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Review Article

Ashwagandha - Phytochemistry, Pharmacological Evidence, Clinical Applications And Safety: An Updated Narrative Review

Sargam Bharti¹, Pankaj Kumar^{1,*}, Basit Fazal², Shantanu Ranjan³ and Sumit Kumar²¹Department of Pharmaceutical Chemistry, Nibha Institute of Pharmaceutical Sciences, Rajgir, Nalanda, India²Department of Pharmacology, Nibha Institute of Pharmaceutical Sciences, Rajgir, Nalanda, India³Department of Pharmaceutics, Nibha Institute of Pharmaceutical Sciences, Rajgir, India

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*Corresponding author:

Pankaj Kumar, Department of
Pharmaceutical Chemistry, Nibha Institute
of Pharmaceutical Sciences, Rajgir, India.

ABSTRACT

Ashwagandha (Withania somnifera (L.) Dunal) is a Solanaceae medicinal plant with a long history of use in Ayurveda as a rasayana and adaptogenic remedy. The present review integrates the botanical and ethnomedicinal information contained in the submitted undergraduate project with contemporary peer-reviewed evidence on phytochemistry, pharmacology, clinical efficacy, quality control and safety. Withanolides, including withaferin A, withanolide A and withanolide D, together with sitoindosides, alkaloids, flavonoids and other metabolites, constitute the major chemically diverse groups reported from W. somnifera. Experimental research supports antioxidant, anti-inflammatory, immunomodulatory, neuroprotective, anticancer, metabolic and cardioprotective activities, although the strength of evidence differs substantially by indication. Evidence for physical performance and reproductive health is promising but remains formulation- and population-dependent. Importantly, the traditional reputation of Ashwagandha as well tolerated should not obscure emerging pharmacovigilance data: rare clinically apparent liver injury has been reported, and authoritative guidance recommends avoiding use during pregnancy and breastfeeding and exercising caution in thyroid and autoimmune disorders and with several medicines. Future research should prioritize authenticated plant material, chemically standardized preparations, transparent reporting of withanolide profiles, clinically meaningful endpoints, longer follow-up and systematic adverse-event surveillance. Taken together, Ashwagandha represents a pharmacologically rich medicinal plant with credible but indication-specific clinical potential rather than a uniformly established treatment for all conditions.

Keywords: *Withania somnifera; Ashwagandha; Withanolides; Withaferin A; Adaptogen; Stress; Sleep; Pharmacology; Safety; Quality control.*

Introduction

Medicinal plants remain important sources of traditional healthcare and bioactive molecules. *Withania somnifera* (L.) Dunal, commonly called Ashwagandha, winter cherry or Indian ginseng, is a small evergreen shrub of the Solanaceae family and is

among the best-known Ayurvedic medicinal plants. The submitted project describes Ashwagandha as a rasayana and summarizes reported adaptogenic, antioxidant, anxiolytic, anti-inflammatory, immunomodulatory, neuroprotective, antimicrobial, cardioprotective, metabolic and anticancer activities. These claims have generated substantial modern research, but contemporary interpretation requires

separation of traditional use, preclinical observations and clinical evidence. [1–4]

The pharmacological interest of *W. somnifera* is closely linked to its steroidal lactones, particularly withanolides. More than a simple single-compound drug, however, *Ashwagandha* is a chemically complex botanical material whose composition varies with plant part, genotype, geography, cultivation, extraction method and processing. Metabolomic and chromatographic investigations therefore have direct relevance to reproducibility and quality control. [5–8] Human studies have expanded from exploratory trials of stress and anxiety to systematic reviews of sleep, physical performance and reproductive outcomes. Recent meta-analyses generally suggest beneficial effects for selected outcomes, but also identify heterogeneity and limited sample sizes. [9–13] At the same time, reports of herb-associated liver injury have altered the safety discussion. The U.S. National Center for Complementary and Integrative Health advises avoidance during pregnancy and breastfeeding and caution in people with thyroid or autoimmune disorders and in those taking medicines that may interact with *Ashwagandha*. [14,15]

The objective of this review is to provide a concise, publication-oriented synproject of the plant's identity, morphology, phytochemistry, mechanisms, pharmacological activities, clinical evidence, safety and research priorities, while retaining the core scope of the submitted project.

Review Methodology

The source project states that the work was designed as a narrative review and that literature was gathered from peer-reviewed articles, review papers, textbooks, scientific databases and government/international publications. Databases identified in the project include PubMed, Google Scholar, Scopus, ScienceDirect, SpringerLink and Wiley Online Library; keywords included *Ashwagandha*, *Withania somnifera*, phytochemistry, pharmacological activities, therapeutic applications, safety, toxicity, adaptogenic activity, antioxidant activity, anti-inflammatory activity and clinical studies. The project included English-language peer-reviewed research, reviews, clinical and experimental studies, books and official publications, while excluding duplicates, insufficiently informative articles, conference abstracts without full text and unverified websites. [16] For this updated article, the project literature was supplemented by targeted searches of PubMed/PMC and authoritative health information through September 2026, emphasizing systematic reviews/meta-analyses, clinical studies, analytical standardization and recent

safety evidence. Because this is a narrative review rather than a registered systematic review, no pooled effect estimate or formal risk-of-bias synproject was independently calculated. The evidence is therefore presented according to study type and clinical relevance.

Botanical Identity, Morphology and Traditional Use

W. somnifera belongs to Kingdom Plantae, family Solanaceae, genus *Withania* and species *W. somnifera* (L.) Dunal. The project describes an erect, evergreen, tomentose shrub approximately 30–150 cm high, with fleshy whitish-brown roots, simple ovate leaves, inconspicuous greenish to yellowish flowers, and small globose orange-red berries enclosed by the persistent calyx. Roots are the principal medicinal part, although leaves and other plant parts are also investigated. [16] The plant occurs widely in the drier regions of India and is also distributed in parts of Africa and the Mediterranean/South Asian region. In Ayurvedic practice, the root is traditionally used as a *rasayana* and for conditions associated with debility, stress and nervous-system complaints. Traditional terminology should not be interpreted as equivalent to modern diagnostic indications; rather, it provides a historical rationale for pharmacological investigation. Plant material can be prepared as powders, decoctions or extracts and is now marketed in capsules, tablets, gummies, beverages and other dosage forms. These preparations are not chemically interchangeable. The extraction solvent, plant part and concentration of marker compounds can substantially change the phytochemical profile and therefore the biological exposure. [5,7,8]

Phytochemistry and Quality Standardization

The project identifies withanolides and alkaloids as major active groups and also lists flavonoids and related glycosides. Contemporary reviews describe *W. somnifera* as a chemically complex plant containing steroidal lactones, withanolides, sitoindosides / glycowithanolides, alkaloids, flavonoids, phenolics, saponins and other specialized metabolites. [2,3,5,6]

Withanolides are C28 steroidal lactones structurally related to the ergostane skeleton. Withaferin A and withanolide D are among the best-characterized constituents, while withanolide A, withanone and other derivatives have been investigated for biological activity. Different tissues can have different metabolite patterns, and analytical studies demonstrate that marker concentrations vary among raw materials and commercial preparations. [3,6–8]

Table 1: Botanical And Pharmacognostic Profile

Parameter	Summary
Botanical name	Withania somnifera (L.) Dunal
Family	Solanaceae
Common names	Ashwagandha; winter cherry; Indian ginseng
Habit	Small woody, evergreen, tomentose shrub
Approximate height	30–150 cm
Principal medicinal part	Root; leaves and other parts are also investigated
Key phytochemical class	Steroidal lactones/withanolides
Traditional positioning	Rasayana; adaptogenic and restorative use in Ayurveda
Major quality concern	Variation in plant part, cultivar, geography, extraction and marker content

Modern quality control therefore requires botanical authentication plus chemical characterization. HPLC and HPTLC methods have been developed for marker compounds, and validated liquid-chromatographic methods can quantify multiple withanolides. Metabolomic approaches using LC-MS, GC-MS and NMR can provide broader fingerprints and may help identify adulteration, geographic effects and batch-to-batch variation. [7,8,17,18]

An important practical point is that a label stating a particular mass of 'Ashwagandha extract' does not, by itself, define the amount of a pharmacologically relevant constituent. Clinical interpretation should consider whether the preparation was root-only or a mixed plant-part product, extraction ratio, solvent, marker specification and whether the clinical formulation has been independently characterized.

Table 2: Major Phytochemical Groups and Representative Relevance.

Chemical group	Representative constituents	Reported relevance
Withanolides / steroidal lactones	Withaferin A, withanolide A, withanolide D, withanone	Anti-inflammatory, redox, cytotoxic and neurobiological actions; major analytical markers
Sitoindosides / glycowithanolides	Sitoindosides VII–X and related glycosides	Adaptogenic, CNS and immunomodulatory activity in experimental studies
Alkaloids	Withanine, somniferine, anaferine, anahygrine and related alkaloids	Contribute to the broad phytochemical profile; biological roles vary by constituent
Flavonoids / phenolics	Quercetin-related compounds, chlorogenic acid and other phenolics	Antioxidant and signaling-related activity
Other metabolites	Saponins, sterols, sugars, amino acids and additional specialized metabolites	May contribute to matrix effects and overall extract fingerprint

Pharmacological Activities and Mechanisms

Adaptogenic, Stress-Relieving and Anxiolytic Activity

Stress regulation is the clinical area in which Ashwagandha has attracted the strongest contemporary interest. Experimental studies have proposed modulation of the hypothalamic–pituitary–adrenal axis, oxidative stress and neurochemical signaling as components of its activity. Clinical trials summarized

in the project generally report reductions in perceived stress, anxiety scores and/or cortisol with standardized root extracts. A 2024 systematic review and meta-analysis of nine randomized controlled trials involving 558 participants found statistically significant improvements in Perceived Stress Scale, Hamilton Anxiety Scale and serum cortisol outcomes compared with placebo; four trials reported mild-to-moderate adverse events. [9]

These results support a clinically relevant signal but should not be interpreted as proof that all Ashwagandha products treat anxiety disorders. The studies differed in extract composition, dose, treatment duration and populations. The most appropriate interpretation is that selected standardized preparations may have stress- and anxiety-related benefits in some adults, while larger, longer and better-standardized trials remain necessary.

Sleep and Neurocognitive Effects

Preclinical work has described antioxidant, neuroprotective and neurite-regenerative effects, while the project summarizes experimental findings in Alzheimer's and Parkinson's disease models. Proposed mechanisms include attenuation of oxidative stress, modulation of inflammatory pathways, effects on cholinergic or dopaminergic signaling and support of neuronal plasticity. [3,19–22]

Human evidence is more limited than preclinical literature. A systematic review and meta-analysis of five randomized controlled trials involving 400 participants found a small but significant overall improvement in sleep, with larger effects in participants with insomnia and in studies using doses of at least 600 mg/day for at least eight weeks. [10] A separate 2024 systematic review/meta-analysis of five RCTs (254 participants) reported improvements in anxiety and several sleep parameters, although substantial heterogeneity was present. [11]

Antioxidant and Anti-Inflammatory Activity

Oxidative stress and inflammation are recurring mechanistic themes in Ashwagandha research. Withanolides and other constituents can influence reactive oxygen species, antioxidant enzymes and inflammatory signaling in experimental models. Withaferin A has received particular attention for modulation of NF- κ B-related signaling and inflammatory mediators. [3,23,24]

These mechanisms are biologically plausible but should be distinguished from demonstrated clinical treatment effects. In vitro inhibition of a signaling pathway or antioxidant activity in a chemical assay does not establish clinical efficacy in humans. The translational value is strongest when mechanistic observations converge with reproducible animal findings and appropriately designed human trials.

Neuroprotective and Neurodegenerative Disease Research

In experimental Alzheimer's models, Ashwagandha-related constituents have been investigated for effects on amyloid processing, neuroinflammation and neuronal survival. In Parkinsonian models, extracts have been associated with lower lipid peroxidation, improved antioxidant defenses and changes in dopaminergic markers and motor behavior. [20–22]

At present, these data support further investigation rather than routine clinical treatment of Alzheimer's or Parkinson's disease. The absence of large disease-modifying clinical trials, together with variability in preparations, prevents extrapolation from animal models to established human therapy.

Physical Performance and Recovery

Several randomized trials have evaluated Ashwagandha in resistance training, athletic or physically active adults. A PRISMA-based systematic review and Bayesian meta-analysis identified 13 eligible studies, with 12 included quantitatively, and concluded that Ashwagandha was more efficacious than placebo across selected physical-performance variables, while also noting the need for more comparable trials. [12]

More recent synproject remains cautious: a 2026 three-level meta-analysis reported an average improvement in exercise performance, with the most consistent evidence for aerobic endurance, while prediction intervals crossed zero and strength, power and muscular-endurance evidence remained less certain. [13] Thus, any performance claim should be linked to the specific extract, dose, training status and outcome measured.

Reproductive and Sexual Health

Traditional use and several clinical investigations have prompted research into male fertility, testosterone and sexual well-being. An evidence-based systematic review found four clinical trials and reported improvements in sperm concentration, semen volume, motility and selected reproductive hormones in infertile men, but the clinical evidence base was small and included only one randomized controlled trial. [25]

More recent systematic review evidence also suggests possible benefits across male and female reproductive outcomes, but emphasizes the need for better long-term and dose-defined studies. [26] Accordingly, Ashwagandha should be considered an investigational adjunct rather than a substitute for diagnostic evaluation and evidence-based management of infertility.

Metabolic, Cardiovascular, Immune and Antimicrobial Activities

Experimental literature summarized in the project reports antidiabetic, hypolipidemic, cardioprotective, hepatoprotective, immunomodulatory and antimicrobial effects. Proposed mechanisms include modulation of oxidative stress, inflammatory mediators, endothelial signaling and immune-cell activity. [3,23,27]

Evidence in humans is considerably less mature for these indications than for stress and sleep. Small studies and heterogeneous preparations limit conclusions about glucose control, lipids, blood pressure, infection prevention or organ protection. These areas warrant adequately powered trials with clinically meaningful endpoints and careful monitoring of concomitant medicines.

Anticancer Research

Withaferin A and other withanolides have shown cytotoxic, pro-apoptotic, anti-angiogenic and cell-cycle effects in multiple experimental cancer models. The project cites studies involving breast cancer, glioblastoma and other tumor systems. [28]

These findings are important for drug-discovery research but do not establish Ashwagandha as an anticancer treatment in humans. Extract composition, pharmacokinetics, tumor biology and therapeutic index remain major barriers to clinical translation. Ashwagandha should therefore not replace oncology-directed treatment.

Clinical Evidence

Table 3: Clinical evidence and key limitations of Ashwagandha.

Indication/outcome	Human evidence	Main finding	Key limitation
Stress/anxiety	Systematic reviews/meta-analyses of RCTs	Improvement in validated stress/anxiety outcomes and cortisol in selected trials	Heterogeneous extracts, doses and trial quality
Sleep	5-RCT meta-analysis; later reviews	Small overall sleep benefit; stronger signal in insomnia and ≥600 mg/day studies	Small samples; heterogeneity; limited long-term data
Physical performance	Systematic reviews/meta-analyses	Possible improvement in selected endurance/strength-related outcomes	Outcome- and population-dependent; prediction intervals may include no effect
Male fertility	Systematic review; small clinical literature	Signals for semen parameters and hormones	Few RCTs and limited sample sizes
Neurodegeneration	Mostly preclinical	Neuroprotective mechanisms and behavioral/biochemical signals	Insufficient disease-modifying human evidence
Diabetes/cardiovascular/immune	Mostly preclinical or small studies	Potential metabolic, endothelial and immune effects	Insufficient evidence for routine therapeutic claims
Cancer	Predominantly experimental	Cytotoxic and signaling effects of withanolides	No basis for replacement of standard cancer therapy

Safety, Adverse Effects and Herb–Drug Interactions

The project describes Ashwagandha as generally well tolerated at recommended doses and notes gastrointestinal symptoms, nausea, diarrhea and drowsiness among reported adverse effects. Short-term clinical trials of standardized extracts have generally

reported acceptable tolerability. For example, a 2024 clinical safety study in 18 healthy men receiving 500 mg twice daily for one month found no clinically important changes in body weight, blood counts, ALT or AST, although a small alkaline-phosphatase change was observed. [15]

However, safety cannot be inferred solely from short-term RCTs. LiverTox, updated in December 2024,

identifies rare clinically apparent liver injury associated with products labeled as containing Ashwagandha. Reported cases commonly begin 2–12 weeks after initiation and often show cholestatic or mixed injury with jaundice and pruritus; most resolve after discontinuation, but severe and fatal cases have occasionally been reported, particularly in people with pre-existing liver disease. [14]

A 2026 scoping review of peer-reviewed clinical literature through December 2025 identified 25 patients across 13 publications and found that cholestatic or mixed patterns predominated. This evidence does not imply that hepatotoxicity is common, but it establishes that the risk should be acknowledged in a publication-ready review and in patient counseling.

Authoritative guidance also recommends avoiding Ashwagandha during pregnancy and not using it while breastfeeding, and advises caution or avoidance in people with autoimmune or thyroid disorders and around surgery. Potential interactions have been described with sedatives, anticonvulsants, immunosuppressants, medicines for diabetes or blood pressure, and thyroid hormone medicines.

From a pharmacovigilance perspective, clinicians should ask about herbal supplements when evaluating unexplained liver-test abnormalities, sedation or endocrine changes. Suspected adverse reactions should be documented with the exact product name, dose, batch information and concomitant medicines whenever possible.

Quality Control and Regulatory Considerations

Chemical variability is one of the central limitations of botanical therapeutics. HPLC methods can quantify withaferin A, withanolide A, withanolide D and other markers, while validated multi-marker methods and metabolomic fingerprints can provide stronger identity and consistency controls. [7,8,17,18]

For research and clinical translation, a minimum quality framework should include authenticated botanical identity, specified plant part, extraction solvent/process, extract ratio, marker-compound assay, microbial and heavy-metal testing, pesticide/adulterant controls and batch traceability. Clinical papers should report the commercial or laboratory preparation sufficiently to allow replication. The phrase 'Ashwagandha 600 mg' is inadequate unless the nature of the extract and its standardization are stated.

Pharmacopeial approaches and validated chromatographic procedures provide a foundation for

Front Multidiscip Res Stud - Vol. 3 - No. 2, Jul-Dec 2026

standardization, but analytical harmonization across manufacturers and trials remains important. [8,18] Future work should combine chromatographic fingerprinting with pharmacological biomarkers and pharmacokinetic characterization.

Research Gaps and Future Directions

Several priorities emerge from the evidence. First, clinical trials should use chemically characterized preparations and report the content of relevant withanolides. Second, trial designs should be adequately powered, preregistered and sufficiently long to assess persistence of benefit and delayed adverse events. Third, outcomes should be clinically meaningful rather than relying only on surrogate biochemical markers. Fourth, adverse-event definitions and laboratory monitoring should be standardized, particularly for liver, thyroid and endocrine outcomes. Fifth, future trials should compare standardized preparations rather than treating all Ashwagandha products as equivalent.

Additional research is needed on pharmacokinetics, active-metabolite exposure, food effects, interactions with commonly prescribed medicines and the influence of genotype, geography and extraction method. For neurodegenerative disease, metabolic disease and cancer, translation should proceed through rigorously designed early-phase studies before broad therapeutic claims are made.

Conclusion

Withania somnifera is a chemically rich medicinal plant whose traditional importance has been accompanied by rapidly expanding pharmacological and clinical research. Its withanolides and associated metabolites provide plausible molecular bases for antioxidant, anti-inflammatory, neuroprotective, immunomodulatory and cytotoxic effects, while human studies provide the clearest contemporary signal for stress, anxiety and sleep-related outcomes. Evidence for exercise performance and reproductive health is promising but remains dependent on formulation and study context, whereas claims for neurodegenerative disease, diabetes, cardiovascular disease and cancer are still substantially preclinical.

The modern evidence base also requires a balanced safety perspective. Most short-term controlled studies report acceptable tolerability, but rare clinically apparent liver injury is documented and clinically important precautions exist for pregnancy, breastfeeding, thyroid or autoimmune disorders and potential drug interactions. Thus, Ashwagandha should be regarded as a promising, indication-specific

botanical intervention whose clinical value depends on authenticated material, standardized preparations, appropriate patient selection and continued pharmacovigilance. Larger, longer and methodologically rigorous trials are needed to define optimal preparations, doses, efficacy and long-term safety.

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Conflict of Interest

None declared.

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