhushan et al., 2024). The leaves, fruit (berries) and seeds are used in the form of tincture, decoction and standard extracts to achieve its pro-health benefits. The pharmacological evaluation of *S. chinensis* has proved its antibacterial, antioxidant, antifatigue, antiproliferative, hepatoprotective, neuroprotective and adaptogenic activities (Skalski et al., 2025). The phytochemical analysis showed that *S. chinensis* contains terpenoids, lignans, flavonoids, polysaccharides, essential oils, organic acids, and vitamins.

Schisandra chinensis (magnolia berry) extract has been studied under ethnopharmacological and ethnobotanical studies and its tincture, decoction and tablets have been effective against respiratory disorder, enervation and mental and physical burnout (Cho et al., 2021). The extract showed effectiveness after 2 - 10 weeks of administration. Moreover, magnolia berry has been tested in 200 patients for its role in nervous disorder, the results elaborated its role in positive mood enhancement, elevated the working capacity and reduced the exhaustion. *S. chinensis* is traditionally prescribed for the treatment of general weakness, improving the sleep cycle and stimulation of appetite these effects have been approved through a clinical pilot study in 95 neurasthenic patients (Zakharov et al., 1956). Table 2 shows plant based adaptogens and their effect on HPA axis, neurotransmitters and oxidative stress.

CLINICAL APPLICATIONS AND EVIDENCE-BASED USE

Adaptogens have been a part of ancient phytotherapy for mental disorders and behavioral anomalies such as anxiety, depression, insomnia and cognitive challenges, without any significant side effects. Clinical trials have been conducted to assess the efficacy of adaptogens and their derivatives on molecular and cellular level in fatigue, cognitive function and mental performance. In a placebo study, SHR-5 extract of *R. rosea* administration has significantly improved attention, insomnia, depression, somatization, better performance in chronic fatigue syndrome and mental performance (Darbinyan et al., 2007). Another most frequently documented adaptogens, *S. chinensis* and *E. senticosus* are most effective in mild fatigue and weakness as their administration has increased the endurance and mental health of the patients (Jurcău et al., 2019). In different regions of the world plant based adaptogens are used by local communities, believed to be beneficial for human immunity, circulatory system and nervous disorders (Liao et al., 2018).

Adaptogens induce specific, effective and significant effects in mental health due to fatigue. *R. rosea* is one of the most documented and tested natural adaptogens. It has been investigated that repeated administration of *R. rosea* is effective against fatigue and has improved attention, mental performance, and concentration ability in the treated experimental groups within four weeks (Polumackanycz et al., 2022). Moreover, *R. rosea* optimizes the salivary cortisol level which is essential for effective cognitive function. Cognitive

impairments have been shown to be associated with significant alterations in corticosteroid levels. *R. rosea* exhibits anti-fatigue properties and enhances attention, mental performance, and concentration, acting as a natural cognitive revitalizer (Bhardwaj et al., 2018). The physiological and pharmacological benefits of adaptogens are shown in Fig. 1.

The reliability of the experimental studies on psychiatric disorders has been questioned and poorly documented, as earlier investigations lacked standardized psychological protocols (Panossian et al., 2025). Although clinical trials have limitations in data collection and interpretation of results, along with several shortcomings in data collection and result interpretation, the available evidence consistently supports that adaptogens are safe and effective as complementary agents in the management of psychiatric disorders. Further large scale, placebo-controlled trials are needed to standardize dosage, confirm long-term safety, and elucidate molecular mechanism of adaptogens in stress and anxiety management.

CONCLUSION

Stress and anxiety are a consequence of environmental pressures or physiological disturbances associated with emotional, psychological, and physical overload, distress in

hypertension, cardiovascular disorders, metabolic imbalance, and age-related chronic neurodegeneration. The pathophysiology of distressed neurons is linked to disrupted mitochondrial function, the redox imbalance, and ATP energy supply, which are associated with multiple molecular targets and signaling pathways in the nervous and endocrine systems. Adaptogens exhibit antistress effects by regulating homeostasis via a multifactorial mechanism of action associated with the hypothalamic–pituitary–adrenal (HPA) axis, and regulation of key mediators such as molecular chaperone (Hsp70), stress-activated protein kinases (JNK, p38 MAPK), transcription factors (FOXO, NF-κB), heat shock factors, cortisol, and nitric oxide. Adaptogens can be recognized as novel pharmacological modulators with potent antistress and anxiolytic properties.

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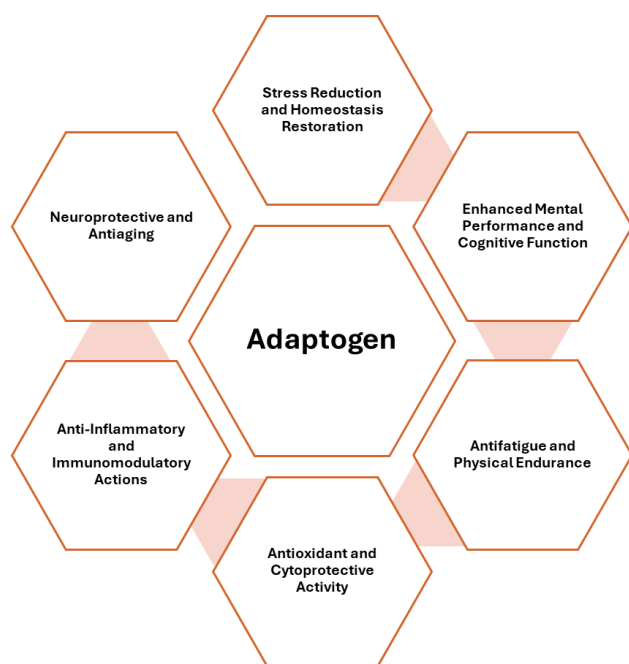


Fig 1. Key physiological and pharmacological benefits of adaptogens

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