

Ashwagandha Supplementation in Healthy Aging and Musculoskeletal Health: Biological Rationale, Clinical Evidence, and Safety Considerations

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ABSTRACT

Aging is accompanied not only by molecular damage but also by progressive loss of sleep quality, stress tolerance, muscle strength, recovery capacity and mobility. These domains are closely connected: chronic stress and poor sleep can worsen fatigue, pain sensitivity, low-grade inflammation and physical inactivity, thereby contributing to musculoskeletal decline. Ashwagandha (*Withania somnifera*) is a botanical adaptogen increasingly used as a supplement for stress reduction, sleep support, vitality and physical performance. This narrative review summarizes the clinical and mechanistic evidence on ashwagandha supplementation in healthy aging, with particular attention to musculoskeletal health, muscle function, recovery and rehabilitation-relevant outcomes. The strongest human evidence supports modest benefits on perceived stress, anxiety and selected sleep outcomes. Preliminary evidence also suggests possible improvements in strength, recovery, VO₂max and body-composition parameters, especially when supplementation is combined with resistance training or regular physical activity. However, current studies are generally small, short-term and heterogeneous in extract composition, dose and population. There is insufficient evidence to claim that ashwagandha reverses biological aging, prevents sarcopenia or treats osteoarthritis. Safety is generally favorable in short-term studies, but rare cases of liver injury and possible endocrine effects require caution. At present, ashwagandha is best considered as a supportive, not curative, intervention within a broader healthy-aging strategy that includes exercise, nutrition, sleep hygiene and medical supervision when appropriate.

KEYWORDS: Ashwagandha; *Withania somnifera*; healthy aging; anti-aging; musculoskeletal health; sarcopenia; physical performance; sleep; cortisol; inflammaging; rehabilitation.

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INTRODUCTION

The goal of anti-aging medicine has shifted from the unrealistic pursuit of chronological age reversal to the more clinically meaningful aim of preserving function, autonomy and resilience across the lifespan. In daily clinical practice, this is often measured less by laboratory markers than by practical abilities: walking independently, climbing stairs, sleeping well, recovering after stress and maintaining enough muscle reserve to remain active. For this reason, the musculoskeletal system deserves a central place in any discussion of healthy aging. Muscle loss, joint pain, reduced

balance and slower recovery are among the changes that most directly limit quality of life in older adults.

Stress and sleep have a central position in this network. Chronic activation of the hypothalamic-pituitary-adrenal (HPA) axis, sustained sympathetic tone and inadequate sleep quality can amplify inflammatory signaling, impair glucose control, worsen pain perception and reduce participation in physical activity. These mechanisms are not purely psychological; they influence muscle protein turnover, post-exercise recovery, rehabilitation tolerance and the subjective experience of fatigue. Interventions that safely improve sleep and stress resilience may therefore

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have indirect but clinically meaningful effects on musculoskeletal health.

Ashwagandha (*Withania somnifera*), also known as Indian ginseng or winter cherry, is a botanical used in Ayurvedic medicine as a rasayana, a term traditionally referring to rejuvenating or restorative substances. Modern interest is mainly related to its adaptogenic, anxiolytic, sleep-promoting, anti-inflammatory and antioxidant effects. The principal bioactive constituents include withanolides, withanosides, sitoindosides, alkaloids and other steroidal lactones. The concentration of these constituents varies substantially according to plant part, extraction method, dose and commercial standardization (3,4).

Because ashwagandha is marketed widely as an anti-aging supplement, a balanced review is needed. The term anti-aging is frequently used in commercial settings more broadly than is justified by clinical evidence. In humans, the best-supported outcomes for ashwagandha concern stress, anxiety and sleep, while data on cognition, endocrine markers, physical performance and musculoskeletal aging remain promising but preliminary. This review therefore focuses on clinically relevant domains rather than unsupported claims of rejuvenation.

METHODS

This article is a narrative review. A literature search was performed in PubMed, Google Scholar and publicly available health-agency resources up to July 2026. Search terms included “*Withania somnifera*”, “ashwagandha”, “healthy aging”, “anti-aging”, “stress”, “anxiety”, “sleep”, “cortisol”, “inflammation”, “oxidative stress”, “cognition”, “physical performance”, “muscle strength”, “sarcopenia”, “musculoskeletal aging”, “osteoarthritis”, “rehabilitation”, “safety”, “liver injury” and “hepatotoxicity”. Priority was given to randomized controlled trials, systematic reviews, meta-analyses, pharmacovigilance reports and official safety summaries. Preclinical data were considered only to explain biological plausibility and were not used as a substitute for clinical efficacy.

Phytochemistry and biological plausibility

The pharmacological profile of ashwagandha is complex. Withanolides such as withaferin A, withanolide A and related glycowithanolides are frequently discussed as active constituents, although the precise contribution of each compound to clinical outcomes remains uncertain. Root extracts are most commonly used in human trials, while leaf-containing preparations may have different chemical profiles and are not automatically interchangeable. This issue is clinically relevant because many trials evaluate branded extracts with defined withanolide content, whereas commercial supplements vary substantially in standardization and quality control (3,4).

Several mechanisms are relevant to healthy aging. First, ashwagandha appears to modulate stress-response pathways. Clinical studies reporting reduced perceived stress and, in some cases, lower cortisol suggest a possible effect on HPA-axis tone (5,6). Second, preclinical studies have described antioxidant and anti-inflammatory actions involving nuclear factor erythroid 2-related factor 2 (Nrf2), nuclear factor kappa B (NF-κB), cytokine modulation and reduced oxidative stress markers (3,7). Third, experimental models suggest potential effects on neuronal plasticity, mitochondrial function and sleep architecture, although these mechanisms remain incompletely confirmed in humans.

These pathways overlap with recognized biology of aging. Chronic inflammation, oxidative damage and neuroendocrine dysregulation are not isolated phenomena; they interact with sarcopenia, frailty, metabolic dysfunction, pain sensitization and cognitive decline. The musculoskeletal relevance is particularly important: skeletal muscle is both a target and a regulator of systemic aging, while inactivity caused by pain or fatigue can rapidly worsen metabolic and functional reserve. Ashwagandha is therefore biologically plausible as a supportive intervention, although plausibility must be separated from proven clinical benefit.

Table 1. Potential mechanisms linking ashwagandha to healthy aging.

Pathway	Potential relevance to aging	Current level of evidence
HPA-axis/stress response	Lower perceived stress, anxiety and possibly cortisol may reduce stress-related fatigue, sleep disturbance and inflammatory activation.	Moderate human evidence for stress outcomes; cortisol effects vary by study.
Sleep regulation	Improved sleep quality and latency may support recovery, cognition, metabolic control and pain modulation.	Moderate but still limited human evidence; strongest in short-term trials.
Inflammation and oxidative stress	Potential downregulation of NF-κB signaling and support of antioxidant defenses may counter components of inflammaging.	Mainly preclinical; limited human biomarker confirmation.

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Musculoskeletal function	Better recovery, strength, body composition and sleep-related pain modulation may support mobility and help counter sarcopenic trajectories when paired with exercise.	Limited human trials, mostly in healthy or physically active adults; direct data in older orthopedic populations are lacking.
Neurocognitive resilience	Potential benefits on memory, attention and processing speed may be relevant to cognitive aging.	Preliminary human evidence; larger independent trials needed.
Endocrine markers	Changes in DHEA-S, testosterone or thyroid hormones may influence vitality but also raise safety considerations.	Preliminary and population-specific evidence.

Clinical evidence: stress, anxiety and cortisol

The most consistent human evidence for ashwagandha concerns stress and anxiety. In a prospective randomized, double-blind, placebo-controlled study, Chandrasekhar et al. reported that high-concentration ashwagandha root extract improved resistance to stress and reduced scores on validated stress and anxiety scales in adults under chronic stress (5). Subsequent trials using different standardized extracts have also reported reductions in perceived stress and anxiety symptoms, with some studies showing decreases in serum or salivary cortisol (6,8).

A health-professional review by the U.S. Office of Dietary Supplements summarized that, overall, studies have found significant reductions in subjectively measured stress and anxiety, sleeplessness, fatigue and serum cortisol compared with placebo, although benefits varied by dose and product (9). Recent systematic reviews have reached similar cautious conclusions: the signal is favorable, but heterogeneity in extract composition, dose, duration and participant characteristics prevents a single dosing or product recommendation for all patients (10).

From an anti-aging perspective, reduced stress is clinically relevant because chronic stress contributes to poor sleep, increased pain sensitivity, altered appetite, impaired recovery and reduced adherence to exercise. Nevertheless, available trials usually enrolled adults with stress or anxiety symptoms, not elderly frail populations or cohorts selected for biological aging markers. Therefore, the stress-reduction data support a role for ashwagandha in resilience rather than proving a direct anti-aging effect.

Clinical evidence: sleep and recovery

Sleep is a key determinant of healthy aging. Short or fragmented sleep is associated with fatigue, reduced cognitive performance, poorer metabolic regulation and impaired tissue recovery. Several randomized trials suggest that ashwagandha may improve sleep quality, sleep onset latency, total sleep time or mental alertness on awakening. In a double-blind, randomized, placebo-controlled trial in healthy volunteers and patients with insomnia, Langade et al. reported improvement in sleep quality and tolerability with ashwagandha root extract (11).

A systematic review and meta-analysis of randomized trials found that ashwagandha extract had a small but significant effect on sleep compared with placebo, with more prominent benefits among individuals with insomnia, treatment durations of at least eight weeks and doses around 600 mg/day of root extract in some studies (12). The U.S. Office of Dietary Supplements similarly notes that evidence from a small number of studies suggests improvements in several sleep parameters, although research remains limited (9).

The clinical relevance of sleep improvement is easy to underestimate. Even modest sleep benefits may translate into better daily energy, mood, recovery from exercise and perceived quality of life. However, most trials are short-term and rely partly on subjective scales. Future studies should include actigraphy or polysomnography, inflammatory markers, pain outcomes and longer follow-up in older adults.

Clinical evidence: cognition and neuropsychological aging

Cognitive aging is influenced by sleep, vascular health, inflammation, neuroendocrine factors and physical activity. Ashwagandha has been investigated in small human studies for memory and cognition. A randomized placebo-controlled trial in adults with mild cognitive impairment reported improvements in immediate and general memory and suggested benefits on executive function, attention and information processing speed (13). More recent early trials of standardized extracts have also suggested improvements in memory domains, although these results require replication in larger independent cohorts (14).

Mechanistically, preclinical studies have proposed neuroprotective effects through antioxidant activity, modulation of inflammatory signaling and support of neuronal plasticity. These findings are biologically plausible but should not be overextended. At present, ashwagandha cannot be recommended as a treatment for dementia or as a proven preventive therapy for neurodegenerative disease. Its possible role is better framed as a supportive intervention for stress-related cognitive fatigue or mild cognitive complaints, pending stronger evidence.

Clinical evidence: musculoskeletal function, physical performance and recovery

Among the domains most relevant to orthopedic and rehabilitation practice, the signal on muscle performance is perhaps the most interesting, but it is also easy to overstate. Healthy aging depends on preserving the capacity to walk, climb stairs, recover after illness or surgery and tolerate regular exercise. Sarcopenia, osteoarthritis and chronic musculoskeletal pain often share the same final pathway: reduced movement. In that context, even a modest improvement in sleep, perceived energy or training response may become clinically relevant if it helps a patient remain active.

A randomized controlled trial by Wankhede et al. found that ashwagandha supplementation during resistance training was associated with greater increases in muscle strength and muscle size and greater reductions in exercise-induced muscle damage compared with placebo (15). A meta-analysis on VO₂max suggested that ashwagandha supplementation may improve aerobic capacity in athletes and healthy adults (16). A later systematic review of physical-performance outcomes concluded that ashwagandha may have beneficial effects on strength, power, cardiorespiratory fitness and fatigue, although the certainty of evidence varies across outcomes and populations (17).

For musculoskeletal aging, these findings should be interpreted as hypothesis-generating. The strongest data do not come from frail older adults with sarcopenia, patients with symptomatic osteoarthritis or postoperative rehabilitation cohorts, but from healthy or physically active adults. Ashwagandha should therefore not be presented as a treatment for sarcopenia, cartilage degeneration or joint disease. A more realistic interpretation is that it may support training adaptation, recovery and perceived vitality in selected individuals, particularly when combined with resistance exercise, adequate protein intake and management of pain generators.

Clinical implications for musculoskeletal aging and rehabilitation

The practical message for musculoskeletal medicine is cautious but useful. Ashwagandha may be considered as an adjunct for selected patients whose main barriers to movement are stress-related fatigue, poor sleep, low perceived recovery or reduced training tolerance. These factors frequently coexist with early osteoarthritis, tendinopathy, nonspecific musculoskeletal pain and age-related deconditioning. A supplement that improves sleep or stress perception may not act directly on cartilage, tendon or bone, but it may improve the behavioral conditions needed for rehabilitation to work.

This distinction matters. In the current evidence base, ashwagandha should not be described as chondroprotective,

osteogenic or disease-modifying in humans. It is better framed as a possible recovery-supporting and resilience-supporting intervention. The most defensible clinical approach is to pair it with resistance exercise, protein adequacy, weight management and structured rehabilitation, while documenting baseline symptoms and functional outcomes. Future orthopedic studies should test whether these indirect benefits translate into measurable improvements in pain, mobility, adherence to exercise and quality of life.

Endocrine and metabolic considerations

Several studies have examined endocrine outcomes. In overweight men aged 40 to 70 years with mild fatigue, Lopresti et al. reported that standardized ashwagandha intake was associated with greater increases in DHEA-S and testosterone compared with placebo, although improvements in fatigue, vigor and psychological well-being occurred over time in both groups without clear between-group differences for all clinical outcomes (18). Another resistance-training trial found increased testosterone alongside strength improvements (15).

These findings may be attractive in the context of male aging, but they must be interpreted cautiously. Endocrine effects may depend on baseline characteristics, sex, age, extract type, dose and duration. In addition, ashwagandha may influence thyroid function in some individuals. Small clinical studies have reported changes in thyroid hormones, and authoritative safety summaries advise caution in patients with thyroid disorders or those taking thyroid medication (9). Therefore, endocrine effects are not automatically beneficial and should be monitored clinically.

Inflammation, oxidative stress and biological aging markers

Inflammaging refers to the chronic, systemic, low-grade inflammatory state that accompanies aging and contributes to frailty, metabolic disease, cardiovascular disease and neurodegeneration (2). Reviews of *Withania somnifera* describe potential modulation of oxidative stress, DNA damage responses, Nrf2 signaling, NF- κ B activity and cytokine pathways (3,7). These mechanisms provide a plausible rationale for healthy-aging research.

However, direct human evidence on validated aging biomarkers is still insufficient. Very few trials have measured epigenetic clocks, telomere dynamics, cellular senescence markers, mitochondrial function, inflammatory panels or long-term clinical endpoints. The currently available evidence is stronger for symptom and functional outcomes than for biological aging outcomes. For this reason, the term “anti-aging” should be used carefully in the manuscript and should be linked to healthspan, resilience and functional preservation rather than literal reversal of aging.

Table 2. Summary of clinically relevant evidence by domain.

Domain	Typical outcomes studied	Overall signal	Practical interpretation
Stress/anxiety	Perceived stress scales, anxiety scales, cortisol	Favorable but heterogeneous	Most supported clinical domain; suitable as a resilience-focused adjunct.
Sleep	Sleep quality, sleep latency, sleep efficiency, total sleep time	Favorable in short-term trials	May be useful when sleep disturbance coexists with stress or fatigue.
Cognition	Memory, attention, executive function	Preliminary favorable signal	Insufficient for disease claims; may justify further trials.
Musculoskeletal performance	Strength, VO2max, recovery markers, body composition, exercise tolerance	Promising but population-specific	Potential adjunct to exercise and rehabilitation, not a substitute for training or disease-specific treatment.
Endocrine markers	DHEA-S, testosterone, thyroid hormones	Variable and clinically nuanced	Monitor in patients with endocrine disease or hormone-sensitive conditions.
Inflammation/oxidative stress	Inflammatory cytokines, antioxidant markers, mechanistic pathways	Strong preclinical rationale, limited clinical proof	Avoid overclaiming biological age reversal.

Dosage and practical supplementation considerations

Human trials have used a wide range of preparations, commonly 250 to 600 mg/day of standardized root extract for 6 to 12 weeks, although some studies used lower-dose high-withanolide extracts or sustained-release preparations. Because different extracts are not interchangeable, the dose should be interpreted together with plant part, extraction method and withanolide standardization. The available evidence does not support a universal “anti-aging dose.”

In clinical practice, if ashwagandha is considered, it should be used as part of a broader lifestyle strategy that includes sleep hygiene, resistance and aerobic exercise, adequate protein intake, weight control, treatment of pain generators and management of cardiometabolic risk. In a musculoskeletal or rehabilitation setting, the supplement should never replace progressive loading, physiotherapy, correction of vitamin D or protein deficiency, or evidence-based treatment of osteoarthritis, osteoporosis or inflammatory disease. The most reasonable candidates are adults with stress-related fatigue, sleep disturbance or poor recovery who are otherwise suitable for supplementation and can be monitored.

Safety, contraindications and pharmacovigilance

Ashwagandha is usually well tolerated in short-term clinical trials. Common adverse effects include gastrointestinal upset, loose stools, nausea and drowsiness. Nevertheless, long-term safety is not established. The U.S. Office of

Dietary Supplements states that ashwagandha appears well tolerated for up to about three months, but long-term safety is unknown and more serious adverse effects, including liver injury, have been reported (9).

LiverTox summarizes that clinically apparent liver injury attributed to ashwagandha is rare but has been reported, typically developing 2 to 12 weeks after starting supplementation with a cholestatic or mixed pattern, jaundice and pruritus; most cases resolve after discontinuation, but severe cases including acute liver failure have been described, particularly in people with pre-existing liver disease (4). An Indian case series and literature review described ashwagandha-induced liver injury, including severe outcomes in patients with underlying chronic liver disease (19). In July 2026, the Therapeutic Goods Administration of Australia warned that cases of liver injury associated with *W. somnifera* continue to be reported and advised avoidance in individuals with existing liver disorders (20).

Other groups requiring caution include pregnant or breastfeeding women, patients with thyroid disease, individuals using sedatives, immunosuppressants, antidiabetic or antihypertensive drugs, and patients with hormone-sensitive prostate cancer or other hormone-sensitive disorders. Because supplements are not regulated with the same rigor as prescription medicines in many countries, product quality, adulteration and variability remain important concerns.

Table 3. Practical safety considerations before ashwagandha supplementation.

Clinical issue	Reason for caution	Suggested approach
Existing liver disease	Rare cases of hepatotoxicity and severe outcomes have been reported.	Avoid use or use only after specialist advice; stop immediately if jaundice, pruritus or dark urine occurs.
Pregnancy/breastfeeding	Safety is insufficient and some authorities advise avoidance.	Avoid supplementation.
Thyroid disorders	Possible changes in TSH, T3 and T4 have been reported.	Monitor thyroid function and medication changes.
Sedatives or CNS depressants	Potential additive drowsiness.	Use caution and avoid combining without medical review.
Diabetes or hypertension therapy	Potential additive metabolic or blood pressure effects.	Monitor glucose and blood pressure.
Multi-ingredient supplements	Adulteration or attribution uncertainty may increase risk.	Prefer single-ingredient, standardized products with quality testing.

Limitations of the current evidence

Several limitations reduce the certainty of conclusions. First, many trials are small and short, commonly lasting 4 to 12 weeks. Second, extracts differ by plant part, extraction method and withanolide content. Third, many studies are industry-funded or product-specific. Fourth, older adults, frail patients and individuals with multimorbidity are underrepresented. Fifth, few studies evaluate hard clinical endpoints such as falls, hospitalization, fracture recovery, postoperative outcomes, sarcopenia progression or long-term cognitive decline. Finally, validated biomarkers of biological aging are rarely included.

Future trials should compare standardized root extracts against placebo in older adults and in clinically relevant populations such as adults with insomnia, chronic stress, sarcopenia risk, osteoarthritis-related inactivity, chronic musculoskeletal pain or post-rehabilitation fatigue. For orthopedic and rehabilitation research, useful endpoints would include gait speed, grip strength, chair-rise testing, muscle mass, patient-reported outcomes such as WOMAC, KOOS or HOOS, analgesic use, return to activity and adherence to exercise programs. Studies should also include longer follow-up and systematic safety monitoring.

CONCLUSION

Ashwagandha is a clinically interesting, biologically plausible nutraceutical for healthy aging, with the strongest human evidence supporting benefits on perceived stress, anxiety and selected sleep outcomes. Preliminary data also suggest potential benefits for physical performance, recovery and muscle-related outcomes, which makes the supplement relevant to discussions of musculoskeletal aging and rehabilitation. However, the evidence is not strong enough to claim reversal of biological aging, prevention of sarcopenia, treatment of osteoarthritis or regeneration of musculoskeletal tissues.

For clinicians and researchers, the value of ashwagandha lies in its possible integration into broader lifestyle, exercise and rehabilitation strategies rather than its use as a standalone anti-aging therapy. Given the heterogeneity of preparations and the emerging safety concerns, particularly liver injury and endocrine effects, supplementation should be individualized, time-limited and monitored in patients with relevant comorbidities or concomitant medications.

Ethical approval

Not applicable. This is a narrative review and did not involve human participants, human data or animal experiments.

Informed consent

Not applicable.

Data availability

No new datasets were generated or analyzed for this article.

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Conflict of interest

The author declares no conflict of interest related to this manuscript.

Author contributions

Michele Bisaccia conceived the topic, reviewed the literature, drafted and approved the final manuscript.

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