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**File: ■ Ashwagandha (*Withania somnifera*)**
**■ Mental Stress**
**■ Cardiovascular Health**

**HC 051456-507**

**Date: October 31, 2014**

**RE: Ashwagandha May Reduce Stress-induced Cardiovascular Changes in Healthy Males; More Study Is Needed**

Pingali U, Pilli R, Fatima N. Effect of *Withania somnifera* extract on mental stress induced changes in hemodynamic properties and arterial wave reflections in healthy subjects. *Curr Top Nutraceutical Res*. 2013;11(4):151-158.

Mental stress adversely affects the circulatory system and cardiovascular health, and impairs the body's antioxidant defense system. Ashwagandha (*Withania somnifera*) is used in Ayurvedic medicine to help the body adapt to stress. It is also used to promote physical and mental health. The purpose of this randomized, placebo-controlled, double-blind, crossover study was to evaluate the effect of ashwagandha on cardiovascular and hemodynamic responses to mental stress in healthy male subjects.

Healthy men (n = 20, mean age 25 years) participated in this study conducted in Panjagutta, Hyderabad, India. The inclusion criteria were as follows: nonsmoker; nonobese (body mass index <23 kg/m$^2$); no hypertension, diabetes, or hyperlipidemia; and not taking antioxidant vitamin supplements for the prior 3 months. Subjects abstained from caffeine and alcohol for 24 hours prior to and during the test days and were trained on ≥ 2 occasions on the study procedures. Subjects received either placebo or 1,000 mg/day (500 mg twice daily) aqueous ashwagandha root and leaf extract (Sensoril®; Natreon Inc.; New Brunswick, New Jersey) for 14 days. The ashwagandha extract was prepared from a genetically uniform withaferin A and withanolide glycoside-dominant chemotype grown in the northern and central provinces of India. The extract was standardized to contain not less than 10% withanolide glycosides, not more than 0.5% withaferin A, and not less than 32% oligosaccharides. The identical placebo capsules contained microcrystalline cellulose, lactose, and magnesium stearate.

At baseline and 3 hours after dosing on day 15, blood pressure, heart rate, arterial stiffness, augmentation index, and augmented pressure of the central (aortic) pressure waveform were measured before and 2 min after the mental stress test was performed. The mental stress test consisted of the following computerized psychometric tests: choice discrimination test, digit symbol substitution test, and digit vigilance test. Blood

was drawn before and after each test to measure high-sensitivity C-reactive protein (hs-CRP), cortisol levels, and safety parameters. Following a 14-day washout period, the subjects were crossed over to the other treatment and the protocol was repeated.

In the placebo group, mental stress increased blood pressure, but did not increase heart rate compared with baseline. According to the authors, post-treatment and post-stress, compared to the placebo group, the ashwagandha group had lower aortic pressure ($P < 0.001$), augmentation index ($P < 0.05$), subendocardial viability ratio (an indicator of myocardial perfusion, $P < 0.05$), radial systolic blood pressure ($P < 0.05$), radial diastolic blood pressure ($P < 0.01$), radial mean pressure ($P < 0.01$), aortic systolic blood pressure ($P < 0.01$), aortic diastolic blood pressure ($P < 0.01$), aortic mean pressure ($P < 0.01$), and aortic pulse pressure ($P < 0.01$). Hs-CRP, which is known to increase with stress, was significantly decreased following stress in the ashwagandha group vs. placebo group ($P < 0.01$). Cortisol and malondialdehyde (MDA) levels, which increase with stress, were decreased following stress in the ashwagandha group vs. placebo group ($P < 0.05$ and $P < 0.01$, respectively), according to the authors. The blood analyses showed that none of the treatments affected safety parameters.

The authors conclude that ashwagandha "can ameliorate the negative change in cardiovascular parameters associated with mental stress." Ashwagandha had a beneficial effect on arterial function by reducing aortic stiffness, wave reflections, and aortic pulse pressure. Also, the decrease in MDA levels supports the hypothesized in vivo antioxidant effect of ashwagandha. However, since the subjects were all healthy young males, the results cannot be generalized to consumers at large.

In the text of the article, it is stated that the changes in the ashwagandha group were significant compared to both baseline and placebo (except for the changes in blood pressure which were said to be significant only in comparison to placebo). However, the data indicating the statistical significance of the changes between pre- and post-placebo and pre- and post-ashwagandha treatment measures (pairwise comparison P-values; the purported purpose of the study) are not presented. It is not clear why the authors chose instead to report P-values for non-pairwise comparisons in the data tables (i.e., comparing post-stress pretreatment measures in the placebo group with post-stress post-treatment measures in the ashwagandha group). In addition, the authors do not report any statistical adjustments for multiple comparisons and therefore the reported significant differences may be biased.

These preliminary results may have been over-interpreted by the authors. Additional studies with larger sample sizes and much more rigorous statistical analyses and reporting are needed to corroborate the results.

*—Heather S. Oliff, PhD*

The American Botanical Council has chosen not to include the original article.