

RESEARCH MONOGRAPH . COMPOUND PROFILE

Ashwagandha (Withania somnifera)

*A root extract from Withania somnifera
standardized to withanolides, with
documented anxiolytic, cortisol-lowering,
and testosterone-supporting effects.*

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COMPOUND CLASS	Ayurvedic adaptogenic root extract

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ABSTRACT

Ashwagandha (*Withania somnifera*) is a small evergreen shrub root used in Ayurvedic medicine for stress, anxiety, fatigue, and physical performance. The active constituents are withanolides (notably withaferin A, withanolide A, and others), with commercial extracts standardized to total withanolide content (typically 5 percent or higher). The KSM-66 (Ixoreal Biomed) and Sensoril (Natreon) extracts are the most extensively studied in clinical trials. Multiple randomized trials demonstrate cortisol reduction, anxiety reduction (DASS-21, Hamilton Anxiety), modest testosterone elevation in men with low baseline, and improvements in muscle strength and endurance. Mechanism is multimodal including GABA-A receptor allosteric modulation, modest serotonergic effects, and HPA axis modulation. Doses are typically 300 to 600 mg of standardized extract per day.

1. Compound Identification

Ashwagandha (*Withania somnifera*) is described as ayurvedic adaptogenic root extract. A root extract from *Withania somnifera* standardized to withanolides, with documented anxiolytic, cortisol-lowering, and testosterone-supporting effects.

1.1 Class summary

Ayurvedic adaptogenic root extract

1.2 Subtitle

A root extract from *Withania somnifera* standardized to withanolides, with documented anxiolytic, cortisol-lowering, and testosterone-supporting effects.

2. Abstract

Ashwagandha (*Withania somnifera*) is a small evergreen shrub root used in Ayurvedic medicine for stress, anxiety, fatigue, and physical performance. The active constituents are withanolides (notably withaferin A, withanolide A, and others), with commercial extracts standardized to total withanolide content (typically 5 percent or higher). The KSM-66 (Ixoreal Biomed) and Sensoril (Natreon) extracts are the most extensively studied in clinical trials. Multiple randomized trials demonstrate cortisol reduction, anxiety reduction (DASS-21, Hamilton Anxiety), modest testosterone elevation in men with low baseline, and improvements in muscle strength and endurance. Mechanism is multimodal including GABA-A receptor allosteric modulation, modest serotonergic effects, and HPA axis modulation. Doses are typically 300 to 600 mg of standardized extract per day.

3. Mechanism of Action

GABA-A allosteric modulation; HPA axis modulation; modest serotonergic effects. Withanolide constituents.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

300 to 600 mg standardized extract per day.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Pratte MA, et al. An alternative treatment for anxiety: a systematic review of human trial results reported for the Ayurvedic herb ashwagandha. J Altern Complement Med 2014.

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