

Herb–Drug Interactions in Polypharmacy: Focus on Ashwagandha in Stress and Cognitive Disorders

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Abstract

Polypharmacy among older adults and patients with chronic diseases increases the likelihood of herb–drug interactions, especially in regions where herbal medicines are widely used. Ashwagandha (*Withania somnifera*), an adaptogenic herb from Ayurvedic medicine, is increasingly popular for managing stress, anxiety, depression, insomnia, and age-related cognitive decline. Its pharmacological actions involve modulation of the hypothalamic–pituitary–adrenal axis, enhancement of antioxidant activity, and neuroprotection. Evidence suggests Ashwagandha may improve cognitive performance and reduce stress, but concurrent use with conventional drugs can alter pharmacokinetics through cytochrome P450 enzyme modulation, thyroid hormone influence, and sedative synergy. This review summarizes mechanisms, clinical evidence, and potential herb–drug interactions to promote safe integration of Ashwagandha in multi-drug regimens.

Keywords: Ashwagandha, *Withania somnifera*, polypharmacy, herb–drug interaction, stress, cognitive disorders.

Introduction

Polypharmacy, the concurrent use of multiple medications, is common among elderly populations and individuals with chronic illnesses. While it addresses complex health needs, it also increases the risk of adverse drug reactions, including herb–drug interactions. In regions such as South Asia and the Caribbean, herbal medicines are frequently combined with prescribed drugs without medical supervision.

Ashwagandha, a key Rasayana herb in Ayurveda, is used for stress reduction, improved cognition, and overall vitality. Its increasing popularity has raised concerns about potential interactions with conventional pharmacotherapy. This paper examines the pharmacological basis, clinical evidence, and interaction risks of Ashwagandha use in polypharmacy.

Mechanisms and Pharmacology

Ashwagandha contains bioactive compounds such as withanolides, alkaloids, and sitoindosides. These compounds exhibit adaptogenic, anti-inflammatory, antioxidant, and neuroprotective activities.

Mechanistically, Ashwagandha reduces cortisol levels, modulates the hypothalamic–pituitary–adrenal axis, enhances cholinergic signaling, and improves mitochondrial function in neurons.

In stress and cognitive disorders, these effects can translate into improved mood, memory, and resilience to oxidative damage. However, its pharmacological effects overlap with several drug classes, including anxiolytics, antidepressants, antiepileptics, thyroid hormones, and immunomodulators, which may lead to clinically significant herb–drug interactions.

Clinical Evidence

Several randomized controlled trials have shown that Ashwagandha supplementation significantly reduces perceived stress and serum cortisol. Chandrasekhar et al. (2012) demonstrated a 44% reduction in stress scores in adults after eight weeks of supplementation.

Cognitive benefits have been reported in patients with mild cognitive impairment, where Ashwagandha improved memory, attention, and information-processing speed. Animal models also support neuroregenerative effects, including dendritic growth and synaptic repair. While these outcomes are promising, concurrent drug therapy can complicate clinical benefits due to altered pharmacokinetics and dynamics.

Herb–Drug Interactions

Cytochrome P450 modulation: May alter metabolism of drugs such as antidepressants, antiepileptics, and anticoagulants.

Sedative synergy: Co-administration with CNS depressants may cause excessive drowsiness.

Thyroid effects: May increase thyroxine levels, interacting with thyroid medication.

Antihypertensive interaction: Can enhance hypotensive effects.

Hypoglycemic interaction: May potentiate effects of antidiabetic agents.

Immunomodulatory interference: Could reduce the efficacy of immunosuppressants.

Discussion

The therapeutic potential of Ashwagandha in stress and cognitive disorders is supported by both traditional use and modern evidence. However, in polypharmacy contexts, the risk of herb–drug interactions must be carefully evaluated.

Clinicians should obtain a complete medication history, including herbal supplements, and educate patients about possible risks. Further studies are needed to clarify interaction mechanisms, define safe dosage ranges, and establish clinical guidelines for combined use.

Conclusion

Ashwagandha is an effective adaptogen with promising benefits in stress reduction and cognitive enhancement. However, its concurrent use with multiple drugs may lead to significant interactions, particularly in populations at risk of polypharmacy. Responsible use, guided by evidence and medical oversight, can help maximize benefits while minimizing risks.

HERB-DRUG INTERACTIONS



Polymedicated
older patients



Polypharmacy



Ashwagandha
Withania somnifera



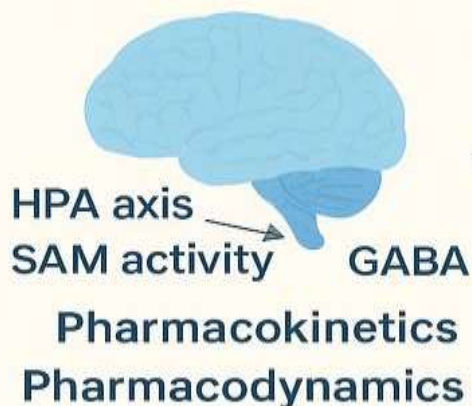
- Stress
- Anxiety
- Depression
- Insomnia
- Cognitive decline



Drug reconciliation



Pharmacovigilance



Keywords: Ashwagandha, Withania somnifera, polypharmacy, herb-drug interactions, cognitive disorders, stress, pharmacokinetics, pharmacodynamics, adaptogen, Caribbean, pharmacovigilance

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