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Therapeutic Potential and Safety Profile of *Withania somnifera* in Health and Sports Science: A Comprehensive Narrative Review

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ABSTRACT

Introduction and Purpose: *Withania somnifera* (Ashwagandha) is a leading adaptogen in phytotherapy and sports nutrition. This review evaluates scientific evidence (2015–2024) regarding its impact on mental health, physical performance, and safety profile.

Material and Methods: A narrative review was conducted using PubMed, Scopus, and Google Scholar, focusing on RCTs, systematic reviews, and meta-analyses published between 2018 and 2024. Twenty-three high-quality sources were selected for analysis.

Results: Ashwagandha supplementation significantly reduces serum cortisol and alleviates symptoms of anxiety and stress. In sports medicine, it is associated with increased muscle strength (1RM) and power, improved VO_2 max, and accelerated recovery, evidenced by

reduced creatine kinase levels. Furthermore, it improves sleep quality and cognitive functions. While generally well-tolerated, rare cases of idiosyncratic hepatotoxicity and clinically significant interactions with thyroid and immunosuppressive medications have been documented.

Conclusion: Ashwagandha exhibits substantial therapeutic potential as an ergogenic and anxiolytic agent. Despite high-level evidence of its efficacy, the risk of rare adverse events and drug interactions necessitates medical supervision. Future research should prioritize long-term safety monitoring and dosing standardization.

Keywords: Ashwagandha; *Withania somnifera*; adaptogens; physical performance; cortisol; safety profile

1. INTRODUCTION

Withania somnifera, widely recognized as Ashwagandha or "Indian Winter Cherry," is a foundational herb in traditional Ayurvedic medicine, where it has been utilized for over 3,000 years as a *Rasayana* – a remedy promoting longevity and revitalization (Mikulska et al., 2023). In modern pharmacology, it is classified as a potent adaptogen, a term used to describe substances that enhance the body's non-specific resistance to biological, chemical, and physical stressors while promoting homeostasis (Speers et al., 2021).

The biological activity of Ashwagandha is primarily attributed to its complex phytochemical profile, particularly a group of steroidal lactones known as withanolides. Among these, withaferin A and withanolide A are considered the most pharmacologically significant, exhibiting anti-inflammatory, neuroprotective, and immunomodulatory properties (Makhlouf et al., 2024; Tharakan et al., 2021). By modulating the hypothalamic-pituitary-adrenal (HPA) axis and enhancing GABAergic signaling, Ashwagandha influences the physiological response to chronic stress, which has become a hallmark of contemporary lifestyle-related disorders.

In recent years, the interest in *Withania somnifera* has extended beyond clinical psychiatry into the realms of sports medicine and physical education. Athletes and physically active individuals increasingly seek natural ergogenic aids to optimize performance, accelerate post-exercise

recovery, and manage the physiological strain of intensive training. Despite its widespread use and growing market availability, the clinical evidence regarding its efficacy across different populations—ranging from sedentary adults to elite athletes—requires comprehensive synthesis. Furthermore, as the use of highly concentrated extracts increases, the evaluation of its safety profile and potential herb-drug interactions becomes a critical concern for healthcare professionals and pharmacists.

The purpose of this study is to provide a comprehensive review of the therapeutic potential of Ashwagandha in the light of current scientific evidence (2018–2024). This article focuses on evaluating its impact on mental health, physical performance, and hormonal balance, while simultaneously analyzing its safety profile and potential contraindications to ensure evidence-based recommendations for its use in health and sport.

2.MATERIAL AND METHODS

The current study is a narrative review based on a comprehensive analysis of scientific literature concerning the therapeutic potential and safety of *Withania somnifera*. To ensure the highest clinical relevance, the search was conducted across major electronic databases, including PubMed, Scopus, Google Scholar, and the Cochrane Library.

Search Strategy

The literature search was performed using a combination of the following keywords and MeSH (Medical Subject Headings) terms: "Ashwagandha", "Withania somnifera", "adaptogens", "physical performance", "muscle strength", "cortisol", "anxiety", "testosterone", and "safety profile". Boolean operators (AND, OR) were applied to refine the search results (e.g., "Ashwagandha AND physical performance").

Inclusion and Exclusion Criteria

The primary focus was placed on articles published between 2018 and 2024 to capture the most recent advancements in the field. The inclusion criteria were:

1. Randomized controlled trials (RCTs),
2. Systematic reviews and meta-analyses,
3. Full-text articles published in English or Polish,
4. Studies involving human subjects.

Exclusion criteria included non-peer-reviewed articles, case reports with insufficient clinical data, and studies published before 2010, unless they provided fundamental pharmacological data.

Data Synthesis and Analysis

Out of the initial search results, 25 key sources were selected for detailed analysis. The collected data were synthesized qualitatively, focusing on three main thematic areas: (1) cognitive and mental health benefits, (2) impact on physical performance and hormonal regulation, and (3) toxicological safety and herb-drug interactions. Each selected study was evaluated for its methodology, sample size, and clinical significance to ensure a balanced and evidence-based perspective.

3. RESULTS

3.1. Chemical composition and pharmacological mechanism of action

The therapeutic efficacy of *Withania somnifera* is primarily attributed to its roots, which contain a wide spectrum of bioactive secondary metabolites. Among these, steroidal lactones known as withanolides—particularly withaferin A and withanolide A—are considered the principal pharmacologically active constituents (Makhlouf et al., 2024). Although structurally distinct, withanolides exhibit functional similarities to ginsenosides found in *Panax ginseng*, which may partly explain the adaptogenic properties shared by both plants.

One of the central mechanisms underlying the adaptogenic effects of Ashwagandha involves modulation of the hypothalamic–pituitary–adrenal (HPA) axis. Supplementation with *W. somnifera* has been associated with the attenuation of HPA axis hyperactivity, resulting in a reduction of circulating cortisol levels, a key biomarker of physiological stress (Lopresti et al., 2019).

In addition, Ashwagandha exerts neuromodulatory effects through interaction with GABAergic signaling pathways. Preclinical and clinical evidence suggests that *W. somnifera* displays GABA-mimetic activity, contributing to inhibitory neurotransmission within the central nervous system and thereby supporting its anxiolytic and sleep-promoting properties (Speers et al., 2021).

Furthermore, the immunomodulatory potential of *W. somnifera* has been linked to the enhancement of innate immune responses, including increased natural killer (NK) cell activity

and regulation of pro-inflammatory cytokine production, indicating a bidirectional influence on immune homeostasis (Tharakan et al., 2021).

3.2. Impact on mental health and sleep quality

3.2. Impact on mental health and sleep quality

The application of *Withania somnifera* in managing psychological distress is among the most extensively studied areas of its use. A recent systematic review and meta-analysis of randomized controlled trials (RCTs) demonstrated that standardized Ashwagandha extracts significantly reduce symptoms of anxiety and perceived stress compared to placebo (Akhgarjand et al., 2022). These effects were consistently observed across validated assessment tools, including the Perceived Stress Scale (PSS) and the Hamilton Anxiety Rating Scale (HAM-A).

Clinical evidence further supports the dose-dependent efficacy of *Withania somnifera* in stress management. A randomized controlled trial by Salve et al. (2019) found that daily supplementation with standardized root extract was associated with reductions in PSS scores and serum cortisol levels in healthy adults. While lower doses (250 mg/day) were effective, higher doses of 600 mg/day appeared to provide more pronounced adaptogenic and anxiolytic effects over an eight-week period.

Beyond stress modulation, Ashwagandha supplementation has been associated with improvements in cognitive performance. Evidence suggests that chronic intake may enhance attention, executive function, and information processing speed in healthy adults (Gopukumar et al., 2021). These outcomes are thought to be linked to the plant's neuroprotective properties, including its antioxidant activity and potential effects on hippocampal function.

Ashwagandha has further gained attention as a natural intervention for sleep disturbances. A meta-analysis by Cheah et al. (2021) reported significant improvements in overall sleep quality following supplementation, including reductions in sleep latency, increases in total sleep time, and enhanced sleep efficiency. Greater benefits were observed in individuals with clinically diagnosed insomnia and at daily doses exceeding 600 mg (Langade et al., 2021). Importantly, available evidence indicates that these sleep-related benefits are not commonly accompanied by residual morning sedation.

Additionally, the therapeutic potential of *Withania somnifera* extends to the management of chronic fatigue, a condition frequently associated with prolonged psychological stress and impaired sleep. A study by Remenapp et al. (2022) found that Ashwagandha supplementation was linked to reductions in both mental and physical fatigue across diverse populations. These effects may be particularly relevant for individuals experiencing exhaustion or burnout, as the adaptogenic properties of the plant may support subjective energy restoration and improved daytime functioning.

3.3. Influence on physical performance and sports medicine

The ergogenic potential of Ashwagandha has been increasingly documented in recent years, positioning it as a multi-modal supplement in sports science. A meta-analysis by Bonilla et al. (2021) provides a comprehensive overview of its effects on neuromuscular performance, demonstrating that chronic supplementation is associated with significant improvements in one-repetition maximum (1RM) strength in both upper and lower body exercises. These gains were particularly evident in movements such as the bench press and leg extension, where individuals receiving standardized Ashwagandha extracts exhibited greater force production compared with placebo groups.

Evidence from resistance training studies further supports the role of Ashwagandha in promoting favorable body composition adaptations. Wankhede et al. (2015) reported significant increases in muscle strength and lean body mass following an eight-week resistance training program combined with Ashwagandha supplementation. The authors suggested that these adaptations may be partially mediated by a more favorable cortisol-to-testosterone balance, reflecting a reduction in training-induced catabolic stress.

From a cardiorespiratory perspective, Ashwagandha supplementation has been associated with improvements in aerobic capacity, commonly assessed via maximal oxygen consumption (VO_2 max). A narrative review by Pérez-Gómez et al. (2020) indicated that VO_2 max improvements have been observed across various populations, including physically active adults and trained athletes. Proposed mechanisms underlying these effects include enhanced oxygen transport capacity and improved mitochondrial efficiency; however, direct evidence from human trials is limited, and mechanisms such as mitochondrial adaptations are largely inferred from preclinical or in vitro studies, warranting further investigation.

Ashwagandha may also support post-exercise recovery and adaptation to intensive training by modulating oxidative stress and physiological responses to exercise-induced muscle damage. In healthy adults, Tiwari et al. (2021) demonstrated that supplementation with Ashwagandha root extract improved VO_2 max and enhanced antioxidant status, suggesting a protective effect against exercise-induced oxidative stress. In resistance training settings, Wankhede et al. (2015) observed attenuated post-exercise increases in serum creatine kinase (CK) levels among participants receiving Ashwagandha, indicating reduced muscle damage. Similarly, the STAR trial conducted by Ziegenfuss et al. (2018) reported improvements in perceived recovery and training adaptations over a 12-week supplementation period in recreationally active men. Collectively, these findings suggest that Ashwagandha may facilitate recovery and support adaptation to structured training programs, although data on specific inflammatory mediators, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), remain inconsistent in human studies, thus limiting conclusions regarding its anti-inflammatory effects.

3.4. Endocrine and metabolic effects

Ashwagandha acts as a potent modulator of the endocrine system, with its most pronounced effects observed in the regulation of the reproductive and thyroid axes. In men, supplementation has been consistently associated with increased testosterone levels. Chauhan et al. (2022) and Wankhede et al. (2015) reported that Ashwagandha supplementation may improve luteinizing hormone (LH) activity and reduce oxidative stress in the testes, leading to enhanced testosterone production and improvements in sperm quality, which is particularly relevant in the management of male infertility (Nasimi Doost Azgomi et al., 2018).

A critical finding for clinical pharmacy and medicine is the plant's impact on thyroid function. A double-blind, placebo-controlled study by Sharma et al. (2018) demonstrated that Ashwagandha root extract can significantly increase serum levels of thyroxine (T4) and triiodothyronine (T3) in patients with subclinical hypothyroidism. While this suggests potential therapeutic benefits for individuals with mild thyroid deficiency, it also necessitates caution and monitoring to avoid potential thyrotoxicosis in sensitive individuals.

From a metabolic perspective, Ashwagandha may contribute to reductions in cortisol through the modulation of the hypothalamic–pituitary–adrenal (HPA) axis. Lopresti et al. (2019) observed that daily supplementation with Ashwagandha extract was associated with significant reductions in stress-related outcomes and morning cortisol levels in adults with self-reported

stress. Chronic elevation of cortisol has been linked to adverse metabolic outcomes, including abdominal fat accumulation, insulin resistance, and dysregulated glucose metabolism. By attenuating cortisol secretion, Ashwagandha may indirectly support metabolic balance and weight management. Additionally, its anti-inflammatory properties—evidenced by reductions in systemic markers such as C-reactive protein (CRP) in clinical studies—may further contribute to overall metabolic and systemic health (Gómez-Afonso et al., 2023).

3.5. Safety profile, side effects, and pharmacological considerations

As the global use of *Withania somnifera* (Ashwagandha) increases, a comprehensive understanding of its safety profile is essential for clinical practice. While generally recognized as safe (GRAS), the dose-response relationship and the quality of the extract are key determinants of its tolerability. Standardized root extracts employed in clinical trials (typically 300–600 mg/day) demonstrate a favorable safety profile, with mild gastrointestinal symptoms, such as dyspepsia or slight nausea, being the most commonly reported adverse effects (Verma et al., 2021; Wankhede et al., 2015; Lopresti et al., 2019; Tiwari et al., 2021).

Recent pharmacovigilance reports, however, have highlighted rare but clinically significant cases of drug-induced liver injury (DILI). Systematic evaluations by Björnsson et al. (2020) and Lubarska et al. (2023) documented idiosyncratic hepatotoxicity presenting with jaundice and a cholestatic or mixed pattern of liver enzyme elevation. Most patients recovered fully upon cessation of the supplement; nevertheless, these findings underscore the importance of monitoring liver function in individuals presenting with unexplained fatigue or abdominal symptoms during supplementation. It is also crucial to differentiate high-quality root extracts from lower-quality products, which may be adulterated with leaves or other plant parts containing higher concentrations of cytotoxic withanolides, such as withaferin A.

From a pharmacological perspective, Ashwagandha exerts notable effects on the endocrine and nervous systems. Its stimulatory action on the thyroid gland may exacerbate hyperthyroidism or interfere with levothyroxine titration in patients with hypothyroidism, potentially leading to thyrotoxicosis (Sharma et al., 2018). Additionally, the plant's GABAergic and serotonergic activity suggests potential pharmacodynamic interactions with psychotropic medications; combining Ashwagandha with benzodiazepines or selective serotonin reuptake inhibitors (SSRIs) may result in excessive sedation or altered cognitive states (Speers et al., 2021). Finally, caution is warranted in patients with autoimmune conditions (e.g., systemic lupus

erythematosus, rheumatoid arthritis), as the immunostimulatory effects observed in healthy adults suggest theoretical considerations for immune modulation (Tharakan et al., 2021).

Therefore, the use of Ashwagandha should be individualized, taking into account the patient's full medical history, concurrent medications, and the quality of the supplement used.

4. DISCUSSION

The findings presented in this review underscore the multi-directional therapeutic potential of *Withania somnifera*, positioning it as a unique pharmacological tool that bridges the gap between mental health support and physical performance enhancement. A key observation across the analyzed literature is the profound impact of Ashwagandha on the human stress response. By stabilizing the HPA axis and reducing serum cortisol levels, the plant provides a physiological foundation for its secondary benefits, such as improved sleep quality and enhanced recovery. The correlation between reduced psychological stress and improved physical outcomes is particularly relevant in the context of professional sports and intensive education, where chronic stress often leads to burnout and overtraining syndrome (Akhgarjand et al., 2022; Mikulska et al., 2023).

In the realm of sports medicine, the evidence regarding muscle strength and VO_2 max is compelling. However, the heterogeneity of results in some studies suggests that the efficacy of Ashwagandha may be highly dependent on the degree of withanolide standardization. Extracts such as KSM-66 or Shoden, which are standardized to specific concentrations, consistently show superior results compared to non-standardized root powders. Furthermore, the duration of supplementation appears to be a critical factor; while some cognitive and anxiolytic effects are visible within weeks, significant hypertrophic and cardiovascular adaptations typically require 8 to 12 weeks of consistent use (Bonilla et al., 2021; Pérez-Gómez et al., 2020).

Despite the favorable evidence, several limitations in current research must be addressed. Many clinical trials involving athletes feature relatively small sample sizes and focus primarily on short-term outcomes. There is a lack of long-term longitudinal studies (lasting more than six months) evaluating the potential for "ceiling effects" or the long-term safety of continuous high-dose supplementation. Additionally, the potential for rare but serious adverse events, such as hepatotoxicity, highlights the need for better regulation and quality control in the herbal supplement industry. From a pharmaceutical perspective, the risk of interactions with thyroid

medications and CNS depressants remains a vital clinical consideration that necessitates professional medical supervision (Björnsson et al., 2020; Sharma et al., 2018).

5. CONCLUSIONS

The analysis of the current scientific literature (2018–2024) leads to the following conclusions:

1. *Withania somnifera* (Ashwagandha) is a highly effective adaptogen that significantly reduces perceived stress and anxiety by modulating the cortisol response and GABAergic signaling.
2. In the context of physical performance, Ashwagandha acts as a potent ergogenic aid, contributing to significant increases in muscle strength, improved VO_2 max, and accelerated post-exercise recovery by reducing markers of muscle damage, such as creatine kinase levels.
3. The plant demonstrates substantial potential in improving sleep quality and cognitive functions, providing valuable support for individuals facing high mental and physical demands.
4. While the safety profile is generally favorable, the potential for rare idiosyncratic hepatotoxicity and significant drug interactions (especially with thyroid and immunosuppressive medications) necessitates that its use be monitored by healthcare professionals.
5. Future research should prioritize long-term safety trials and the global standardization of dosing protocols to fully establish Ashwagandha's place in modern evidence-based phytotherapy and sports nutrition.

Disclosure

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