

REVIEW ARTICLE/ DERLEME

POTENTIAL EFFECTS OF ADAPTOGENIC PLANTS ON HEALTHY AGING
*ADAPTOJEN BİTKİLERİN SAĞLIKLI YAŞLANMA ÜZERİNE OLASI ETKİLERİ*Gülhanım HIZARCI¹, Sine YILMAZ^{2,*}

Geliş tarihi/Received: 20.04.2026 • Kabul tarihi/Accepted: 23.05.2026

ABSTRACT

The global increase in life expectancy and the growing aging population have brought the concept of healthy aging to the forefront of contemporary scientific research. Current approaches focus not only on extending lifespan but also on increasing the number of years lived free from disease and disability. Aging is shaped by interconnected biological processes, including oxidative stress, chronic low-grade inflammation, mitochondrial dysfunction, and dysregulation of stress-response pathways. This review aims to evaluate the potential role of adaptogenic plants as natural agents that may support healthy aging. In particular, *Rhodiola rosea*, *Panax ginseng*, and *Withania somnifera* are discussed with regard to their possible effects on stress response, the hypothalamic–pituitary–adrenal axis, immune function, mitochondrial activity, and neuroprotective mechanisms. Current evidence suggests that these plants may help modulate oxidative stress and inflammatory responses, support energy metabolism, and contribute to cognitive and physical performance. However, much of the available evidence is derived from preclinical studies or human studies with limited sample sizes and heterogeneous designs. Therefore, further well-designed, large-scale clinical studies are needed to clarify the potential contribution of adaptogenic plants to healthy aging strategies.

Keywords: Healthy aging, Adaptogenic plants, *Rhodiola rosea*, *Panax ginseng*, *Withania somnifera*

ÖZET

Küresel ölçekte yaşam süresinin uzaması ve yaşlı nüfusun artması, sağlıklı yaşlanma kavramını güncel bilimsel araştırmaların odak noktalarından biri haline getirmiştir. Günümüzde temel amaç yalnızca yaşam süresini uzatmak değil, aynı zamanda hastalık ve işlev kaybı olmadan geçirilen yılların artırılmasını sağlamaktır. Yaşlanma süreci; oksidatif stres, kronik düşük dereceli inflamasyon, mitokondriyal disfonksiyon ve stres yanıtı yollarındaki düzensizlikler gibi birbiriyle ilişkili biyolojik mekanizmalar tarafından şekillenmektedir. Bu derlemenin amacı, adaptojen bitkilerin sağlıklı yaşlanmayı destekleyebilecek doğal ajanlar olarak potansiyel rollerini güncel literatür doğrultusunda değerlendirmektir. Bu kapsamda özellikle *Rhodiola rosea*, *Panax ginseng*

*Correspondence/İletişim: Sine YILMAZ, Doç. Dr., Ankara Medipol Üniversitesi, Sağlık Bilimleri Fakültesi, Beslenme ve Diyetetik Bölümü, Ankara, Türkiye, e-posta: sine.yilmaz@ankaramedipol.edu.tr • ORCID: <https://orcid.org/0000-0002-2592-9057>

1. Gülhanım HIZARCI, Ankara Medipol Üniversitesi, Sağlık Bilimleri Fakültesi, Beslenme ve Diyetetik Bölümü, Ankara, Türkiye

2. Sine YILMAZ, Doç. Dr., Ankara Medipol Üniversitesi, Sağlık Bilimleri Fakültesi, Beslenme ve Diyetetik Bölümü, Ankara, Türkiye

• ORCID: <https://orcid.org/0000-0002-2592-9057>

ve *Withania somnifera*; stres yanıtı, hipotalamus-hipofiz-adrenal aks, bağışıklık fonksiyonları, mitokondriyal aktivite ve nöroprotektif mekanizmalar açısından ele alınmıştır. Güncel bulgular, bu bitkilerin oksidatif stres ve inflamatuvar yanıtların düzenlenmesine katkı sağlayabileceğini, enerji metabolizmasını destekleyebileceğini ve bilişsel ile fiziksel performans üzerinde olumlu etkiler gösterebileceğini düşündürmektedir. Bununla birlikte, mevcut kanıtların önemli bir bölümü prelinik çalışmalara ya da sınırlı örneklem büyüklüğüne ve heterojen tasarıma sahip insan çalışmalarına dayanmaktadır. Bu nedenle, adaptojen bitkilerin sağlıklı yaşlanma stratejilerindeki olası katkısını daha net ortaya koyabilmek için iyi tasarlanmış, geniş örneklemli klinik çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Sağlıklı yaşlanma, Adaptojen bitkiler, *Rhodiola rosea*, *Panax ginseng*, *Withania somnifera*

INTRODUCTION

The global increase in longevity and the growing proportion of older adults have positioned healthy aging as a central issue in contemporary scientific and public health discourse (1). However, longer lifespan does not necessarily correspond to healthier years. Many individuals experience chronic diseases, functional limitations, and increased dependency in later life, placing substantial pressure on healthcare systems, long-term care services, and social security structures (2). This discrepancy highlights the need for strategies that promote not only survival but also functional independence and quality of life (3,4).

Aging is an inevitable yet highly heterogeneous physiological process. It involves progressive biological decline, increased susceptibility to disease, and a greater risk of mortality (5). The rate and clinical manifestations of aging vary substantially among individuals and are shaped by genetic predisposition, lifestyle behaviors, environmental exposures, and access to healthcare services (5). At the population level, this issue has become increasingly relevant. Projections indicate that the number of people aged 60 years and older will exceed 2.1 billion by 2050 and account for more than 21% of the global population, underscoring the importance of preventive and supportive approaches (7).



The World Health Organization defines healthy aging as the process of developing and maintaining the functional ability that enables well-being in older age (1). Within this framework, understanding the biological mechanisms underlying aging is essential. Oxidative stress, chronic low-grade inflammation, mitochondrial dysfunction, and impaired neuroendocrine regulation represent major biological determinants of this process (8). In particular, the persistent age-related inflammatory state known as “inflammaging” contributes to several chronic conditions, including type 2 diabetes, cardiovascular diseases, neurodegenerative disorders, sarcopenia, and certain cancers (8,9). These interconnected mechanisms have intensified interest in interventions that can modulate multiple biological pathways simultaneously.

Adaptogenic plants have emerged as promising bioactive agents due to their capacity to enhance physiological resilience against physical, chemical, and biological stressors (10). By modulating stress response, immune function, oxidative damage, inflammation, mitochondrial activity, and cognitive performance, these plants may influence key pathways involved in healthy aging. Among them, *Rhodiola rosea*, *Panax ginseng*, and *Withania somnifera* are particularly notable because of their bioactive constituents and multifaceted mechanisms of action. Therefore, this review examines the potential role of these adaptogenic plants in supporting healthy aging, with particular emphasis on stress regulation, inflammatory control, mitochondrial function, and neuroprotective mechanisms (10).

METHODS

A narrative literature search was conducted between November 2025 and January 2026 using PubMed, Web of Science, Scopus, ScienceDirect, and Google Scholar. The search primarily included studies published between 2014 and 2025, while earlier foundational studies were also incorporated where scientifically relevant. Search terms included “adaptogens”, “adaptogenic plants”, “healthy aging”, “aging”, “oxidative stress”, “inflammation”, “inflammaging”, “mitochondrial dysfunction”, “autophagy”, “HPA axis”, “stress response”, “neuroprotection”, “*Rhodiola rosea*”, “*Panax ginseng*”, and “*Withania somnifera*”. Clinical, experimental, and review studies related to healthy aging and the selected biological mechanisms were included.



MAJOR ADAPTOGENIC PLANTS ASSOCIATED WITH HEALTHY AGING

Rhodiola rosea

Rhodiola rosea is among the adaptogenic plants that have been used for centuries in traditional medicine practices across Russia, China, and the Scandinavian countries. Its contemporary evaluation by the European Medicines Agency within a clinical context has further increased scientific interest in this plant (10). Its ability to survive under harsh environmental conditions has been linked to the concept of biological adaptation, contributing to its classification as an adaptogen (10,14,15). To date, approximately 140 distinct chemical constituents have been identified in *Rhodiola rosea*, with particular emphasis placed on phenylethanoids and phenylpropanoids in relation to its adaptogenic effects (16).

The principal bioactive compounds of *Rhodiola rosea* include salidroside, rosavin, rosin, and rosarin. Salidroside is one of the key phenylethanoid glycosides, notable for its antioxidant, anti-inflammatory, and neuroprotective properties. Experimental studies have demonstrated that salidroside may reduce oxidative damage, modulate neurotransmitter levels, and support mitochondrial function (16). Compounds within the rosavin group function as characteristic chemical markers of *Rhodiola rosea* and have been associated with enhanced stress tolerance and mood stabilization (11,16,17). In addition, various phytochemical constituents—including flavonoids, organic acids, tannins, terpenes, and essential oils—are also thought to contribute to the plant's overall biological activity (16,18,19).

Current evidence suggests that *Rhodiola rosea* extract may contribute to the reduction of oxidative stress. Oligomeric proanthocyanidins present in the extract exhibit free radical scavenging activity, enhance the activity of antioxidant enzymes such as glutathione peroxidase and superoxide dismutase, and reduce malondialdehyde levels (20). Furthermore, supplementation with *Rhodiola rosea* has been associated with decreased lactate levels, attenuation of exercise-induced fatigue, and improved adaptation to physical activity (10,21). Additionally, *Rhodiola rosea* may exert regulatory effects on the gut microbiota and neurotransmitter pathways (10,22). Mechanistically, it may



support intestinal barrier integrity by upregulating tight junction proteins such as ZO-1 and occludin, while also modulating gut microbial composition and increasing beneficial short-chain fatty acids. These gut-related effects may contribute to neurotransmitter regulation through microbiota-derived metabolites, alongside increased activity and expression of monoamine neurotransmitters and opioid peptides (10). Experimental data also indicate that *Rhodiola rosea* glycosides may preserve mitochondrial function and reduce intracellular reactive oxygen species formation (24).

The potential effects of *Rhodiola rosea* in the context of healthy aging are primarily explained through its roles in mitochondrial biogenesis, oxidative stress regulation, and modulation of the stress response.

Jiang et al. (2021) provided mechanistic evidence that *Rhodiola rosea* extract enhanced longevity and stress resistance in *Caenorhabditis elegans* by activating the SKN-1/Nrf2-related signaling pathway. The extract reduced oxidative damage markers and increased antioxidant enzyme activities, indicating improved cellular defense against oxidative stress. As SKN-1 is the functional homolog of mammalian Nrf2, these findings suggest that *Rhodiola rosea* may contribute to cellular protection and repair-related responses by strengthening endogenous antioxidant defense mechanisms linked to lifespan extension.

Zhao et al. (2019) demonstrated that salidroside, one of the principal bioactive constituents of *Rhodiola rosea*, may exert cytoprotective effects partly through activation of the AMPK/SIRT1 signaling pathway. In ox-LDL-treated human umbilical vein endothelial cells, salidroside increased phosphorylated AMPK levels, whereas AMPK silencing attenuated its protective effects and further reduced SIRT1 expression. These findings suggest that SIRT1 may be regulated, at least in part, downstream of AMPK activation. Taken together, the AMPK/SIRT1 axis may represent a key molecular mechanism through which salidroside contributes to the antioxidant, mitochondrial protective, and potentially anti-aging effects attributed to *Rhodiola rosea*.

The plant's effects on the hypothalamic–pituitary–adrenal axis are also noteworthy. In particular, it may help maintain homeostatic balance under stress by limiting excessive cortisol secretion (14). In addition, the regulatory effects of salidroside and rosavin on



serotonin, dopamine, and norepinephrine levels support the biological basis for their potential positive effects on mood, attention, and mental fatigue (14,27).

Panax ginseng

Panax ginseng is one of the adaptogens that has been used for many years in traditional Chinese medicine and is currently regarded as one of the most widely recognized herbal products worldwide (28). Its traditional use has largely been shaped within the framework of supportive therapies, and it can be utilized in different processed forms such as white, red, and black ginseng (29,30). Processing methods influence the plant's chemical composition and, consequently, its biological activity (30).

Ginsenosides constitute the major saponin compounds in *Panax ginseng*, with root-derived Rb1, Rg1, Re, Rf, and Ra2 representing the principal bioactive constituents (31).

The biological effects of *Panax ginseng* have been extensively investigated, particularly in relation to stress response, cognitive functions, and neuroendocrine regulation. Ginsenosides Rb1 and Rg1 are thought to be among the primary compounds responsible for these effects. Lee and Rhee (2017) showed that, in a rat model of post-traumatic stress disorder, ginsenoside Rb1 attenuated anxiety-like behaviors, suggesting that ginseng-derived bioactive compounds may contribute to stress adaptation by modulating hypothalamic–pituitary–adrenal axis-related responses (32).

Similarly, interventions containing Rg1 have been shown to suppress the stress response and exert beneficial effects on anxiety-like behaviors (32). These findings suggest that *Panax ginseng* may enhance the organism's capacity for stress adaptation.

Evidence from human studies also indicates that *Panax ginseng* may exert beneficial effects on certain stress-related outcomes. In a 12-week randomized, double-blind, placebo-controlled study conducted in individuals with high stress levels, the effects of *Panax ginseng* extract on both subjective and physiological stress indicators were evaluated (32). At the end of the intervention, a significant reduction in perceived stress was observed in the *Panax ginseng* HRG80 group compared with the placebo group. While improvements were noted in self-reported stress measures, changes in cognitive



performance-related stress outcomes, including the d2 attention-test error rate and computerized memory-test accuracy, were more pronounced (32). These findings suggest that *Panax ginseng* may serve as a potential adaptogen contributing to stress management.

In addition, the effects of HRG80—a form of red ginseng obtained through advanced processing techniques—on cognitive performance have also been investigated. Short-term use has been associated with reduced error rates in attention tests and improvements in mental performance (32). Therefore, *Panax ginseng* emerges as a notable adaptogen not only through its role in regulating the stress response but also through its potential to support mental resilience and cognitive function (32).

Withania somnifera

Withania somnifera, commonly known as Ashwagandha, is one of the key adaptogenic plants that has been used in Ayurvedic practices for over 3000 years (33). The root is the most frequently utilized part of the plant, and root extracts are predominantly preferred in modern phytotherapeutic approaches as well (33). The principal bioactive constituents of *Withania somnifera* include withanolides such as withaferin A, withanone, and withanolide A, which modulate various biological pathways involved in the aging process (36). In addition, the plant has been suggested to possess neuroprotective, cardioprotective, hypoglycemic, antimicrobial, and anticancer properties (34,35).

The effects of *Withania somnifera* associated with healthy aging are primarily discussed in relation to the maintenance of cellular proteostasis, telomere biology, and mitochondrial functions. Certain bioactive compounds, particularly withanone, may activate heat shock proteins, thereby supporting the refolding of damaged proteins and reducing protein aggregation (36). Furthermore, findings such as the suppression of telomere shortening and increased telomerase activity strengthen the mechanistic basis for the plant's potential geroprotective effects (36).

From a mitochondrial perspective, *Withania somnifera* is thought to activate the Nrf2 pathway, thereby protecting mitochondria against oxidative damage and contributing to the maintenance of energy production by limiting cellular damage induced by reactive



oxygen species (36). Evidence from human studies also supports these preclinical observations. In individuals performing resistance exercise, daily supplementation with 600 mg of Ashwagandha has been associated with increases in muscle strength, muscle cross-sectional area, and lean body mass, as well as reductions in exercise-induced muscle damage (36). Additionally, evidence suggests improvements in skin hydration and elasticity, regulation of hormonal balance, and reductions in menopausal symptoms (36).

Its effects on cognitive function have further increased interest in *Withania somnifera*. Evidence from individuals with mild cognitive impairment and healthy adults indicates that Ashwagandha supplementation may improve cognitive domains such as memory, attention, and reaction time (13). Administration of 300 mg twice daily has been associated with significant improvements in various cognitive parameters—particularly working memory and verbal memory—compared to placebo (13). These effects are thought to arise through mechanisms including inhibition of acetylcholinesterase leading to enhanced cholinergic transmission, support of synaptic plasticity, and limitation of neuronal damage via antioxidant and anti-inflammatory pathways (13).

The potential role of *Withania somnifera* in neurodegenerative diseases is also noteworthy. In Alzheimer's disease models, root extract may reduce amyloid-beta accumulation, alleviate behavioral impairments, and enhance amyloid-beta clearance from the brain (13). In Parkinson's disease models, it has been shown to reduce dopaminergic neuron loss, improve motor function, and attenuate neuroinflammation by suppressing microglial activation (13). Regarding its effects on the immune system, it has been suggested that the plant may reduce C-reactive protein levels, suppress pro-inflammatory markers such as IL-6 and TNF- α , and support natural killer cell activity as well as T-cell responses (13).

Its effects on the stress response represent one of the most prominent features of *Withania somnifera*. In an eight-week randomized, double-blind, placebo-controlled clinical trial, supplementation in the range of 125–500 mg/day was associated with reductions in stress, anxiety, and depression scores, as well as improvements in biochemical stress markers such as cortisol, ACTH, and salivary amylase (37). These findings indicate that *Withania somnifera* may be characterized as a promising adaptogen, particularly due to its potential



roles in stress regulation, cognitive support, and modulation of biological processes associated with healthy aging.

MAIN BIOLOGICAL MECHANISMS AFFECTING HEALTHY AGING

The concept of healthy aging involves not only the extension of lifespan but also the preservation of cellular and systemic function. Therefore, understanding the biological mechanisms that shape aging is essential for evaluating the potential effects of adaptogenic plants. Increased production of reactive oxygen species, bioenergetic insufficiency, telomere shortening, loss of proteostasis, impaired autophagy, epigenetic alterations, cellular senescence, and chronic inflammation are among the major biological determinants of aging (23,38).

Chronic inflammation plays a central role among these mechanisms. The persistent, low-grade inflammatory state that develops with aging reflects changes in immune regulation and contributes to many age-related pathological processes. Together with oxidative stress, chronic inflammation promotes DNA damage and genomic instability. These alterations are associated not only with cancer development but also with tissue dysfunction and accelerated biological aging (38). In this context, inflammation acts as both a driver and an outcome of the aging process.

The interaction between inflammation and cellular repair mechanisms is particularly important for autophagy. Autophagy maintains cellular homeostasis by removing damaged intracellular components. However, its efficiency declines with age. Inflammation-related disruption of autophagy contributes to the pathogenesis of neurodegenerative diseases, including Parkinson's disease, Alzheimer's disease, and Huntington's disease (38). Tumor necrosis factor- α (TNF- α) suppresses microglial autophagy through the mTOR signaling pathway, whereas autophagy activation may support a shift toward the anti-inflammatory M2 phenotype (38). In addition, persistent microglial activation promotes the accumulation of α -synuclein and Tau proteins, linking aging-related inflammation to neurodegeneration (38,39).



The hypothalamic–pituitary–adrenal (HPA) axis is another key regulatory system involved in aging. This axis regulates the stress response and cortisol secretion (40). However, chronic or prolonged stress can disrupt the physiological balance of this axis, leading to sustained elevations in cortisol levels. Elevated cortisol may adversely affect the gut microbiota, intestinal barrier integrity, and the microbiota–gut–brain axis by altering microbial composition and increasing intestinal permeability. This may weaken epithelial barrier function and facilitate inflammatory signaling, while reduced SCFA-mediated support may further impair barrier integrity and neuroendocrine regulation. (41). During aging, increased cortisol levels, weakened negative feedback mechanisms, and circadian rhythm disruption make stress adaptation more fragile in older adults (42).

Overall, oxidative stress, chronic inflammation, impaired autophagy, mitochondrial dysfunction, and neuroendocrine dysregulation interact closely in the aging process. These interconnected mechanisms provide a biological basis for evaluating adaptogenic plants as potential supportive agents in healthy aging.

SAFETY PROFILE OF ADAPTOGENS AND THEIR USE IN DAILY LIFE

Adaptogenic plants may carry the potential for pharmacological interactions with certain medications due to their rich content of bioactive compounds. Therefore, particular caution is required when adaptogens are used concomitantly, especially in individuals taking prescription medications (46). Drug interactions may, in some cases, lead to an exacerbation of adverse effects or alterations in therapeutic response. Clinical monitoring is particularly recommended for individuals with psychiatric disorders who are using multiple psychotropic medications, due to the potential interactions of adaptogens with antidepressants and other centrally acting agents (12).

Available evidence suggests that most adverse effects associated with long-term use of adaptogens are generally mild and transient in nature (45). The most frequently documented side effects include headache, dry mouth, sleep disturbances, gastrointestinal complaints, and restlessness (12).



However, given their potential effects on the endocrine and immune systems, more careful evaluation is warranted in special conditions such as pregnancy, lactation, hormone-sensitive disorders, and autoimmune diseases (12). In such populations, potential risks and benefits should be assessed on an individual basis prior to use.

In daily practice, adaptogens are available in various forms, including capsules, powders, teas, and liquid extracts (44). However, the appropriate dosage may vary depending on the specific plant species, the level of standardization of the preparation, individual tolerance, and the person's overall health status (12). Although the literature commonly cites dosage ranges of 100–450 mg per day, this range should not be generalized as a universal recommendation for all adaptogens (12).

Additionally, some sources indicate that usage is often structured in cycles of 4–8 weeks, and intermittent use may help prevent the development of tolerance (45). Nonetheless, the safe and effective use of adaptogens should be planned under the guidance of a healthcare professional, taking into account variables such as product standardization, duration of use, comorbid conditions, and concurrent medication use (12,43,44).

This precaution is particularly relevant because plant-derived bioactive compounds may induce or inhibit hepatic cytochrome P450 enzymes, including CYP3A4 and CYP2D6, thereby altering drug metabolism and increasing the risk of pharmacokinetic herb–drug interactions (48). In addition, *Withania somnifera* may affect thyroid hormone regulation; in a randomized placebo-controlled pilot study, 600 mg/day ashwagandha root extract for 8 weeks significantly improved serum TSH, T3, and T4 levels in patients with subclinical hypothyroidism, suggesting the need for caution in individuals with thyroid disorders or those using thyroid-related medications (49).

CONTRIBUTIONS OF ADAPTOGENIC PLANTS TO HEALTHY AGING

Healthy aging refers not only to the extension of lifespan but also to the preservation of physical, cognitive, and psychosocial functions in later life to the greatest extent possible. Contemporary perspectives acknowledge that aging is an inevitable process; however, its rate and clinical outcomes can be modulated to a certain extent through lifestyle factors,



environmental influences, and biological adaptation mechanisms. Within this context, adaptogenic plants represent notable complementary agents that may support healthy aging by enhancing the organism's capacity to adapt to stressors. In particular, a substantial proportion of current clinical studies has focused on the effects of adaptogens on stress-related outcomes (13).



Table 1. Recent Randomized Controlled Trials Investigating the Effects of Adaptogenic Plants on Stress (13)

Researchers	Study Design	Participants	Age	Location	Adaptogen	Groups	Duration	Outcome
Baek et al., 2019	Double-blind RCT	Nurses & firefighters with high occupational stress	20–60	South Korea	<i>Panax ginseng</i>	2 g (28) vs placebo (27)	42 days	No difference in stress levels.
Sung et al., 2020	Double-blind RCT	Adults with chronic fatigue	19–65	South Korea	<i>Panax ginseng</i>	3 g (24) vs placebo (23)	42 days	Improved perceived fatigue.
Jówko et al., 2018	Double-blind RCT	Students during exams	Mean 20–21	Poland	<i>Rhodiola rosea</i>	600 mg (13) vs placebo (13)	28 days	No change in cortisol.
Gopukumar et al., 2021	Double-blind RCT	Healthy adults with moderate stress	20–55	India	<i>Withania somnifera</i>	300 mg (62) vs placebo (63)	90 days	Reduced stress levels.
Remenapp et al., 2022	Double-blind RCT	Healthy adults (PSS ≥14)	18–54	USA	<i>Withania somnifera</i>	225 mg (19) & 400 mg (19) vs placebo (19)	30 days	Reduced cortisol.



Disruption of cellular homeostasis, increased oxidative stress, chronic low-grade inflammation, mitochondrial dysfunction, and impaired neuroendocrine balance are among the principal biological determinants of the aging process. The significance of adaptogenic plants arises from their potential to simultaneously influence multiple of these mechanisms rather than targeting only a single pathway. In particular, it is suggested that the stress response may be rendered more balanced through regulation of the hypothalamic–pituitary–adrenal (HPA) axis, inhibition of NF- κ B, activation of Nrf2, and support of neurotrophic mechanisms (3). Maintaining cortisol levels within physiological limits has been proposed to contribute to the attenuation of aging-related outcomes such as muscle loss, insulin resistance, cognitive decline, and immune dysfunction (3).

The preservation of mitochondrial function also constitutes a fundamental component of healthy aging. Bioactive compounds present in adaptogens, including salidroside, ginsenosides, and withanolides, may contribute to mitochondrial biogenesis, antioxidant defense, and improved cellular energy efficiency (3,16,25,26,36). These effects are of particular importance in slowing age-related fatigue, loss of muscle strength, and metabolic deterioration. In addition, certain adaptogens may modulate immune responses by supporting natural killer cell activity and T-lymphocyte function while reducing proinflammatory cytokine production (3,13).

Table 2. Key Effects of Adaptogenic Plants on Health (3)

Category	Description
Sleep	Contributes to improved sleep and reduction of fatigue.
Stress	Supports stress management and helps reduce anxiety.
Longevity	Supports longevity by exerting anti-aging effects.
Performance	Enhances physical performance and supports recovery.
Cognitive	Contributes to the improvement of cognitive functions and memory.

However, the majority of the available evidence is based on short-term interventions, small sample sizes, and heterogeneous study designs. In addition, variations in the



standardization of the preparations used make it difficult to directly compare the obtained results. Therefore, although the potential effects of adaptogenic plants on healthy aging appear promising, there is a need for long-term, well-designed studies conducted with standardized preparations in order to more clearly demonstrate these effects at the clinical level (3,13).

LIMITATIONS OF THE STUDIES

A substantial portion of the existing literature on adaptogenic plants is limited by heterogeneous study designs, small sample sizes (often fewer than 100 participants), short intervention and follow-up periods (mostly restricted to approximately 4–12 weeks), and preparations with varying levels of standardization. These methodological limitations restrict the generalizability of findings and prevent firm conclusions regarding optimal dose, duration, product standardization, and long-term efficacy. (3,13). This represents one of the main factors limiting the comparability and generalizability of the findings. In particular, differences in the bioactive compound content of extracts used for *Rhodiola rosea*, *Panax ginseng*, and *Withania somnifera* across studies make it difficult to clearly determine which specific component or biological mechanism is responsible for the observed effects. Furthermore, the fact that a substantial proportion of current clinical data focuses on indirect outcomes such as stress, fatigue, cognitive function, and physical performance limits the direct evaluation of the true clinical effects of adaptogens on healthy aging.

In addition, although strong mechanistic findings obtained from preclinical studies are valuable, direct extrapolation of these results to human physiology is not always feasible. Therefore, future research should prioritize well-designed, long-term randomized controlled trials involving larger sample sizes and the use of standardized preparations (3,13,45).

CONCLUSION

Current evidence regarding the potential effects of adaptogenic plants on healthy aging suggests that these agents may exert beneficial effects through multidimensional mechanisms, including regulation of the stress response, reduction of oxidative damage,



suppression of inflammatory processes, support of mitochondrial function, and preservation of cognitive and immune functions. In particular, findings related to *Rhodiola rosea*, *Panax ginseng*, and *Withania somnifera* indicate that these plants may play a complementary role in strategies aimed at promoting healthy aging.

However, existing clinical evidence is largely based on short-term interventions and indirect clinical outcomes; therefore, these effects should be interpreted primarily in terms of biological and functional parameters associated with healthy aging rather than direct impacts on lifespan. Although their safety profiles appear generally favorable, careful evaluation is required—especially in older populations—due to factors such as polypharmacy, the burden of chronic diseases, and the potential for pharmacological interactions (12,45,46).

In conclusion, while adaptogenic plants appear promising in supporting healthy aging, further research involving standardized preparations, larger sample sizes, longer durations, and high methodological quality is necessary to more clearly establish their true clinical value. In the future, personalized approaches that take into account individual variability and the heterogeneous nature of aging may contribute to a more precise definition of the role of adaptogens in healthy aging strategies.

Abbreviations

ACTH: Adrenocorticotrophic hormone

AMPK: AMP-activated protein kinase

CYP2D6: Cytochrome P450 2D6 enzyme

CYP3A4: Cytochrome P450 3A4 enzyme

CYP450: Cytochrome P450

HPA axis: Hypothalamic–Pituitary–Adrenal axis

HRG80: A processed red ginseng preparation of *Panax ginseng*

IL-6: Interleukin-6

M2 phenotype: Anti-inflammatory M2 macrophage/microglial phenotype

mTOR: Mammalian target of rapamycin

NF- κ B: Nuclear factor kappa B

Nrf2: Nuclear factor erythroid 2–related factor 2



ox-LDL: Oxidized low-density lipoprotein

PSS: Perceived Stress Scale

SCFA: Short-chain fatty acids

SIRT1: Sirtuin 1

SKN-1: Skinhead-1 / *C. elegans* Nrf2 homolog

TNF- α : Tumor necrosis factor alpha

TSH: Thyroid-stimulating hormone

ZO-1: Zonula occludens-1

Çıkar çatışması: Yazarlar, bu araştırma ile ilgili herhangi bir çıkar çatışması bulunmadığını beyan eder.

Finansal Destek: Yazarlar herhangi bir finansal destek almadıklarını beyan ederler.

Yazar katkısı / Author contributions: Araştırmanın tüm aşamalarında (tasarım, yazım ve revizyon) tüm yazarlar eşit derecede katkı sağlamıştır. / All authors contributed equally to all stages of the research (design, data collection, analysis, writing, and revision).

KAYNAKLAR

1. Beard JR, Officer A, de Carvalho IA, Sadana R, Pot AM, Michel JP, et al. Concepts and definitions of healthy ageing: A systematic review and synthesis of theoretical models. *EClinicalMedicine*. 2022;52:101611.
2. Cesari M, Araujo de Carvalho I, Thiyagarajan JA, Cooper C, Martin FC, Reginster JY, et al. How to promote healthy aging across the life cycle. *Eur J Intern Med*. 2025;122:17.
3. Sharma R, Panossian A. Unlocking nature's potential: The power of adaptogens in enhancing modern health and wellness. *J Ayurveda Integr Med*. 2025;16(2):100872.
4. Nutt D, Carhart-Harris R, Erritzoe D, Allen M, McQueen G. Psychedelic drugs—A new era in psychiatry? *Dialogues Clin Neurosci*. 2019;21(2):139–147.
5. Cesari M, Canevelli M. Aging, longevity, and healthy aging: The public health approach. *Aging Clin Exp Res*. 2025.
6. Gu D, Dupre ME, eds. *Encyclopedia of gerontology and population aging*. Springer; 2021.



7. United Nations. World social report 2023: Leaving no one behind in an ageing world. United Nations Publications; 2023.
8. Franceschi C, Garagnani P, Parini P, Giuliani C, Santoro A. Inflammaging, hormesis and the rationale for anti-aging strategies. *Ageing Res Rev.* 2020;64:101142.
9. Fulop T, Larbi A, Dupuis G, Le Page A, Frost EH, Cohen AA, *et al.* Immunosenescence and inflammaging in the aging process: Friends or foes? *Ageing Res Rev.* 2021;68:101268.
10. Panossian A, Hamm R, Wikman G, Efferth T. *Rhodiola rosea*: A review in the context of predictive, preventive and personalized medicine (PPPM). *EPMA J.* 2024.
11. Panossian A, Wikman G, Sarris J. Effects of adaptogens on the central nervous system and the molecular mechanisms associated with their stress-protective activity. *Curr Clin Pharmacol.* 2014;9(3):200–216.
12. Namusisi NNH. Narrative review of plant-based adaptogens in stress management. *Eurasian Exp J Med Med Sci.* 2025;7(1):177–185.
13. Zhang Y, Hu J, Yang Z, Wang J. The effect of adaptogenic plants on stress: A systematic review and meta-analysis. *J Herb Med.* 2023;38:100695.
14. Amsterdam JD, Panossian AG. *Rhodiola rosea* as a medicinal adaptogen: A review of clinical studies. *Phytomedicine.* 2016;23(7):770–783.
15. Brinckmann JA, Cunningham AB, Harter DEV. Running out of time to smell the roseroots: Reviewing threats and trade in wild *Rhodiola rosea* L. *J Ethnopharmacol.* 2021;269:113686.
16. Ćmil M, Karchut W, Furtak G, Daniszewski W, Knobelsdorf W, Pogoda M, *et al.* *Rhodiola rosea* as a natural adaptogen: A review of its effects on stress reduction, mood enhancement, and cognitive function. *Int J Innov Technol Soc Sci.* 2025;3(47).
17. Lee J, Choi J, Kim H. Adaptogens on depression-related outcomes: A systematic integrative review and rationale of synergism with physical activity. *Nutrients.* 2022;14(17):3521.
18. Jówko E, Długołęcka B, Makaruk B, Cieśliński I. Effects of the combined supplementation of caffeine and *Rhodiola rosea* with resistance training on lower limb explosive power in male volleyball players. *Nutrients.* 2025;17(4):681.



19. Smeriglio A, Trombetta D, Cornara L, Denaro M. Controlled cultivation confers *Rhodiola rosea* synergistic activity on muscle cell homeostasis, metabolism and antioxidant defense. *Antioxidants (Basel)*. 2024;13(8):1000.
20. Wu T, Zhou Y, Liu S, Li X. Free radical-scavenging activities of oligomeric proanthocyanidin from *Rhodiola rosea* L. and its antioxidant effects in vivo. *J Ethnopharmacol*. 2014;155(1):474–482.
21. Abidov M, Crendal F, Grachev S, Seifulla R, Ziegenfuss T. Effect of *Rhodiola rosea* and *Panax ginseng* on metabolic parameters of rats subjected to swimming. *Phytomedicine*. 2006;13(5):413–418.
22. Zhang X, Zhao Y, Xu J, Xue Z, Zhang M, Pang X, et al. The dietary supplement *Rhodiola crenulata* extract alleviates DSS-induced colitis by mediating gut barrier integrity and reshaping the gut microbiome. *Food Funct*. 2021;12(6):2517–2529.
23. Liguori I, Russo G, Curcio F, Bulli G, Aran L, Della-Morte D, et al. ROS: Basic concepts, sources, cellular signaling, and its implications in aging pathways. *Oxid Med Cell Longev*. 2022;1225578.
24. Li X, Wang Y, Wang Y, Zhang Y, Zhang Z. Salidroside inhibits high-glucose-induced proliferation of vascular smooth muscle cells via inhibition of mitochondrial fission and oxidative stress. *Vasc Pharmacol*. 2020;127:106659.
25. Huangfu ZM, Xu Q, Wang X, Wang EP, Feng Y, Zeng J, et al. Salidroside improves lung injury in mouse models of chronic intermittent hypoxia. *Chin J Tissue Eng Res*. 2019;23(31):5036–5040.
26. Ma Y, Liu J, Pan T. Protective effect and mechanism of salidroside on H9C2 cardiomyocytes under oxidative stress and hyperglycemia. *J Nanjing Univ Tradit Chin Med*. 2019;35(4):442–447.
27. Marchev AS, Dimitrova PA, Koycheva IK, Georgiev MI, Panossian A. Phenolic compounds of *Rhodiola rosea* L. as potential alternative therapy in chronic diseases. *Antioxidants (Basel)*. 2023;12(9):1703.
28. Kim JH. Pharmacological potential of ginseng and its major component ginsenosides. *J Ginseng Res*. 2018;42(3):263–271.
29. Fan S, Zhang Z, Su H, Xu P, Qi H, Zhao D, et al. *Panax ginseng* clinical trials: Current status and future perspectives. *Biomed Pharmacother*. 2020;132:110832.



30. Wang Y, Chen Y, Zeng Q. *Panax ginseng* and its ginsenosides: Potential candidates for prevention and treatment of chemotherapy-induced side effects. *Phytomedicine*. 2021;91:153685.
31. Lu L, Chen Y, Shi J, Wang R, Yang Y, Yang L, *et al.* Biosynthesis of rare ginsenosides through engineered *Escherichia coli*. *J Ginseng Res*. 2019;43(1):116–124.
32. Reay JL, Kennedy DO, Scholey AB. Efficacy of *Panax ginseng* Meyer herbal preparation HRG80 in preventing stress-induced failure of cognitive functions. *Pharmaceuticals (Basel)*. 2020;13(4):57.
33. Kumar R, Gupta A, Dubey N. *Withania somnifera* root extract confers beneficial effects on healthspan and lifespan in *Caenorhabditis elegans*. *Drug Target Insights*. 2023.
34. Zhang L, Li Y, Zhang C, Wang Y. Ashwagandha (*Withania somnifera* (L.) Dunal) root extract containing withanolide A alleviates depression-like behavior in mice by enhancing the BDNF pathway under chronic mild stress. *J Ethnopharmacol*. 2024;327:117522.
35. Uthirapathy S, Tahir TF. *Withania somnifera*: Correlation of phytoconstituents with hypolipidemic and cardioprotective activities. *ARO Sci J Koya Univ*. 2021;9(2):15–21.
36. Singh N, Bhalla M, de Jager P, Gilca M. Enhancing healthspan with Ashwagandha (*Withania somnifera*): A comprehensive review of its multifaceted geroprotective benefits. *Nutrients*, 2024;16(12):1813. <https://doi.org/10.3390/nu16121813>
37. Lopresti AL, Smith SJ, Drummond PD, Mills JG. Effects of *Withania somnifera* extract in chronically stressed adults: A randomized controlled trial. *Nutrients*. 2024;16(9):1293.
38. Ferrucci L, Gonzalez-Freire M, Fabbri E, Simonsick E, Tanaka T, Moore Z, *et al.* Chronic inflammation and the hallmarks of aging. *Trends Endocrinol Metab*. 2023;34(5):389–403.
39. Frasca D, Blomberg BB. Inflammaging: Exploring the role of gut microbiota, environmental factors, and sex differences. *Biomedicines*. 2024;12(8):1716.
40. Sun N, Youle RJ, Finkel T. Mitophagy in aging and disease: MitophAging. *Front Cell Dev Biol*. 2020;8:239.



41. Cryan JF, O’Riordan KJ, Cowan CSM, Sandhu KV, Bastiaanssen TFS, Boehme M, et al. Signalling cognition: The gut microbiota and the hypothalamic–pituitary–adrenal axis. *Front Endocrinol (Lausanne)*. 2023;14:1130689.
42. Aguilera G, Liu Y. Editorial: The HPA axis and aging: Individual features and age-related pathology. *Front Endocrinol (Lausanne)*. 2023;14:1222033.
43. Ajala TO. The effects of adaptogens on the physical and psychological symptoms of chronic stress. *Discovery (Georgia State Univ)*. 2017;4(2).
44. Panossian A, Hamm R, Kadioglu O, Wikman G, Efferth T. Synergy and antagonism of active constituents of ADAPT-232 at the transcriptional level. *Front Neurosci*. 2013;7:16.
45. Panossian A, Seo EJ, Efferth T. Clinical evidence for the adaptogenic effects of *Withania somnifera* and *Rhodiola rosea*. *Ann Agric Environ Med*. 2023.
46. Neuner J, et al. Effects of an adaptogenic extract on brain electrical activity in elderly subjects with mild cognitive impairment. *J Alzheimers Dis*. 2020;73(3):1239–1253.
47. Li Y, et al. Impact of *Rhodiola rosea* on biomarkers of diabetes, inflammation, and gut microbiota. *Nutrients*. 2024.
48. Wanwimolruk S, Prachayasittikul V. Cytochrome P450 enzyme mediated herbal drug interactions (Part 1). *EXCLI Journal*. 2014;13:347–391.
49. Sharma AK, Basu I, Singh S. Efficacy and safety of ashwagandha root extract in subclinical hypothyroid patients: A double-blind, randomized placebo-controlled trial. *J Altern Complement Med*. 2018;24(3):243–248.

