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Phytochemistry and Pharmacology of *Withania somnifera*: An Updated Review

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ABSTRACT

Withania somnifera, known in Ayurveda as ashwagandha, is among the most widely used medicinal plants of South Asia, and its roots and leaves have attracted steady laboratory interest over several decades. This narrative review brings together published work on its chemistry and pharmacology and asks how far the reported activities can be trusted as evidence for use in people. The plant is rich in withanolides, steroidal lactones of which withaferin A and withanolide A are the best studied, together with withanosides, sitoindosides and a minor alkaloid fraction, and the profile differs between roots and leaves and between populations. Cell and animal studies describe effects on stress responses, neuronal growth, inflammation, immune function and cancer cell survival, and a few small human studies point in similar directions. Most of this work rests on crude extracts of uncertain composition, on concentrations that are hard to relate to doses taken by people, and on trials that are short and small. The review concludes that the chemistry is well characterised, that the pharmacology is plausible but unevenly supported, and that standardised extracts, reported composition and adequately sized controlled trials are the main gaps. It reports no new data.

Keywords: *Withania somnifera*; Ashwagandha; Withanolides; Withaferin A; Adaptogen; Ethnopharmacology; Narrative review

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Article Class: Review Article

1. Introduction

Few medicinal plants have as long a recorded history as ashwagandha. *Withania somnifera* (L.) Dunal, a shrub of the nightshade family, grows in the drier parts of India, the Middle East and Africa, and its root has been used in Ayurveda for centuries as a Rasayana, a rejuvenating

tonic (1, 2). Its roots, leaves and fruit all appear in traditional preparations, and it is often called Indian ginseng (3).

A large share of the drugs introduced in recent decades trace back, directly or indirectly, to natural products (4, 5), and a herb with a thousand-year reputation is an obvious place to look for new chemistry.



The laboratory literature on ashwagandha has grown accordingly, with reports of activity against stress, neurodegeneration, inflammation, infection and cancer (6).

Growth in the number of papers is not the same as growth in knowledge, however. A report that an extract kills cancer cells in a dish, or calms a stressed rat, says little about what a capsule does in a person. This review sets out what is known about the chemistry of the plant, summarises the main pharmacological findings, and asks how much weight each can carry. The aim is a fair account of what is known and what is merely repeated. No local or original data are reported here.

2. Literature Review

2.1 Botany and Traditional Use

In Ayurvedic practice it is given alone or in compound formulas, and it is classed among the plants thought to build resilience rather than treat a single complaint (1). That framing helps explain why modern studies so often look for general effects on stress and ageing instead of a specific disease target. Traditional use is a reason to study a plant, not a result of having studied it. Ayurveda and other traditional systems use concepts of balance that do not map neatly onto biomedical outcomes (2).

2.2 Constituents of the Plant

The characteristic compounds are the withanolides, a family of steroidal lactones built on an ergostane skeleton. Withaferin A, with its epoxide and unsaturated ketone in the first ring, and withanolide A are the best known (7). Alongside them are glycosylated withanolides called withanosides, acylsterylglucosides called sitoindosides, a dimeric thiowithanolide named ashwagandhanolide, and a small alkaloid fraction (1, 8). Table 1 gives the main classes and the plant parts from which they are usually reported.

Quantities are another matter. Chromatographic methods for withanolides in the plant show that content differs considerably between samples and between plant parts (9), and metabolic fingerprinting of leaf and root extracts confirms that the two organs carry rather different chemical profiles (10). A study of leaves may therefore examine different chemistry from a study of roots. Such differences look small on paper, yet they decide which chemistry a given study was really examining.

Table 1. Main constituent classes reported from *Withania somnifera*.

Class	Examples	Plant part
Withanolides	Withaferin A, withanolide A (7, 9)	Leaf and root
Withanolide glycosides	Withanosides (10)	Mainly root
Acylsterylglucosides	Sitoindosides (11)	Root
Dimeric withanolides	Ashwagandhanolide (8)	Root
Alkaloids	Minor fraction (1)	Root
Phenolics and sugars	Present, little studied (10)	Leaf and root

Note: Qualitative summary of the cited phytochemical literature. Content varies with plant part, population and growing conditions, so no amounts are given.

2.3 Effects on the Nervous System and Stress

The most frequently cited claim is that ashwagandha acts as an adaptogen, a term for substances said to raise non-specific resistance to stress (12). In rats subjected to chronic stress, treatment with a root extract was reported to reduce several stress-related disturbances (11), and glycowithanolide preparations produced anxiolytic and antidepressant-like effects in standard behavioural tests (13). Reduced lipid peroxidation in stressed animals has also been described (14).



Work on neurons goes a step further. Withanolide A was reported to promote regrowth of neurites and the reconstruction of synapses in cultured cells damaged by amyloid peptide (15), and withanamides from the fruit protected cultured cells from beta-amyloid toxicity (16). Defined extracts altered cholinergic markers in rat brain (17). These are leads from cell and rodent work, and the step from a protected cell line to a person with a neurodegenerative disease is long and has rarely been tested.

2.4 Immune and Inflammatory Activity

Several groups have reported that extracts alter immune function. Early work in mice described effects on immune parameters (18, 19), and an aqueous extract was later reported to favour Th1-type activity (20). A small study in healthy volunteers reported changes in markers of lymphocyte activation (21). The direction of change depends on the extract and the model.

2.5 Anticancer Activity

Withaferin A has driven much of the interest in cancer. It was reported to inhibit angiogenesis (22), to target the proteasome (23), to dampen NF-kappaB signalling through IkappaB kinase (24, 25), and to cause oxidative stress and apoptosis in leukaemia cells (26). Withanolides from the leaves inhibited growth of several human tumour cell lines (27), and a leaf extract killed cancer cells more readily than normal cells in culture (28, 29).

Those results have to be read alongside a caution. Withaferin A carries a reactive enone, and such compounds can hit many targets non-specifically (30). Selective killing in a dish is a long way from a treatment, and the concentrations used in culture are often hard to relate to anything achievable in the body (31). The point is not that a study is poor, only that its result travels less far than its abstract suggests.

Other reports describe antioxidant activity (32), altered thyroid hormone concentrations in mice (33), improved semen quality in a study of infertile men (34), and better physical performance in healthy young adults given a combination product (35). The human studies are small and short.

3. Materials and Methods

3.1 Scope and Question

The review asks two linked questions. What is the chemistry of *Withania somnifera* as reported in the published literature, and what pharmacological activities have been described for its extracts and constituents? It does not attempt to estimate treatment effects.

3.2 Literature Assembly

This is a narrative synthesis. No formal systematic search was run, no registered protocol exists and no database was searched with a fixed string. Sources were gathered from the authors' knowledge of the field and by following citations from reviews, a route that finds relevant work efficiently but reproduces the biases of its starting papers (36). Only work published up to 2012 is considered. A systematic review would follow a standard such as PRISMA (37), which this one does not claim to meet. None of these steps is difficult, but each one is easy to skip.

3.3 Appraisal Framework

Each body of evidence was read with a short set of questions: was the material identified and its composition reported, was the dose relevant to human exposure, was the design able to support a causal reading, and was the study reported completely enough to judge bias? The questions draw on guidance for randomised trials (38, 39) and on critiques of small studies (40), and were applied informally. Table 2 and Table 3 summarise



the result.

Table 2. Reported activities and the kind of evidence behind each.

Activity	Main evidence	Caveat
Anti-stress, anxiolytic	Rodent models (11, 13)	Crude extracts; doses vary
Neuronal growth	Cultured neurons (15, 16)	Concentrations high
Immune modulation	Mice, cells, a human study (19, 21)	Direction depends on model
Antitumour	Cell lines (23, 28)	Selectivity unclear in vivo
Reproductive function	Small human study (34)	Design limits inference
Physical performance	Healthy adults (35)	Combined product

Note: The final column is the authors' reading of the cited studies, not a ranking of their quality.

4. Results

4.1 From Plant Material to Claim

Reading across the literature, the path from plant to clinical claim has five steps, and Figure 1 shows each with the check that belongs to it. Many reports are strong at one step and silent on the next: an extract is characterised carefully and then tested at an unrealistic concentration, or tested in people without saying what the capsule contained.

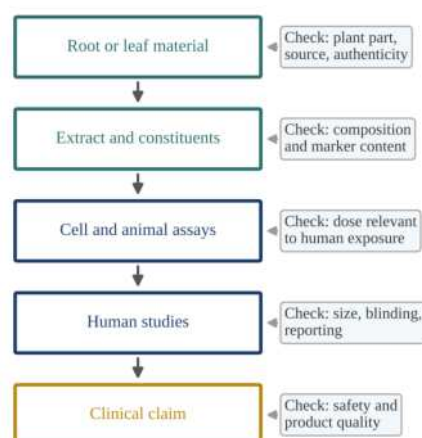


Figure 1. From plant material to a clinical claim, with the checks that sit between the steps (schematic, not data).

4.2 What the Activities Rest On

Figure 2 sets the main activities against the level at which they have been studied. Anti-stress and neuronal effects rest mostly on rodent and cell work. Antitumour effects rest almost entirely on cell lines, and human data, where they exist, are thin. The matrix records relative volume of work and nothing more.

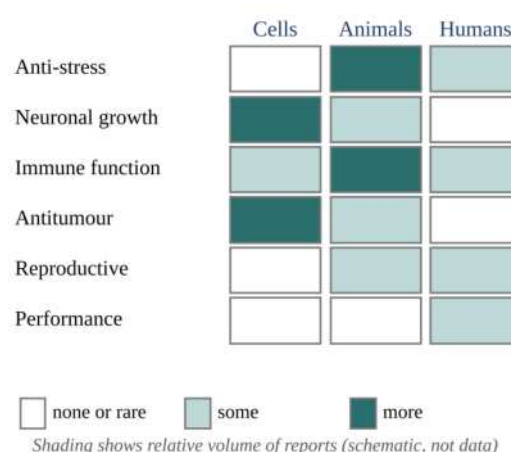


Figure 2. Qualitative matrix of reported activity by level of evidence (schematic, not data).

4.3 Quality of the Evidence

Table 3 collects the recurring weaknesses. The first is that extracts are often described only by name, so a second laboratory cannot tell whether it has the same material (9, 10). The second is dose: in vitro concentrations frequently exceed what could plausibly reach tissue after oral dosing (31). This is why the same plant can look impressive in one report and unremarkable in the next.

Small trials add their own problem. When samples are small, the effects that reach publication tend to be exaggerated, and positive findings are more likely to be false than they look (40). Trial reports that omit allocation or blinding details make bias impossible to judge (38, 39). Read this way, the absence of an effect in a small trial is not evidence of absence.

**Table 3.** Common weaknesses in the evidence and what would address them.

Weakness	Consequence	Remedy
Unstandardised extract	Dose and identity unknown (9, 10)	Report marker content
Unrealistic in vitro dose	Effect may not translate (31)	Relate to exposure
Reactive compounds	Non-specific activity (30)	Counter-screens
Small trials	Exaggerated effects (40)	Adequate sample size
Incomplete reporting	Bias hard to judge (38, 39)	Follow reporting guides
Contaminated products	Safety risk (41, 42)	Test each batch

Note: Weaknesses are those discussed in the cited methodological literature, not attributed to any single study.

4.4 Safety and Product Quality

Toxicity work in rats and mice reported tolerance of root extract at the doses tested (43), and the human studies cited above did not highlight serious harm. Absence of reported harm in short studies is not proof of safety. The broader herbal literature warns that natural does not mean harmless (44) and that herbs can interact with prescribed drugs (45).

Quality is a separate matter. Surveys of Ayurvedic products sold in Western markets found detectable lead, mercury or arsenic in a notable share of those tested (41, 42). These surveys were not specific to ashwagandha, but they show that label and capsule can differ. These points apply with equal force to any herbal product, not only to this one. It is a habit worth keeping even when the answer seems obvious.

5. Discussion

5.1 Interpretation

The reading that best fits the literature is a conditional one. The chemistry of ashwagandha is solidly characterised, and several of its constituents have shown real

biological activity under laboratory conditions. Figure 3 expresses how the claims depend on one another: a clinical claim sits on top of human trials, which sit on animal and cell work, which sit on well-identified material. If the base is weak, everything above inherits the weakness. A reader weighing a report needs an answer to a plain question: would this result hold for a person taking the herb?

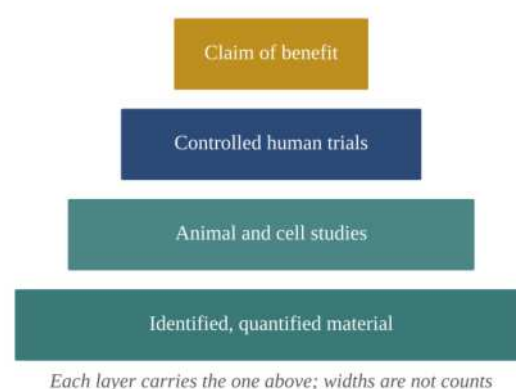


Figure 3. Layered view of what a claim of benefit rests on (schematic, not data).

5.2 Limitations

This review inherits the limits of its method. The literature was not searched systematically, so relevant studies may be missing, and the selection may favour well-known groups and journals. Quality was judged informally, and work after 2012 is not covered. Much of the evidence is on extracts, so findings on one preparation should not be read onto another. That is a modest claim, and it is the one the evidence will currently bear. Reviews of this kind are more useful when they say where the evidence stops than when they smooth it over.

5.3 Future Work

Three needs stand out. The first is standardisation: extracts used in research should be defined by marker content, plant part and origin, and ideally deposited so



others can obtain the same material (9, 10). The second is better preclinical practice, with realistic concentrations and counter-screens for non-specific activity (30, 31). The third is adequately sized, blinded, fully reported human trials of well-defined products (39, 45). Nothing in this reading argues against further work on ashwagandha; it argues for measuring carefully what the plant does.

6. Conclusion

Ashwagandha is a chemically rich plant with a long traditional history and a real, if uneven, body of laboratory work behind it. The human evidence is still thin, and the claims most often repeated in marketing rest on the weakest links. Defined material, realistic doses and properly reported trials would turn plausible findings into established ones.

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9. Conflict of Interest

The authors declare no conflict of interest.

10. Author Contributions

L.C. conceived the review and wrote the sections on pharmacology. L.S. wrote the sections on botany and phytochemistry. T.B. wrote the sections on extract quality, product safety and appraisal. All authors revised the manuscript and approved the final version.

11. Ethics Statement

This is a review of published literature. No human participants or animals were involved and no ethical approval was

required.

12. Data Availability

No new data were generated. All sources are cited in the reference list.

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