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

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RE: Ashwagandha Reduces Perceived Stress and Cortisol Levels in Healthy Adults

Chandrasekhar K, Kapoor J, Anishetty S. A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of ashwagandha root in reducing stress and anxiety in adults. *Indian J Psychol Med*. 2012;34(3):255-262.

Ashwagandha (*Withania somnifera*, Solanaceae) root is an adaptogen, which is a substance that helps the body cope with stress. This study was published in 2012, and the authors state that at that time clinical trials evaluating ashwagandha for the treatment of stress and anxiety were limited. Hence, the purpose of this prospective, randomized, double-blind, placebo-controlled study was to evaluate the safety and efficacy of a full-spectrum extract of ashwagandha root in reducing stress and anxiety in healthy adults.

Subjects (n = 64; aged 18-54 years) with a history of chronic stress participated in this study conducted at Asha Hospital; Hyderabad, India. The subjects were "a wide cross-section of the population, which included doctors, students, self-employed persons, executives and employees of information technology firms," who attended a stress-management talk. Included subjects had no psychiatric conditions other than stress, < 15 points on the World Health Organization-5 well-being index (WHO-5), and ≥ 14 points on the Perceived Stress Scale (PSS). Excluded subjects had any chronic physical, hormonal, or psychiatric illness; were using "certain" hormonal birth control; were taking any medication on a regular basis; were taking any herbal preparations or formulations containing ashwagandha, ginseng (*Panax* spp., Araliaceae) root, ginkgo (*Ginkgo biloba*, Ginkgoaceae) leaf, bacopa (brahmi; *Bacopa monnieri*, Plantaginaceae) aerial plant parts, or related herbs; were pregnant or lactating; had substance dependence; or had abnormal laboratory or electrocardiogram (ECG) test results.

Subjects (41 males and 23 females) were randomly assigned to receive placebo ("capsules containing a neutral substance") or 600 mg/day ashwagandha root extract (KSM-66® ashwagandha extract; Ixoreal Biomed; Hyderabad, India) for 60 days. The extract "is produced by a unique extraction process, based on the principles of 'green chemistry', without using alcohol or any synthetic solvents," and standardized to contain at least 5% withanolide. The effect of ashwagandha on stress was evaluated by assessing (at baseline and day 60) serum cortisol levels and scores on the PSS questionnaire, the Depression Anxiety Stress Scale (DASS) questionnaire, and the 28-item version of the General Health

Questionnaire (GHQ-28). Safety of the ashwagandha extract was assessed based on laboratory findings and incidence of adverse events (AEs).

A total of 61 subjects completed the trial; an accounting of the dropouts was not given. Compliance data was not reported.

At baseline, the mean score for self-perceived stress on the PSS was classified as "moderate" for both groups; however, the mean score was significantly higher in the placebo group ($P = 0.009$). At study end, the ashwagandha group had a significantly greater reduction in total PSS score compared with the placebo group ($P < 0.0001$). It is not clear whether the higher score for the placebo group at baseline had an impact on the outcome.

There was no significant difference between groups in GHQ-28 or DASS scores. At study end, the ashwagandha group had a significantly greater reduction in GHQ-28 total score and each item-subset score (somatic, anxiety and insomnia, social dysfunction, and severe depression) compared with placebo ($P \leq 0.0001$ for all). Similarly, the ashwagandha group had a significantly greater reduction in the DASS total score and each item-subset score (depression, anxiety, and stress) compared with placebo ($P < 0.0001$ for all).

A strength of this study is that the 3 instruments used to assess self-perceived stress were all ratio scales (based on the frequency of stress-signaling events, with a score of 0 indicating a total absence of events). Therefore, each score may be interpreted as the absolute degree of self-assessed stress.

Cortisol is used as a biological marker of stress, and as such, provides an objective measure of stress. At study end, the ashwagandha group had a significantly greater reduction in cortisol levels compared with the placebo group ($P = 0.002$).

AEs were mild, infrequent, and considered unrelated to treatment; there was no significant difference in the incidence of AEs between groups. There were no clinically significant changes in laboratory parameters.

The authors conclude that this specific full-spectrum ashwagandha root extract can safely improve resistance to stress, and as a result, improve self-assessed quality-of-life measures. Strengths of the study are the use of 3 instruments to measure self-assessed stress, the evaluation of cortisol levels to provide an objective measure of stress, and that the treatment was evaluated under real-world conditions rather than artificially induced experimental stress. Limitations of the study were the relatively small population size (n = 32/group), the relatively short duration, that 64% of the population were men, and that compliance, dropout, and full demographic data were not provided. The study should be repeated in a larger, gender-balanced population for a longer period of time.

—Heather S. Oliff, PhD

Referenced article can be accessed at http://www.ijpm.info/article.asp?issn=0253-7176;year=2012;volume=34;issue=3;spage=255;epage=262;aulast=Chandrasekhar.