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An Exploratory and Future Perspective Review of Adaptogens: A Multifaceted Approach to Enhancing Human Health and Performance

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ABSTRACT

Adaptogens, a class of natural substances derived primarily from plants, have gained significant attention for their potential to enhance human health and performance. These compounds are believed to help the body adapt to stress, improve cognitive function, boost immunomodulation and promote overall well-being. This review article is aimed to discuss the diverse world of adaptogens, exploring their historical use, mechanisms of action and scientific evidence supporting their efficacy. A range of adaptogens will be examined and discussed, including well-known examples like *Withania somnifera* (Ashwagandha), *Rhodiola rosea* and *Panax ginseng*, as well as lesser known but promising candidates. The highlights of the key potential benefits of adaptogens in various health conditions, such as anxiety, depression, fatigue and cognitive decline will be addressed. Additionally, the critical evaluation of the available scientific evidence will be mentioned, highlighting the need for rigorous clinical trials to further validate the claims surrounding adaptogens. By synthesizing information from diverse references, including traditional medicine, modern pharmacology and clinical research, this review aims to provide a comprehensive understanding of adaptogens and their potential applications in promoting human health and performance.

INTRODUCTION

Adaptogens are a class of herbs and plants that have been used in traditional medicine systems for centuries to help the body adapt to various forms of stress. The concept of adaptogens originated in Ayurvedic and Traditional Chinese Medicine (TCM) practices, where certain plants were recognized for their ability to enhance the body's resistance to physical, chemical and biological stressors (Schütz et al., 2006; Panossian & Wikman, 2010). In recent years, there has been a growing interest in adaptogens due to the increasing prevalence of stress-related disorders in modern society and the recognition of their potential health benefits (Simkin & Arnold, 2020). Numerous studies have investigated the effects of adaptogens on the body's response to stress, immune function and overall well-being, suggesting that they may help to maintain homeostasis and support overall health (Nocerino et al., 2000; Panossian & Wikman, 2008). There has been a resurgence of interest in adaptogens in recent years, highlighting the growing recognition of their potential benefits in managing stress-related disorders.

The term "adaptogen" was coined by Soviet scientist N.V. Lazarev in the 1940s to describe substances that help the body adapt to various stressors, both physical and psychological. While there is no universally accepted definition, adaptogens are generally characterized by the following important properties (Lazarev, 1958; Brekhman & Dardymov, 1969; Todorova et al., 2021):

i. Non-specific action: Adaptogens are believed to exert a broad spectrum of effects on the body, rather than targeting specific symptoms or diseases.

ii. Normalization: They help to normalize physiological functions, bringing them back to optimal levels.

iii. Increased resistance to stress: Adaptogens enhance the body's ability to cope with various stressors, including physical, chemical and biological stressors.

Mechanisms of Action

Adaptogens are a class of natural substances that have gained significant attention for their ability to help the body adapt to various stressors (Winston, 2019). These stressors can be physical, such as fatigue and intense exercise, chemical, such as toxins and pollutants or biological, such as infections (Kruk et al., 2019). By enhancing the body's resilience to these stressors, adaptogens can promote overall well-being and improve quality of life (Yance, 2013). The exact mechanisms by which adaptogens exert their effects are complex and not fully understood (Panossian et al., 2018). However, several proposed mechanisms have been identified that work on cellular levels and summarized in Table 1.

Neurotransmitter Modulation

Adaptogens have been found to influence the levels of key neurotransmitters such as dopamine, serotonin, and norepinephrine, which are crucial for regulating mood, cognition and the body's response to stress (Ray et al., 2021). Dopamine is associated with pleasure and reward mechanisms in the brain, affecting motivation and focus (Esch & Stefano, 2004). Serotonin, often referred to as the "feel-good" neurotransmitter, contributes to feelings of well-being and happiness (Dsouza et al., 2020). Norepinephrine is involved in the body's fight-or-flight response, influencing alertness and energy levels (Gruner & Sarris, 2014). By modulating these neurotransmitters, adaptogens can help improve mood, enhance cognitive function and reduce the negative effects of stress (Gulati et al., 2016). This modulation can lead to a more balanced and resilient mental state, making it easier to cope with daily challenges and stressors (Palamarchuk & Vaillancourt, 2021). For example, *Rhodiola rosea*, an adaptogen, has been shown to increase the levels of serotonin and dopamine, thereby improving mood and reducing symptoms of depression and anxiety (Khanum et al., 2005).

Hormonal Regulation

Adaptogens can play a significant role in hormonal regulation, particularly by modulating the Hypothalamic-Pituitary-Adrenal (HPA) axis (Singh et al., 2017). The HPA axis is a central part of the body's stress response system, controlling the production and release of stress hormones such as cortisol (DeMorrow, 2018). Chronic stress can lead to dysregulation of the HPA axis, resulting in elevated cortisol levels and a range of negative health effects, including anxiety, depression and immune suppression (Guilliams & Edwards, 2010). Adaptogens help to normalize the function of the HPA axis, reducing the overproduction of cortisol and promoting a more balanced stress response (Emudainohwo et al., 2023). This hormonal regulation can help mitigate the adverse effects of chronic stress, support mental health and improve overall well-being (Stansbury et al., 2012). For instance, Ashwagandha, a well-known adaptogen, has been shown to lower cortisol levels, thereby reducing stress and anxiety (Gomes, 2023).

Table 1. Summary of potential main mechanism of actions for selected adaptogens

Mechanism*	**Example Adaptogen**	**Effect**
HPA Axis Modulation	Ashwagandha (*Withania somnifera*)	Decreased cortisol levels
Neurotransmitter Regulation	Rhodiola (*Rhodiola rosea*)	Increased serotonin and dopamine levels
Antioxidant Pathways	Schisandra (*Schisandra chinensis*)	Reduction of oxidative stress
Immune Modulation	Ginseng (*Panax ginseng*)	Increased natural killer (NK) cell activity

Note: *Key potential pathways of adaptogen action.

Antioxidant and Anti-Inflammatory Effects

Many adaptogens possess potent antioxidant and anti-inflammatory properties, which are crucial for protecting cells from damage caused by oxidative stress and inflammation (Wróbel-Biedrawa & Podolak, 2024). Oxidative stress occurs when there is an imbalance between free radicals and antioxidants in the body, leading to cellular damage and contributing to aging and various diseases (Sadiq, 2023). Inflammation is a natural response to injury or infection, but chronic inflammation can lead to numerous health issues, including cardiovascular disease, diabetes and autoimmune disorders (Bennett et al., 2018). Adaptogens help to neutralize free radicals, reduce oxidative stress and prevent cellular damage (Panossian, 2017). Their anti-inflammatory effects help to reduce chronic inflammation, promoting healing and preventing disease (Pawar & Shivakumar, 2012; Wróbel-Biedrawa & Podolak, 2024). By providing these protective benefits, adaptogens support overall health and longevity, enhancing the body's resilience to environmental stressors and improving quality of life (Panossian et al., 2021). For example, *Schisandra chinensis*, an adaptogen, has been shown to have strong antioxidant properties, protecting the liver from damage and reducing inflammation (Nowak et al., 2019).

Immune system modulation: Adaptogens may enhance immune function by modulating the activity of immune cells and cytokines (Ratan et al., 2021). This modulation can help the body fight off infections and recover more quickly from illness (Isokauppila & Broida, 2024). Adaptogens support the immunomodulation by increasing the production and activity of white blood cells, which are crucial for defending against pathogens (Panossian & Brendler, 2020). They also help regulate the production of cytokines, which are signaling molecules that mediate and regulate immunity and inflammation (Kaur et al., 2017). By supporting the body's natural defense mechanisms, adaptogens contribute to overall well-being and a healthier lifestyle (Provino, 2010). For instance, *Eleutherococcus senticosus* (Siberian ginseng) has been shown to enhance immune function by increasing the activity of natural killer cells, which play a key role in the body's defense against infections and cancer (Murray, 2020a). This immune-boosting effect helps the body maintain homeostasis and resilience in the face of various stressors.

Overview of Major Adaptogens

The increasing interest in adaptogens is evident in the rising number of scientific studies and consumer demand for adaptogen-containing products (Sama et al., 2022). These adaptogens offer a range of health benefits and can be used to support overall well-being, enhance resilience to stress and improve physical and mental performance (Tóth-Mészáros et al., 2023). This section will provide a brief overview of some of the most well-studied and widely used adaptogens, including:

Ashwagandha (Withania somnifera)

Ashwagandha, scientifically known as *Withania somnifera*, is a perennial shrub native to India, North Africa and the Middle East. It has been extensively used in Ayurvedic medicine for centuries, revered for its rejuvenating and adaptogenic properties (Kumar et al., 2013a, 2023).

Historical use in Ayurvedic medicine

In Ayurvedic medicine, Ashwagandha is considered a Rasayana, a class of herbs believed to promote longevity, vitality and overall well-being (Durg et al., 2015). It has been traditionally used to address a wide range of health issues, including stress, anxiety, insomnia and inflammation (Zahiruddin et al., 2020).

Potential benefits for stress, anxiety and cognitive function

Modern research has begun to validate the traditional uses of Ashwagandha (Joshi & Joshi, 2021). Numerous studies have explored its potential benefits for stress, anxiety and cognitive function (Speers et al., 2021; Arumugam et al., 2024; Lopresti et al., 2019; Akhgarjand et al., 2022; Guo & Rezaei, 2024). It is believed to modulate the HPA axis, a key regulatory system involved in stress response (Sobota et al., 2024). By reducing the levels of cortisol, the primary stress hormone, Ashwagandha may help alleviate symptoms of stress and anxiety (Majeed et al., 2023). Additionally, it has been shown to enhance cognitive function, including memory, attention and reaction time (Xing et al., 2022).

Mechanisms of action, including modulation of the HPA axis and neurotransmitter systems

The mechanisms of action of Ashwagandha are complex and multifaceted. Key mechanisms include (Singh et al., 2011; Chandrasekhar et al., 2012; Pratte et al., 2014; Guo & Rezaei, 2024; Wiciński et al., 2024): HPA Axis Modulation: Ashwagandha can help normalize the HPA axis, reducing excessive cortisol production and promoting a balanced stress response. It may influence the levels of neurotransmitters such as γ-aminobutyric acid (GABA), serotonin and dopamine, which are involved in mood regulation, sleep and cognitive function. Ashwagandha possesses potent antioxidant and anti-inflammatory properties, which can help protect cells from oxidative damage and reduce inflammation.

Clinical evidence supporting its efficacy

Several clinical trials have investigated the efficacy of Ashwagandha in various health conditions. Studies have shown that Ashwagandha can effectively reduce stress, anxiety and symptoms of depression (Lopresti & Smith, 2021). It has also been found to improve cognitive function, particularly in individuals with mild cognitive impairment (Ng et al., 2020). Additionally, Ashwagandha may have potential benefits for physical performance, immune function and reproductive health (Długołęcka et al., 2023). Several clinical trials have provided robust evidence supporting the efficacy of Ashwagandha in various health conditions. A randomized, double-blind, placebo-controlled study by Chandrasekhar et al. (2012) demonstrated that high-concentration full-spectrum Ashwagandha root extract significantly reduced stress and anxiety levels in adults. Participants taking Ashwagandha showed a 44% reduction in stress scores compared to a 5.5% reduction in the placebo group.

A study by Choudhary et al. (2017) investigated the effects of Ashwagandha on cognitive function in adults with mild cognitive impairment. The results indicated significant improvements in memory, executive function, attention and information processing speed in the Ashwagandha group compared to the placebo group (Choudhary et al., 2017). Wankhede et al. (2015) conducted a randomized, double-blind, placebo-controlled trial to assess the impact of Ashwagandha on cardiorespiratory endurance and physical performance in healthy athletic adults. The study found that Ashwagandha supplementation significantly improved VO_2 max (maximum oxygen consumption volume by body during exercise) and overall physical performance.

A study by Davis & Kuttan (2000) explored the immunomodulatory effects of Ashwagandha. The findings revealed that Ashwagandha enhanced the proliferation of lymphocytes and increased the activity of natural killer cells, suggesting a boost in immune function. A clinical trial by Ahmad et al. (2010) examined the effects of Ashwagandha on male fertility. The study reported significant improvements in sperm count, motility and overall semen quality in men treated with Ashwagandha, indicating its potential benefits for reproductive health. These studies collectively highlight the diverse therapeutic potential of Ashwagandha, making it a valuable addition to integrative health practices.

Rhodiola rosea

R. rosea is a popular adaptogen used in traditional medicine to reduce stress, improve mood and enhance cognitive function. It is often found in cold regions, such as the Arctic and mountainous areas (Anghelescu et al., 2018; Brinckmann et al., 2021).

Traditional use in Scandinavian and Russian folk medicine

R. rosea, also known as "golden root" or "arctic root," has a long history of use in Scandinavian and Russian folk medicine. It was traditionally used to enhance physical endurance, work productivity, longevity and resistance to high altitude sickness. In Siberia, it was given to couples before marriage to enhance fertility and ensure the birth of healthy children. The Vikings reportedly used it to boost their strength and stamina (Panossian et al., 2010; Elise, 2020).

Potential benefits for fatigue, stress and cognitive performance

R. rosea is renowned for its adaptogenic properties, which help the body resist physical, chemical and environmental stress. It has been shown to reduce fatigue, alleviate stress and improve cognitive function. Studies have indicated that Rhodiola can enhance mental performance, particularly under stressful conditions and may also help with symptoms of burnout and mild to moderate depression (Van De Walle & Lamoreux, 2024; Anonymous, 2024a).

Mechanisms of action, including antioxidant and anti-inflammatory effects

The beneficial effects of *R. rosea* are attributed to its active compounds, such as rosavins and salidroside. These compounds exhibit antioxidant properties, protecting cells from oxidative damage. Rhodiola also modulates the stress-response system, reducing cortisol levels and enhancing the production of neurotransmitters like serotonin and dopamine. Additionally, it has anti-inflammatory effects, which contribute to its overall health benefits (Li et al., 2017a; Bernatoniene et al., 2023).

Clinical evidence supporting its efficacy

Clinical studies have demonstrated the efficacy of *R. rosea* in reducing symptoms of stress, fatigue and depression (Panossian & Wikman, 2014; Ivanova Stojcheva & Quintela, 2022). A randomized controlled trial (RCT) conducted by Darbinyan et al. (2000) evaluated the effects of *R. rosea* on stress-induced fatigue in physicians during night shifts. The study found that Rhodiola significantly improved mental performance and reduced fatigue compared to placebo (Darbinyan et al., 2000). Participants reported enhanced cognitive function and reduced symptoms of burnout, indicating Rhodiola's potential as an adaptogen for stress management. Another RCT by Shevtsov et al. (2003) investigated the impact of Rhodiola on mental fatigue in young, healthy cadets. The study demonstrated that a single dose of Rhodiola extract improved capacity for mental work against a background of fatigue and stress. This suggests that Rhodiola can enhance cognitive function and mental clarity under stressful conditions.

A systematic review by Ishaque et al. (2012) assessed the efficacy of Rhodiola in improving physical and mental fatigue. The review included multiple RCTs and controlled clinical trials, concluding that Rhodiola supplementation could enhance physical performance and reduce fatigue in both healthy individuals and clinical populations. The adaptogenic properties of Rhodiola were highlighted as beneficial for improving endurance and overall physical capacity. A study by Cropley et al. (2015) explored the effects of Rhodiola on symptoms of depression and anxiety. The results indicated that Rhodiola significantly reduced depressive symptoms and anxiety levels in participants, supporting its use as a complementary treatment for mood disorders. The study emphasized Rhodiola's role in modulating neurotransmitter levels, which may contribute to its antidepressant effects.

A multicenter study by Spasov et al. (2000) examined the effects of Rhodiola on stress symptoms in a diverse population. The study reported significant improvements in stress-related symptoms, including fatigue, irritability and cognitive impairment. Participants experienced enhanced well-being and reduced stress levels, further validating Rhodiola's adaptogenic properties. These studies collectively provide robust evidence for the efficacy of *R. rosea* in managing stress, fatigue, and depression. The adaptogenic effects of Rhodiola make it a valuable addition to integrative health practices, particularly for individuals experiencing high levels of stress and mental fatigue.

Ginseng (Panax ginseng and Eleutherococcus senticosus)

Panax ginseng is a highly valued medicinal herb in traditional Chinese and Korean medicine. It is often used to improve cognitive function, boost energy levels and enhance overall well-being (Coleman et al., 2003). Siberian ginseng is another popular adaptogen used in TCM (Liao et al., 2018). It is often used to boost energy levels, improve mental clarity and enhance immune function.

Diverse species with distinct properties

P. ginseng (Asian ginseng) and *Eleutherococcus senticosus* (Siberian ginseng) are two distinct species with unique properties. *P. ginseng* is known for its potent adaptogenic effects, enhancing physical and mental performance and supporting overall vitality. *Eleutherococcus senticosus*, although not a true ginseng, shares similar adaptogenic properties but is considered milder and more suitable for younger individuals (Huizen & French, 2017; Powers, 2022).

Potential benefits for cognitive function, immune function and energy levels

Both *P. ginseng* and *Eleutherococcus senticosus* are used to boost cognitive function, enhance immune response and increase energy levels (Huizen & French, 2017). *P. ginseng* has been shown to improve memory, concentration and overall mental performance (Gaffney et al., 2001). It also supports immune function by enhancing the activity of natural killer cells (Choi et al., 2017). *Eleutherococcus senticosus* is known for its ability to reduce fatigue, improve physical endurance and support immune health (Gerontakos et al., 2021).

Mechanisms of action, including modulation of neurotransmitter systems and antioxidant effects

The active compounds in *P. ginseng*, known as ginsenosides and the eleutherosides in *Eleutherococcus senticosus*, contribute to their health benefits (Arouca & Grassi-Kassisse, 2013). These compounds modulate neurotransmitter systems, enhancing the release of dopamine and serotonin, which improve mood and cognitive function. They also exhibit antioxidant properties, protecting cells from oxidative stress and reducing inflammation (Smith et al., 2014; Anonymous, 2025).

Clinical evidence supporting its efficacy

Clinical trials have shown that *P. ginseng* can improve cognitive function, reduce fatigue and enhance physical performance. For example, a study found that *P. ginseng* improved cognitive performance in healthy volunteers. Similarly, *Eleutherococcus senticosus* has been shown to enhance physical endurance and reduce the severity of colds and flu (Kennedy et al., 2004; Bleakney, 2008; Ernst, 2010; Bach et al., 2016). These findings support the use of both herbs as effective adaptogens.

Schisandra chinensis

The plant that is called *Schisandra chinensis*, also known as Chinese magnolia vine or five-flavor berry (Sun et al., 2021; Park et al., 2021).

Traditional use in Chinese medicine

Schisandra chinensis, known as "Wu Wei Zi" in Chinese medicine, has been used for centuries to enhance vitality, improve mental clarity and increase physical endurance (Jafernik et al., 2021). It is considered one of the 50 fundamental herbs in TCM and is used to balance the body's energies, support liver function and improve respiratory health (Thompson, 2014; Wu Wei Zi, 2025).

Potential benefits for liver health, respiratory function and cognitive performance

Schisandra is known for its hepatoprotective properties, making it beneficial for liver health. It helps detoxify the liver and protect it from damage. Additionally, Schisandra supports respiratory function by improving lung capacity and reducing cough. It also enhances cognitive performance by improving concentration, memory and mental clarity (Whelan, 2018; Kung, 2019; Levy, 2023).

Mechanisms of action, including antioxidant and anti-inflammatory effects

The active compounds in Schisandra, such as schisandrin, exhibit strong antioxidant and anti-inflammatory properties. These compounds protect the liver from oxidative stress, enhance detoxification processes and reduce inflammation. Schisandra also modulates neurotransmitter levels, which can improve mood and cognitive function (Zhang et al., 2018; Kopustinskiene & Bernatoniene, 2021).

Clinical evidence supporting its efficacy

Clinical studies have shown that Schisandra can improve liver function, enhance cognitive performance and support respiratory health (Wang et al., 2024). For instance, research has demonstrated that Schisandra extract can protect the liver from damage caused by toxins and improve symptoms of chronic hepatitis (Addissouky et al., 2024). Other studies have indicated its potential to enhance mental performance and reduce stress (Yan et al., 2017; Jurcău et al., 2019).

Other notable adaptogens

Apart from Moringa (Masiysa) - which is fast-growing tree is native to areas around the Himalayas, but its cultivation has spread throughout the world, including regions in Egypt – there are other more powerful adaptogens (Alshoaibi, 2021). Moringa leaves are a good source of vitamins and minerals and are sometimes considered an adaptogen due to potential health benefits (Van Wyk, 2019; Meireles et al., 2020). Some of the other common adaptogens could be summarized non-exclusively herein.

Licorice root (Glycyrrhiza glabra)

Licorice root is known for its anti-inflammatory and immune-boosting properties (Darvishi et al., 2022). *Glycyrrhiza glabra* possesses potent antiviral and anti-inflammatory properties, making it a valuable tool in managing respiratory conditions like the common cold, flu, and bronchitis. It effectively soothes irritated mucous membranes in the throat and lungs, alleviating symptoms such as coughing (Otieno, 2019). Licorice root is available in various forms, including teas, tinctures and supplements. However, it's important to exercise caution, as extended use of licorice root can elevate blood pressure and disrupt electrolyte balance, particularly for individuals with hypertension (Otieno, 2019). It is used to soothe gastrointestinal issues, reduce inflammation and support adrenal function (Murray, 2020b). Licorice roots also have antiviral properties, making it useful in treating respiratory infections (Zhang et al., 2021a).

Holy basil (Ocimum sanctum)

Holy basil, also known as Tulsi, is revered in Ayurvedic medicine for its adaptogenic properties (Kumar et al., 2013b). It helps the body cope with stress, supports immune function and improves mental clarity (Thakur & Thapa, 2024). Holy basil also has anti-inflammatory and antioxidant effects, which contribute to its overall health benefits (Yadav et al., 2024).

Astragalus membranaceus

Astragalus is a key herb in TCM, known for its immune-boosting and anti-aging properties (Alipour & Farokhimanesh, 2024). It enhances the body's resistance to stress, supports cardiovascular health and improves energy levels (Shahrajabian et al., 2019). Astragalus is also used to support kidney function and improve overall vitality (Lui et al., 2015).

Cordyceps militaris

Cordyceps is a medicinal mushroom known for its energy-boosting and immune-enhancing properties (Kumar & Kushwaha, 2023). It improves physical performance, supports respiratory health and enhances stamina (Thongsawang et al., 2021). Cordyceps also has antioxidant and anti-inflammatory effects, which contribute to its adaptogenic benefits (Shashidhar et al., 2013). While it's often referred to as a "mushroom," it's more accurately classified as a fungus (Holliday, 2017). *Cordyceps militaris* is a parasitic fungus that grows on insects, particularly caterpillars (Shrestha et al., 2012). It showcases the distinctive orange, club-shaped fruiting bodies that emerge from the infected insect host (Wellham, 2021). *Cordyceps militaris* has gained popularity in recent years due to its potential health benefits, including improved athletic performance, enhanced immune function and anti-aging properties (Abdullah & Kumar, 2023).

Reishi mushroom (Ganoderma lucidum)

Reishi mushroom is a powerful adaptogen used to enhance immune function, reduce stress and improve sleep (Petitto, 2020). It has anti-inflammatory and antioxidant properties, which support overall health and longevity (Luo et al., 2024). Reishi is also known for its ability to improve mental clarity and promote relaxation (Ahmad et al., 2021). It's a type of fungus, not a plant (Mizuno et al., 1995). The characteristic features of Reishi mushrooms, including their distinctive shelf-like shape, red-brown color and white underside (Subramaniam, 2013). Reishi mushrooms are highly valued in TCM for their potential health benefits, such as boosting immunomodulation, reducing stress and improving sleep quality (Zeng et al., 2019).

Adaptogens and Health Conditions

It would be expected from the previously proposed mechanisms by which adaptogens exert their effects some benefits in various health conditions, including the following in this section and Table 2 provides a detailed overview of various adaptogens, their chemical structures, the parts of the organism they are derived from and their medicinal uses. Adaptogens are known for their ability to modulate the body's stress response. They help reduce the secretion of stress hormones like cortisol, which can lower overall stress levels (Panossian & Wikman, 2009). By balancing neurotransmitter levels, adaptogens such as Ashwagandha and *R. rosea* improve mood and emotional well-being (Wal et al., 2019). These herbs enhance resilience to stress by supporting the HPA axis, which regulates the body's response to stress (Lopresti et al., 2022). Adaptogens can significantly enhance cognitive function (Dimpfel et al., 2020). Herbs like *P. ginseng* and *R. rosea* have been shown to improve memory, attention and focus (Joshi Pranav, 2013). They enhance cognitive performance, especially under stressful conditions, by modulating neurotransmitter activity and promoting neurogenesis (Tabassum et al., 2012). Additionally, adaptogens possess neuroprotective effects, protecting brain cells from oxidative stress and inflammation, which can help prevent cognitive decline (Panossian et al., 2019).

Adaptogens play a crucial role in boosting immune function (Sharma et al., 2021). They increase the activity of immune cells such as natural killer cells and macrophages, enhancing the body's resistance to infections (Brindha, 2016). Adaptogens like Astragalus and Reishi mushroom also reduce inflammation by modulating cytokine production and supporting the immune-neuro-endocrine system (Pasdaran et al., 2023). This helps maintain a balanced immune response and prevents chronic inflammation (Tewari et al., 2011). Adaptogens are effective in combating fatigue and boosting energy levels (Ayales, 2019). Herbs like *P. ginseng* and cordyceps improve physical performance and endurance by enhancing mitochondrial function and increasing ATP production (Choi et al., 2020). They help reduce fatigue and exhaustion by supporting adrenal function and HPA axis regulation (Kariatsumari, 2019). This leads to increased vitality and sustained energy throughout the day (Yu et al., 2023). Adaptogens offer a range of additional health benefits. For cardiovascular health, adaptogens like hawthorn and *R. rosea* help regulate blood pressure and improve heart function (Kshirsagara et al., 2023). For liver health, herbs such as schisandra and milk thistle support detoxification and protect against liver damage (Rudzinska & Bogacz, 2012). Adaptogens like maca and *Tribulus terrestris* enhance sexual function by balancing hormones and improving libido (Oyedokun et al., 2024). Additionally, adaptogens have anti-aging properties, reducing oxidative stress and inflammation, which can slow down the aging process (Panossian & Gerbarg, 2016).

Table 2. Summary of adaptogen compounds and their medicinal uses

Adaptogen*	Active Principle/Class	Typical Daily Dosage	Part Used	Organism	Medicinal Uses
Ashwagandha	Withanolides (steroidal lactones)	300–600 mg (root extract, 5% withanolides)	Root	*Withania somnifera*	Reduces stress, anxiety, improves cognitive function, enhances physical performance
Ginseng	Ginsenosides (triterpene saponins)	200–400 mg (root extract)	Root	*Panax ginseng*	Boosts immune function, reduces fatigue, improves cognitive function, anti-inflammatory
Rhodiola	Rosavins, salidroside (phenylpropanoids)	200–600 mg (root extract, 3% rosavins)	Root	*Rhodiola rosea*	Reduces fatigue, enhances mental performance, improves mood, increases physical endurance
Eleuthero	Eleutherosides (saponins)	300–400 mg (root/stem bark extract)	Root, stem bark	*Eleutherococcus senticosus*	Enhances physical performance, reduces stress, boosts immune function
Schisandra	Schisandrins (lignans)	500–1500 mg (berry extract)	Berries	*Schisandra chinensis*	Improves concentration, coordination, endurance, liver protection
Holy Basil	Eugenol, ursolic acid (phenylpropanoids, triterpenoids)	500–1000 mg (leaf extract)	Whole herb	*Ocimum sanctum*	Reduces anxiety, improves focus, boosts immune function
Licorice Root	Glycyrrhizin (triterpene saponin)	200–800 mg (root extract)*	Root	*Glycyrrhiza glabra*	Anti-inflammatory, immune modulation, supports adrenal function
Maca	Macamides, macamides (alkaloids)	1500–3000 mg (root powder)	Root	*Lepidium meyenii*	Enhances libido, improves mood, boosts energy and endurance
Astragalus	Astragalosides (triterpene saponins)	500–1000 mg (root extract)	Root	*Astragalus membranaceus*	Immune boosting, anti-inflammatory, supports cardiovascular health
Cordyceps	Cordycepin (nucleoside analog)	1000–3000 mg (mushroom extract)	Mushroom	*Cordyceps sinensis*	Enhances physical performance, boosts energy, supports respiratory health

Note: *References for given adaptogens are: Størmer et al. (1993), Panossian et al. (1999), Darbinyan et al. (2000), Gonzales et al. (2002), Block & Mead (2003), Cicero et al. (2004), Reay et al. (2005), Coates et al. (2010), Chandrasekhar et al. (2012), Cohen (2014).

Different natural remedies provide different pharmacological approaches in the treatment. For comparative efficiency purpose, it should be noted for example that Ashwagandha primarily modulates the HPA axis, reducing cortisol levels (Chandrasekhar et al., 2012), while *R. rosea* enhances neurotransmitter activity (serotonin/dopamine) to combat fatigue (Darbinyan et al., 2000). For stress-related cognitive decline, Ashwagandha improves memory consolidation, whereas Rhodiola optimizes acute mental performance under fatigue. Ginseng excels in immune enhancement (Reay et al., 2005), whereas Schisandra offers superior hepatoprotection (Panossian et al., 1999).

Overview of Adaptogens and Structure-Activity Relationships (SAR)

Withanolides (Ashwagandha) are steroidal lactones with a C28 ergostane skeleton, featuring a δ-lactone ring at C-22 and C-26 (Kumar et al., 2024). Ginsenosides (Ginseng) are triterpene saponins with a dammarane skeleton, consisting of a four-ring structure (Chopra et al., 2023). Rosavins (Rhodiola) are cinnamyl glycosides, with a phenylpropanoid backbone (Bi et al., 2022). Eleutherosides (Eleuthero) are a group of compounds including saponins and glycosides (Huang et al., 2022). Schisandrins (Schisandra) are dibenzocyclooctadiene lignans (Kortesoja et al., 2019). Eugenol (Holy Basil) is a phenylpropanoid with a methoxy group and an allyl chain (Bendre et al., 2016). Glycyrrhizin (Licorice Root) is a triterpenoid saponin with a glycoside linkage (Li et al., 2020). Macamides (Maca) are fatty acid amides with a benzylamide structure (Alasmari et al., 2019). Astragalosides (Astragalus) are triterpene glycosides with a cycloartane skeleton (Graziani et al., 2019). Cordycepin (Cordyceps) is a nucleoside analog of adenosine, lacking the 3′ hydroxyl group (Du et al., 2021). These structures represent the core chemical frameworks of the compounds found in these adaptogens.

Adaptogens are natural substances known for their ability to help the body adapt to stress and exert a normalizing effect upon bodily processes (Panossian, 2013). The chemical structures of adaptogens play a crucial role in determining their biological activity. The concept of Structure-Activity Relationship (SAR) is fundamental in medicinal chemistry and pharmacology, as it explores the relationship between a compound's chemical structure and its biological effects (Ferro et al., 2006). Withanolides (Ashwagandha) are steroidal lactones that interact with various biological targets, including the HPA axis, to reduce stress and anxiety (Guehairia & Taleb, 2023). The lactone ring and the steroidal backbone are essential for binding to receptors and exerting their adaptogenic effects (Kumar et al., 2024). Ginsenosides (*P. ginseng*) are triterpene saponins that modulate immune function, reduce fatigue and improve cognitive performance (Kennedy & Scholey, 2003). The dammarane skeleton and sugar moieties are critical for their interaction with cell membranes and receptors (Verstraeten et al., 2020). For instance, ginsenoside Rg1, with fewer sugar moieties, is more effective in enhancing cognitive function, while ginsenoside Rb1, with more sugar moieties, has stronger anti-inflammatory properties (Zarneshan et al., 2022; Fan et al., 2024).

Rosavins (*R. rosea*) are phenylpropanoids that enhance mental performance and reduce fatigue (Hamidpour et al., 2015). The presence of glycoside groups enhances the solubility and bioavailability of rosavins (Aktar et al., 2024). Salidroside, a major active component, has been shown to improve mental performance and reduce fatigue more effectively due to its higher bioavailability compared to other rosavins (Zhang et al., 2021b). Eleutherosides (*Eleutherococcus senticosus*) are saponins that enhance physical performance and boost immune function. The aglycone part of eleutherosides is crucial for their adaptogenic effects (Bernatoniene et al., 2023). Modifications in the sugar moieties can alter the compound's ability to enhance physical performance and immune function (Wang et al., 2023). For example, eleutheroside E has been found to be particularly effective in boosting endurance. Schisandrins (*Schisandra chinensis*) are lignans that improve concentration, coordination, and endurance (Goulet & Dionne, 2005). The unique dibenzocyclooctadiene structure of schisandrins is essential for their antioxidant and hepatoprotective activities (Liu et al., 2023a).

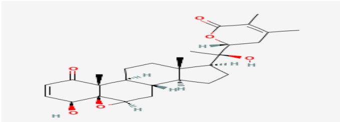
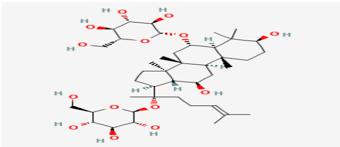
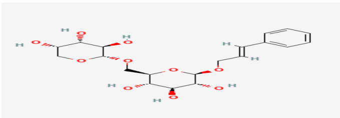
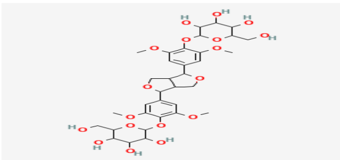
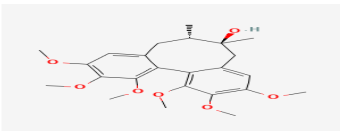
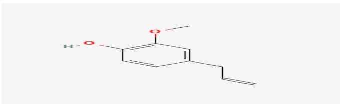
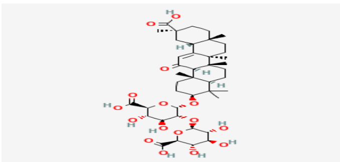
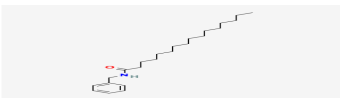
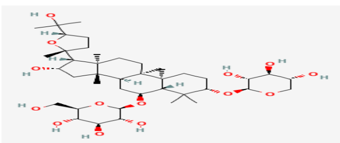
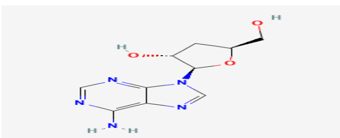
Eugenol (Holy Basil) is a phenylpropanoid with anti-inflammatory and anxiolytic properties. The methoxy group and allyl chain are important for its interaction with enzymes and receptors involved in inflammation and stress response (Saini & Dhiman, 2022). Glycyrrhizin (*Glycyrrhiza glabra*) is a triterpene saponin that modulates immune function and supports adrenal health (Xie et al., 2023). The glycoside linkage and triterpene backbone are critical for its bioactivity and interaction with glucocorticoid receptors (Schwarz et al., 2011). Macamides (*Lepidium meyenii*) are alkaloids that enhance libido and improve mood. The benzylamide structure is essential for their neuroactive properties and interaction with neurotransmitter systems (Pino-Figueroa et al., 2010). Astragalosides (*Astragalus membranaceus*) are triterpene saponins that boost immune function and support cardiovascular health. The cycloartane skeleton and sugar moieties are important for their immunomodulatory effects (Dong et al., 2023). Cordycepin (*Cordyceps sinensis*) is a nucleoside analog that enhances physical performance and supports respiratory health. The absence of the 3′ hydroxyl group in cordycepin is crucial for its ability to inhibit RNA synthesis, which contributes to its anti-cancer and anti-inflammatory properties (Paterson, 2008). Understanding the SAR of these compounds helps in optimizing their therapeutic potential and developing new derivatives with enhanced efficacy and reduced side effects (Singh et al., 2022). These relationships illustrate how specific structural features of adaptogen compounds are directly related to their biological activities, making them valuable additions to integrative health practices.

Table 3 shows simplified examples of adaptogens such as Withanolide D (IUPAC Name[192-201]: (1S,2R,6S,7R,9R,11S,12S,15S,16S)-15-[(1R)-1-[(2R)-4,5-dimethyl-6-oxo-2,3-dihydropyran-2-yl]-1-hydroxyethyl]-6-hydroxy-2,16-dimethyl-8-oxapentacyclo[9.7.0.02,7.07,9.0 12,16]octadec-4-en-3-one), Ginsenoside Rg1 (IUPAC Name: ((2R,3R,4S,5S,6R)-2-[[(3S,5R,6S,8R,9R,10R,12R,13R,14R,17S)-3,12-dihydroxy-4,4,8,10,14-pentamethyl-17-[(2S)-6-methyl-2-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyhept-5-en-2-yl]-2,3,5,6,7,9,11,12,13,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-6-yl]oxy]-6-(hydroxy methyl)oxane-3,4,5-triol), Rosavidin (IUPAC Name: (2R,3R,4S,5S,6R)-2-[(E)-3-phenylprop-2-enoxy]-6[[(2S,3R,4S,5S)-3,4,5-trihydroxyoxan-2-yl]oxymethyl]oxane-3,4,5-triol), Acanthoside D (IUPAC Name: 2-[4-[6-[3,5-dimethoxy-4-[3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyphenyl]-1,3,3a,4,6,6a-hexahydrofuro[3,4-c]furan-3-yl]-2,6-dimethoxyphenoxy]-6-(hydroxymethyl) oxane-3,4,5-triol), Schisandrin (IUPAC Name: (9S,10S)-3,4,5,14,15,16-hexamethoxy-9,10-dimethyltricyclo[10.4.0.02,7]hexadeca-1(16),2,4,6,12,14-hexaen-9-ol), 4-Allyl-2-methoxyphenol (IUPAC Name: 2-methoxy-4-prop-2-enylphenol), Glycyrrhizic acid (IUPAC Name: (2S,3S,4S,5R,6R)-6-[(2S,3R,4S,5S,6S)-2-[[(3S,4aR,6aR,6bS,8aS,11S,12aR,14aR,14bS)-11-carboxy-4,4,6a,6b,8a,11,14b-heptamethyl-14-oxo-2,3,4a,5,6,7,8,9,10,12,12a,14a-dodecahydro-1H-picen-3-yl]oxy]-6-carboxy-4,5-dihydroxyoxan-3-yl]oxy-3,4,5-trihydroxyoxane-2-carboxylic acid), Macamide B (IUPAC Name: (N-benzylhexadecanamide), Astragaloside IV (IUPAC Name: (2R,3R,4S,5S,6R)-2-[[(1S,3R,6S,8R,9S,11S,12S,14S,15R,16R)-14-hydroxy-15-[(2R,5S)-5-(2-hydroxypropan-2-yl)-2-methyloxolan-2-yl]-7,7,12,16-tetramethyl-6-[(2S,3R,4S,5R)-3,4,5-trihydroxyoxan-2-yl]oxy-9-pentacyclo[9.7.0.01,3.03,8.012,16]octadecanyl]oxy]-6-(hydroxymethyl)oxane-3,4,5-triol) and 3′-Deoxyadenosine (IUPAC Name: (2R,3R,5S)-2-(6-aminopurin-9-yl)-5-(hydroxymethyl)oxolan-3-ol).

Overview of Adaptogen Interactions, Contraindications, and Adverse Effects

Adaptogens are widely used for their potential health benefits, but it is crucial to understand their interactions with drugs, contraindications, and possible side effects (Winston, 2019). The following tables provide a detailed overview of these aspects, supported by scientific references in Tables 3-6. Table 4 summarizes the interactions between various adaptogens and drugs, highlighting the potential side effects and adverse reactions (Siwek et al., 2023). Table 5 summarizes the contraindications for various adaptogens, highlighting the conditions and situations where their use should be avoided (Størmer et al., 1993; Panossian et al., 1999; Gonzales et al., 2002; Block & Mead, 2003; Cicero et al., 2004; Reay et al., 2005; Coates et al., 2010; Chandrasekhar et al., 2012; Cohen, 2014; Pratte et al., 2014). Table 6 summarizes the side or adverse effects of various adaptogens and these effects are dose dependent (Størmer et al., 1993; Panossian et al., 1999; Darbinyan et al., 2000; Gonzales et al., 2002; Block & Mead, 2003; Cicero et al., 2004; Reay et al., 2005; Coates et al., 2010; Chandrasekhar et al., 2012; Cohen, 2014).

Table 3. Simplified 2D structures of adaptogens and links to databases for further exploration

Adaptogen	Compound	Chemical Structure (Simplified)	Chemical Formula
Ashwagandha	Withanolides		$C_{28}H_{38}O_6$
Ginseng	Ginsenosides		$C_{42}H_{72}O_{14}$
Rhodiola rosea	Rosavins		$C_{20}H_{28}O_{10}$
Eleuthero	Eleutherosides		$C_{34}H_{46}O_{18}$
Schisandra	Schisandrins		$C_{24}H_{32}O_7$
Holy Basil	Eugenol		$C_{10}H_{12}O_2$
Licorice Root	Glycyrrhizin		$C_{42}H_{62}O_{16}$
Maca	Macamides		$C_{23}H_{39}NO$
Astragalus	Astragalosides		$C_{41}H_{68}O_{14}$
Cordyceps	Cordycepin		$C_{10}H_{13}N_5O_3$

Note: Information for given adaptogens were obtained from National Center for Biotechnology Information (2024a, b, c, d, e, f, g, h, i, j). The structures provided here are simplified representations and may not reflect the full complexity of the molecules. Many of these compounds exist in various forms and isomers, each with its own specific chemical structure.

Table 4. Drug-adaptogen interactions, based on current scientific evidence

Adaptogen*	Drug	Interaction
Withania somnifera	Reboxetine	Testicle pain, ejaculatory dysfunctions
	Sertraline	Severe diarrhea
	Escitalopram	Myalgia, epigastric pain, nausea, vomiting, restless legs syndrome, severe cough
	Paroxetine	Generalized myalgia, ophthalmalgia, ocular hypertension
Eleutherococcus senticosus	Duloxetine	Upper gastrointestinal bleeding
	Paroxetine	Epistaxis
	Sertraline	Vaginal hemorrhage
	Agomelatine	Irritability, agitation, headache, dizziness
Schisandra chinensis	Bupropion	Arthralgia, thrombocytopenia
	Amitriptyline	Delirium
	Fluoxetine	Dysuria
Tribulus terrestris	Citalopram	Generalized pruritus
	Escitalopram	Galactorrhea
	Trazodone	Psoriasis relapse
Coptis chinensis	Mianserin	Arrhythmias
	Mirtazapine	Edema of lower limbs, myalgia
	Fluoxetine	Gynecomastia
Cimicifuga racemosa	Mianserin	Restless legs syndrome
	Paroxetine	Gynecomastia, mastalgia
	Venlafaxine	Hyponatremia
Bacopa monnieri	Agomelatine	Back pain, hyperhidrosis
	Moclobemide	Myocardial infarction
Gynostemma pentaphyllum	Duloxetine	Back pain
Cordyceps sinensis	Sertraline	Upper gastrointestinal bleeding
Lepidium meyenii	Mianserin	Restless legs syndrome
Scutellaria baicalensis	Bupropion	Seizures

Note: * Concluded and extrapolated from Siwek et al. (2023).

That is why it is important for the patients to consult with a healthcare professional before combining adaptogens with medications to ensure safety and efficacy.

Clinical Evidence and Future Directions

The clinical evidence supporting the efficacy and safety of adaptogens is growing, yet it remains limited and often inconsistent (Panossian et al., 2021). Many studies have demonstrated the potential benefits of adaptogens in reducing stress, enhancing cognitive function and boosting immune response (Sánchez et al., 2023). For instance, and as could be extrapolated earlier, clinical trials have shown that *R. rosea* can significantly reduce symptoms of stress-related fatigue and improve mental performance in stressful conditions (Ishaque et al., 2012). Similarly, *P. ginseng* has been found to enhance cognitive function and physical performance (Oliynyk & Oh, 2013). However, these studies often vary in their methodologies, sample sizes and outcome measures, which complicates the interpretation and generalization of the results (Panossian & Wagner, 2005). One of the primary strengths of the existing clinical evidence is the demonstration of adaptogens' ability to modulate the stress response. Adaptogens like ashwagandha and *R. rosea* have been shown to lower cortisol levels, which is a key indicator of stress reduction (Wal et al., 2019). Additionally, adaptogens have been found to improve markers of immune function, such as increased activity of natural killer cells and enhanced resistance to infections (Ramakrishnan et al., 2022). These findings are promising and suggest that adaptogens could play a valuable role in managing stress and supporting overall health.

Table 5. Summary table showing known potential contraindications of various adaptogens, based on current scientific evidence

Adaptogen*	Contraindications
Ashwagandha (*Withania somnifera*)	Pregnancy, hyperthyroidism, autoimmune diseases (e.g., rheumatoid arthritis, lupus)
Ginseng (*Panax ginseng*)	Hypertension, bleeding disorders, insomnia, pregnancy
Rhodiola rosea	Bipolar disorder, pregnancy, breastfeeding
Eleuthero (*Eleutherococcus senticosus*)	Hypertension, sleep disorders, pregnancy, breastfeeding
Schisandra chinensis	Epilepsy, peptic ulcers, pregnancy, breastfeeding
Holy Basil (*Ocimum sanctum*)	Hypoglycemia, anticoagulant therapy, pregnancy, breastfeeding
Licorice Root (*Glycyrrhiza glabra*)	Hypertension, hypokalemia, pregnancy, breastfeeding
Maca (*Lepidium meyenii*)	Hormone-sensitive conditions (e.g., breast cancer, uterine fibroids), pregnancy, breastfeeding
Astragalus (*Astragalus membranaceus*)	Autoimmune diseases, transplant recipients, pregnancy, breastfeeding
Cordyceps (*Cordyceps sinensis*)	Autoimmune diseases, bleeding disorders, pregnancy, breastfeeding

Note: *References for given adaptogens are: Størmer et al. (1993), Panossian et al. (1999), Darbinyan et al. (2000), Gonzales et al. (2002), Block & Mead (2003), Cicero et al. (2004), Reay et al. (2005), Coates et al. (2010), Chandrasekhar et al. (2012), Cohen (2014).

Table 6. Summary showing known dose-dependent side or adverse effects of various adaptogens based on current scientific evidence.

Adaptogen*	Side/Adverse Effects
Ashwagandha (*Withania somnifera*)	Nausea, diarrhea, abdominal pain, drowsiness, headache, allergic reactions
Ginseng (*Panax ginseng*)	Insomnia, headaches, gastrointestinal issues, changes in blood pressure, allergic reactions
Rhodiola rosea	Dry mouth, dizziness, excessive salivation, restlessness, insomnia
Eleuthero (*Eleutherococcus senticosus*)	Drowsiness, headache, gastrointestinal upset, changes in blood pressure
Schisandra chinensis	Gastrointestinal upset, skin rash, allergic reactions
Holy Basil (*Ocimum sanctum*)	Hypoglycemia, nausea, diarrhea, allergic reactions
Licorice Root (*Glycyrrhiza glabra*)	Hypertension, hypokalemia, edema, headache, fatigue
Maca (*Lepidium meyenii*)	Gastrointestinal upset, headache, mood changes
Astragalus (*Astragalus membranaceus*)	Gastrointestinal upset, rash, itching, allergic reactions
Cordyceps (*Cordyceps sinensis*)	Dry mouth, nausea, diarrhea, gastrointestinal upset

Note: *References for given adaptogens are: Størmer et al. (1993), Panossian et al. (1999), Darbinyan et al. (2000), Gonzales et al. (2002), Block & Mead (2003), Cicero et al. (2004), Reay et al. (2005), Coates et al. (2010), Chandrasekhar et al. (2012), Cohen (2014).

Despite these positive findings, there are significant limitations in the current body of research. Many studies on adaptogens are small-scale, short-term and lack rigorous controls. There is also a high degree of variability in the quality and standardization of adaptogen preparations used in these studies. This variability can lead to inconsistent results and makes it difficult to compare findings across different studies (Jarry, 2022). Furthermore, the placebo effect is a notable concern in adaptogen research, as many studies do not adequately control for this factor. Looking forward, there are several challenges and opportunities in conducting high-quality clinical trials on adaptogens. One major challenge is the standardization of adaptogen extracts (Pandey & Tripathi, 2014). Adaptogens are often complex mixtures of bioactive compounds and the concentration of these compounds can vary significantly between different preparations. Standardizing these extracts to ensure consistent potency and composition is crucial for reliable research (Jonas et al., 2023). Additionally, determining the optimal dosage and duration of adaptogen use is essential for understanding their long-term safety and efficacy.

Another important consideration is the selection of appropriate outcome measures. Many studies rely on subjective measures of stress and fatigue, which can be influenced by individual perceptions and biases. Incorporating objective biomarkers, such as cortisol levels and immune cell activity, can provide more reliable and quantifiable data. Moreover, long-term studies are needed to assess the sustained effects of adaptogens and their potential side effects over extended periods. Hence, while the current clinical evidence on adaptogens is promising, more rigorous and standardized research is needed to fully understand their efficacy and safety. Addressing the challenges of standardization, dosage and outcome measures will be critical in advancing the field of adaptogen research (Prinsen et al., 2016; Panossian, 2017; Jarry, 2022; Gerontakos et al., 2020). Future studies should focus on large-scale, long-term clinical trials with well-defined protocols to provide more definitive evidence on the health benefits of adaptogens.

Adaptogens and Personalized Medicine

Personalized medicine, also known as precision medicine, is an innovative approach that tailors medical treatment to the individual characteristics of each patient. This approach considers genetic, environmental and lifestyle factors to provide more effective and targeted therapies (MedlinePlus, 2024). Adaptogens, with their diverse range of bioactive compounds, fit well into the personalized medicine paradigm (Vicente et al., 2020). By understanding an individual's specific stressors and physiological responses, healthcare providers can select the most appropriate adaptogens to support their health.

Genetics play a crucial role in how individuals respond to adaptogens. Genetic variations can influence the metabolism, efficacy and safety of adaptogens. For instance, polymorphisms in genes encoding for enzymes involved in the metabolism of adaptogens can affect how these compounds are processed in the body (Anonymous, 2024b). Cytochrome P450 enzymes, which are responsible for the metabolism of many drugs and natural compounds, exhibit genetic variability that can lead to differences in adaptogen metabolism (Anonymous, 2024c). Understanding these genetic variations can help in selecting the right adaptogen and dosage for each individual (Hossam Abdelmonem et al., 2024).

Environmental and lifestyle factors also significantly impact the effectiveness of adaptogens (Cybel, 2024). Factors such as diet, stress levels, physical activity and exposure to toxins can influence how the body responds to adaptogens (Anonymous, 2024d). For example, individuals with high levels of chronic stress might benefit from adaptogens like Ashwagandha, which has been shown to modulate the HPA axis and reduce cortisol levels (Plante, 2024). Conversely, those needing cognitive support might find *R. rosea* more beneficial due to its effects on mental performance and fatigue reduction (Ishaque et al., 2012; Turner, 2024). Personalized medicine can also consider potential interactions between adaptogens and other medications, ensuring safe and effective use tailored to the individual's unique health profile.

Biomarkers are measurable indicators of biological processes, and they play a critical role in personalized medicine (Jain, 2021). By identifying specific biomarkers, healthcare providers can tailor adaptogen therapy to the individual's needs (Yance, 2013; Jamal, 2023). For example, cortisol levels can be used as a biomarker to assess stress and determine the effectiveness of adaptogens like Ashwagandha in reducing stress (Haber et al., 2024). Similarly, inflammatory markers such as C-reactive protein (CRP) can help in selecting adaptogens with anti-inflammatory properties, such as ginseng or turmeric (Garcia-Bailo et al., 2011).

Several case studies and clinical trials have demonstrated the benefits of personalized adaptogen therapy (Winston, 2019). For instance, a study on the use of *R. rosea* in individuals with chronic fatigue syndrome showed significant improvements in fatigue levels and overall well-being when the adaptogen was tailored to the individual's specific needs (Ayales, 2019; Elise, 2020). Another study on the use of Ashwagandha in individuals with high stress levels found that personalized dosing based on cortisol levels resulted in better outcomes compared to standard dosing (Quinones et al., 2025).

Integrating adaptogens into personalized medicine involves a comprehensive assessment of the individual's health status, including genetic testing, biomarker analysis and lifestyle evaluation (Panossian & Efferth, 2022). This holistic approach ensures that the selected adaptogens are well-suited to the individual's unique needs (Yance, 2022). Healthcare providers can use tools such as genetic testing kits, wearable devices for monitoring physiological parameters and personalized health apps to gather data and make informed decisions about adaptogen therapy.

While the integration of adaptogens into personalized medicine holds great promise, there are several challenges to consider (Yance, 2013; Jamal, 2023; Balkrishna et al., 2024). One of the main challenges is the variability in the quality and standardization of adaptogenic products (Kurkin & Ryazanova, 2021). Ensuring that adaptogens are sourced from reputable suppliers and standardized for their active compounds is crucial for their effectiveness and safety (Nunez, 2024). Additionally, more research is needed to understand the long-term effects of adaptogen use and their interactions with other medications (Panossian et al., 2021). Future directions in personalized adaptogen therapy include the development of advanced diagnostic tools and technologies for real-time monitoring of biomarkers and physiological responses (Pokushalov et al., 2024). The use of artificial intelligence and machine learning algorithms to analyze data and predict the most effective adaptogen combinations is another exciting area of research (Siddiqui et al., 2025). As our understanding of the human genome and the mechanisms of adaptogens continues to grow, personalized adaptogen therapy will become increasingly precise and effective.

Adaptogens and Nanotechnology

Nanotechnology, the manipulation of matter on an atomic or molecular scale, offers exciting possibilities for enhancing the efficacy and delivery of adaptogens (Teli et al., 2024). By incorporating adaptogens into nanoparticles, researchers can improve their bioavailability, stability and targeted delivery to specific tissues or cells (Stanisz et al., 2024). This approach can maximize the therapeutic benefits of adaptogens while minimizing potential side effects (Milicic et al., 2022).

One of the main challenges with adaptogens is their bioavailability, which refers to the proportion of a substance that enters the bloodstream and has an active effect (Potoroko et al., 2018; Panossian et al., 2021). Many adaptogens have low bioavailability due to poor solubility, instability in the gastrointestinal tract or rapid metabolism (Ayub et al., 2024). Nanotechnology can address these issues by encapsulating adaptogens in nanoparticles, which can protect them from degradation and enhance their absorption (Chatterjee & Khan, 2025). For example, curcumin, the active compound in Turmeric, has low bioavailability due to its poor solubility and rapid metabolism (Abd El-Hack et al., 2021). Researchers have developed curcumin nanoparticles that significantly enhance its bioavailability and therapeutic effects (Kakkar et al., 2011; Abd El-Hack et al., 2021). Similar approaches can be applied to other adaptogens to improve their efficacy (Uddin, 2024).

Nanoparticles can be engineered to target specific tissues or cells, enhancing the therapeutic effects of adaptogens while reducing side effects (Sheik et al., 2021). This targeted delivery is achieved by modifying the surface of nanoparticles with ligands that bind to specific receptors on the target cells244. For instance, nanoparticles can be designed to target cancer cells, delivering adaptogens with anti-cancer properties directly to the tumor site (Abdul Azeez et al., 2018; Anarjan, 2019). A study on the use of nanoparticle-encapsulated Ginseng extract demonstrated enhanced anti-cancer activity and reduced toxicity compared to free Ginseng extract (Jeon et al., 2023). This targeted delivery approach can be applied to other adaptogens to treat various health conditions more effectively.

Nanotechnology can also enable the sustained release of adaptogens, providing a steady and prolonged therapeutic effect. This is particularly beneficial for adaptogens that require consistent levels in the bloodstream to be effective. Sustained release formulations can reduce the frequency of dosing and improve patient compliance. For example, sustained release nanoparticles of Ashwagandha extract have been developed to provide a prolonged anti-stress effect. This approach ensures that the adaptogen remains active in the body for an extended period, enhancing its therapeutic benefits (Manjunath et al., 2023).

Biological barriers, such as the blood-brain barrier (BBB), can limit the effectiveness of adaptogens in treating certain conditions. Nanoparticles can be designed to cross these barriers, delivering adaptogens to otherwise inaccessible sites. This is particularly relevant for adaptogens used in neuroprotection and cognitive enhancement. A study on the use of nanoparticles encapsulated *R. rosea* extract demonstrated its ability to cross the BBB and exert neuroprotective effects in a model of Alzheimer's disease (Shilo et al., 2015; Tang et al., 2017; Liu et al., 2023b). This opens up new possibilities for using adaptogens in the treatment of neurological disorders.

While nanotechnology offers numerous benefits for adaptogen delivery, it is essential to consider the safety and efficacy of nanoparticle formulations (Arifin et al., 2019). The size, shape and surface properties of nanoparticles can influence their interaction with biological systems and their potential toxicity (Albanese et al., 2012). Rigorous testing and evaluation are necessary to ensure that nanoparticle-based adaptogen formulations are safe for human use (Sukhanova et al., 2018).

The integration of nanotechnology with adaptogens represents a promising frontier in both botanical medicine and advanced therapeutic delivery systems (de Jesus Silva et al., 2023). Future research will focus on optimizing nanoparticle formulations, exploring new materials for nanoparticle construction, and conducting clinical trials to evaluate the safety and efficacy of these advanced delivery systems (Liu et al., 2024). Additionally, the development of multifunctional nanoparticles that combine adaptogens with other therapeutic agents or diagnostic tools is an exciting area of research (Pięta et al., 2023). These multifunctional nanoparticles can provide synergistic effects, enhancing the overall therapeutic outcome (Gupta et al., 2022). At the end, the combination of adaptogens and nanotechnology holds great potential for improving the effectiveness and precision of natural therapies. By enhancing bioavailability, enabling targeted delivery, providing sustained release and overcoming biological barriers, nanotechnology can maximize the therapeutic benefits of adaptogens and open up new possibilities for their use in personalized medicine and beyond.

Incorporation of Nanorobotics and Adaptogens in Space Travel: A Scientific Perspective

Space travel presents a unique set of challenges that can significantly impact human health (Eissa, 2018). The harsh environment of space, characterized by microgravity, radiation, isolation and confinement, poses risks to astronauts' physical and mental well-being (Shah et al., 2024). To mitigate these risks, innovative solutions are required. The incorporation of nanorobotics and adaptogens in space travel is a scientifically logical approach that holds great promise for enhancing astronaut health and performance during long-duration missions (Kalia, 2022).

Space travel exposes astronauts to a variety of stressors that can affect their health (Arone et al., 2021). These include:

(i) *Microgravity*: Prolonged exposure to microgravity leads to muscle atrophy, bone density loss and fluid shifts that can affect vision and cardiovascular function (Iwase et al., 2020).

(ii) *Radiation*: Space radiation, including galactic cosmic rays and solar particle events, increases the risk of cancer, central nervous system effects and other health issues (Cucinotta et al., 2014).

(iii) *Isolation and Confinement*: The psychological effects of isolation and confinement can lead to stress, anxiety and depression (Pagel & Choukèr, 2016).

(iv) *Distance from Earth*: The vast distance from Earth complicates medical interventions and emergency responses (Clément, 2011).

(v) *Hostile/Closed Environments*: The closed environment of spacecraft can lead to issues with air quality, microbial contamination and limited resources (Mogul & Moeller, 2022).

Nanorobotics involves the use of nanoscale robots (nanobots) that can perform tasks at the molecular level (Eissa, 2025). These nanobots can be designed for various applications, including drug delivery, diagnostics and repair of biological tissues (Li et al., 2017b). In the context of space travel, nanorobots offer several advantages:

(i) *Targeted Drug Delivery*: Nanobots can deliver adaptogens and other medications directly to specific tissues or cells, enhancing their efficacy and reducing side effects (Wahi et al., 2024).

(ii) *Real-Time Monitoring*: Nanobots equipped with sensors can monitor astronauts' health in real-time, detecting early signs of health issues and providing immediate feedback (Roda et al., 2018).

(iii) *Repair and Maintenance*: Nanobots can repair damaged tissues, close micro-holes in spacecraft and perform maintenance tasks, reducing the need for risky extravehicular activities (EVAs) (Chui & Kissner, 2000).

The integration of adaptogens and nanorobotics in space travel can create a synergistic effect, enhancing the overall health and performance of astronauts (Kalia, 2022). There are several approaches through which this integration can be achieved:

(i) *Enhanced Bioavailability of Adaptogens:* Nanotechnology can improve the bioavailability of adaptogens, ensuring that they are effectively absorbed and utilized by body (Babii et al., 2017). For example, encapsulating adaptogens in nanoparticles can protect them from degradation and enhance their absorption in the gastrointestinal tract (Bandiwadekar et al., 2022).

(ii) *Targeted Delivery of Adaptogens:* Nanobots can deliver adaptogens directly to specific tissues or cells, enhancing their therapeutic effects (Anto et al., 2025). For instance, nanobots can target the brain to deliver adaptogens that improve cognitive function and reduce stress (Kakkar et al., 2016).

(iii) *Sustained Release of Adaptogens:* Nanotechnology can enable the sustained release of adaptogens, providing a steady and prolonged therapeutic effect (Li et al., 2021; NASA, 2020; NASA Spinoff, 2024). This is particularly beneficial for adaptogens that require consistent levels in the bloodstream to be effective (Shimer, 2004; Smart Adaptogen, 2024).

(iv) *Real-Time Health Monitoring:* Nanobots equipped with sensors can monitor astronauts' health in real-time, detecting early signs of stress, fatigue or other health issues (NASA, 2020; NASA Spinoff, 2024). This information can be used to adjust adaptogen therapy as needed, ensuring optimal health and performance (Shimer, 2004; Smart Adaptogen, 2024).

(v) *Repair and Maintenance:* Nanobots can repair damaged tissues and perform maintenance tasks, reducing the need for risky EVAs. This can help maintain the health and safety of astronauts during long-duration missions (Palencia, 2020; Hutson, 2023; White, 2024; Space Voyage Ventures Team, 2024).

Finally, industrialization of these technologies requires stringent and consistent quality that could be achieved using Statistical Process Control (SPC) techniques. SPC methodologies have been used extensively in various fields, including industrial and non-industrial sectors (Eissa, et al, 2022; Eissa, 2023a, 2023b). They provide indispensable means to monitor, adjust, control and improve various inspection characteristics to yield products of high safety, quality and efficacy with reproducible and predictable properties.

CONCLUSION

Adaptogens are promising natural substances that enhance health and performance by modulating neurotransmitter systems, hormonal balance, and immune function. Traditional medicine values them, and modern research supports their benefits. However, consulting healthcare professionals and conducting rigorous clinical trials are essential to establish their efficacy and safety. Standardizing extracts and identifying optimal dosages are critical challenges. Objective biomarkers in trials can validate adaptogens' effects. Future research should explore their synergistic effects with other treatments. Adaptogens fit well into personalized medicine and can be enhanced with nanotechnology for better delivery and efficacy, benefiting both terrestrial and space medicine. Embracing SPC tools for industrialization will be crucial to achieve large and widespread use of this unique technologies in a safe, predictable and consistent inspection properties through appropriate quality tests.

Compliance with Ethical Standards

Conflict of Interest

The author declares that there is no conflict of interest.

Ethical Approval

For this type of study, formal consent is not required.

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Data Availability

Data availability is not applicable to this article as no new data were created or analyzed in this study.

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AI-assisted technology was not used in the preparation of this work, except for grammar and spelling checks as an assistant writing tool & organizer.

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