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File: ■ Ashwagandha (*Withania somnifera*, Solanaceae)
■ Stress and Anxiety
■ Safety Profile

HC 052611-787

Date: June 30, 2026

RE: Ashwagandha Root Extract Was Found to Be Generally Safe and Well-tolerated by Adults Diagnosed with Borderline to Moderate Stress and Anxiety

Pakhale K, Salve J, Ademola J, Parraca, Langade D. Safety of 8-week administration with ashwagandha (*Withania somnifera*) root extract in adults with stress and anxiety: findings from a prospective, randomized, multi-center, double-blinded, placebo-controlled study. [published online April 6, 2026.] *Phytother Res*. doi: 10.1002/ptr.70315.

Ashwagandha (*Withania somnifera*, Solanaceae) is an adaptogenic herb traditionally used to treat fatigue, weakness, insomnia, and anxiety. It has been used in Ayurvedic medicine to enhance longevity, vitality, and mental well-being. Studies show that ashwagandha root extract (ARE) has anxiolytic, neuroprotective, antioxidant, and anti-inflammatory effects. Previous studies have reported transient adverse effects (AE) from ARE; however, safety and tolerability were not fully addressed in some of those studies. Therefore, this prospective, randomized, multi-center, double-blind, placebo-controlled trial assessed the safety and tolerability of ARE for treating adults diagnosed with borderline to moderate stress and anxiety.

The multi-center study was conducted from June 25, 2020 through April 4, 2024. Study locations included sites in India, Australia, the United States, Portugal, and Africa. Most of the patients were from India (80%). Participants were recruited through outpatient departments, referrals, posters placed at hospitals and clinics, community advertisements, and digital methods. Patients aged 18 to 65 years with a baseline Hamilton Anxiety Rating Scale (HAM-A) total score between 14 and 30 and a Cohen's Perceived Stress Scale (PSS) score ≥ 13 were eligible. Patients experiencing signs and symptoms of high stress and who were willing to participate were also included. Patients with depressive episodes, suicidal tendencies, panic disorder, social phobia, obsessive-compulsive disorder, alcohol dependency, schizophrenia, mania, or post-traumatic stress disorder were excluded. Additionally, those with a history of drug or alcohol abuse, taking medications or supplements, or who consumed a diet that may interfere with the study medication were ineligible. Finally, patients diagnosed with chronic or malignant disease, who had undergone surgery during the prior year, or who practiced meditation or relaxation techniques for ≥ 3 months were also excluded.

A total of 1002 patients were randomized to the ARE (n = 498) or placebo (n = 504) group. Patients assigned to the ARE group consumed KSM-66® (300 mg; Ixoreal Biomed; Los Angeles, California). Patients in the placebo group were given starch capsules (300 mg). Both groups were instructed to take their respective capsules twice daily, after breakfast and dinner, for eight weeks. Patients were seen at baseline and eight weeks. Hematological parameters were assessed at baseline and eight weeks. AEs and severe AEs (SAEs) were recorded during each visit and over the phone at four weeks. Adherence was assessed during the phone call at four weeks.

Primary outcome measures were safety and tolerability and changes in laboratory parameters. Results of the Global Assessment of Tolerability to Therapy (GATT) assessment were secondary outcome measures. Hematological parameters included white blood cell count, red blood cell count, hematocrit, hemoglobin, platelet count, serum aspartate aminotransferase (AST), and alanine aminotransferase (ALT).

For the 892 participants (474 ARE and 418 placebo) with laboratory data available, no significant changes were observed within or between the two groups. There were no significant differences in the GATT assessments between groups. The ARE was well-tolerated; patients generally rated the treatment as “good” or “excellent.”

No SAEs were recorded. Seventy-four (7.4%) AEs were reported, including 46 (9.2%) in the placebo group and 28 (5.6%) in the ARE group. Nausea, dry mouth, and headache were the most reported AEs. Of those who experienced AEs, 33 patients in the placebo and 24 in the ARE groups reported one AE, five in the placebo and two in the ARE groups reported two AEs, and one patient in the placebo group reported three AEs. There were no significant differences between the two groups in terms of reported AEs or relative risk of experiencing an AE.

The authors conclude that KSM-66 is safe and well-tolerated for adults diagnosed with borderline to moderate stress and anxiety. Several study limitations were noted, including its short duration, primary Indian population, and incomplete paired laboratory data. This study concentrated on within-group comparisons; therefore, between group comparisons should be interpreted with caution. Extended studies are needed to assess long-term safety and efficacy of ashwagandha root extract to treat mild to moderate stress and anxiety.

The authors declare no conflicts of interest.

—*Samaara Robbins*

Referenced article can be accessed at <https://onlinelibrary.wiley.com/doi/10.1002/ptr.70315>.