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File: ■ Ashwagandha (*Withania somnifera*)
■ Stress
■ Adaptogens

HC 070593-387

Date: October 30, 2009

RE: Ashwagandha Extract Dose-Dependently Improves Stress Parameters

Auddy B, Hazra J, Mitra A, Abedon B, Ghosal S. A standardized *Withania somnifera* extract significantly reduces stress-related parameters in chronically stressed humans: A double-blind, randomized, placebo-controlled study. *JANA.* 2008;11(1):50-56.

Ashwagandha (*Withania somnifera*) has an antistress adaptogenic effect. According to Ayurvedic medicine, it promotes stress relief, restores homeostasis, and increases resistance to adverse environmental factors. However, it has not been evaluated in a randomized, controlled trial of chronically stressed people. Hence, the objective of this study was to evaluate the effect of ashwagandha on indicators of stress and anxiety in chronically stressed adults.

Men and women (n = 130, aged 18 to 60 years) with a Bengali version of a modified Hamilton anxiety (mHAM-A) scale for stress score of 24 to 42 participated in this double-blind, randomized, placebo-controlled study between November 2004 and October 2006. The study was conducted at the Central Research Institute (Ayurveda), Ministry of Health and Family Welfare, Bidhan Nagar, Kolkata, India. Patients were treated with placebo (excipients) or 125 mg/day, 250 mg/day, or 500 mg/day ashwagandha (Sensoril®; Natreon Inc.; New Brunswick, New Jersey and Essentra®; NutraGenesis, LLC; Brattleboro, Vermont) for 60 days. Ashwagandha was standardized to a minimum of 8% withanolide glycosides and 32% oligosaccharides, and a maximum of 2% withaferin A. Stress and anxiety were assessed with the mHAM-A and blood was drawn to measure biochemical markers of stress and anxiety.

A total of 32 patients dropped out of the study including 10 who were lost to follow-up, 6 from protocol violations, and 4 due to doctor's decisions. The other 12 withdrew due to lack of efficacy, and 9 of these were in the placebo group. Dropouts were not included in the analysis. Patients treated with ashwagandha had improved well-being at day 30 and 60. There was a statistically significant dose-dependent improvement in mHAM-A scores

of patients in the ashwagandha groups, whereas the placebo group had no significant improvement over the course of the study. Even the lowest dose (125 mg/day) had a significant decrease ($P < 0.001$) in mean sum mHAM-A score from baseline (29.9) to Day 30 (18.1, -39.5%) to Day 60 (11.3, -62.2%) compared to placebo.

Similarly, there was a dose-dependent effect on the biochemical parameters of stress. Between baseline and Day 60, the 125 mg/day group decreased significantly ($P < 0.05$) more than the placebo group for mean serum cortisol (-14.5%), serum very low-density lipoprotein cholesterol (VLDL-C) (-8.9%), systolic blood pressure (-1.6%), diastolic blood pressure (-5.6%), and ($P < 0.001$) serum C-reactive protein (-31.6%) and pulse rate (-6.0%), and increased significantly ($P < 0.05$) more than the placebo group for mean serum dehydroepiandrosterone sulfate (DHEAS) (13.2%) and hemoglobin (6.3%). In addition to these improvements, the 250 mg/day group had significantly ($P < 0.05$) greater reductions, compared to the placebo group, in mean fasting blood glucose (-4.7%), serum total cholesterol (-7.0%), serum triglycerides (-9.5%), and serum LDL-C (-9.0%). In addition to all of the aforementioned improvements, the 500 mg/day group had a significantly ($P < 0.001$) greater increase in mean serum high-density lipoprotein cholesterol (HDL-C) compared to the placebo group (17.3%). Cardiac risk ratios for the 2 higher doses were significantly less ($P < 0.05$) than for placebo after 60 days. There was no significant change over time in the placebo group for any biochemical parameter. There were no adverse events reported for any group.

The authors conclude that all doses tested support traditional claims of an antistress-adaptogenic effect. In this study, the cortisol levels declined over the course of the study in patients treated with ashwagandha. This indicates that ashwagandha may be working through the hypothalamic-pituitary-adrenal axis. Cortisol also regulates blood sugar levels. Patients in the 250 and 500 mg/day groups had reductions in fasting blood glucose. Also, chronic stress reduces serum DHEAS, a marker of stress. Patients in this study treated with ashwagandha had increased concentrations of DHEAS at study end compared with the placebo group. Chronic stress is associated with high levels of serum C-reactive protein, a systemic marker of inflammation associated with various chronic diseases. All doses of ashwagandha decreased levels of serum C-reactive protein. The authors conclude that daily use of ashwagandha may help people with chronic stress with no adverse side effects. Long-term safety and efficacy need to be determined.

—Heather S. Oliff, PhD

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