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File: ■ Ashwagandha (*Withania somnifera*)
■ Safety
■ Tolerability

HC 121264-472

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RE: Ashwagandha in Healthy Humans: Physiological Effects and Safety

Raut AA, Rege NN, Tadvi FM, et al. Exploratory study to evaluate tolerability, safety, and activity of ashwagandha (*Withania somnifera*) in healthy volunteers. *J Ayurveda Integr Med*. July 2012;3(3):111-114.

In traditional Ayurvedic medicine, ashwagandha (*Withania somnifera*) root is used to promote general strength and vitality. Several human studies have been published in recent years, collectively showing that this plant's root, ingested either in dried form or in extract form, decreased stress and improved quality of life,[1] improved sexual function in males,[2] increased immunity,[3] improved cardiorespiratory endurance and neuromuscular coordination,[4] and alleviated fatigue and weakness in peri- and postmenopausal women.[5] The ashwagandha root has also been reported to be an adaptogen.[6]

The present observational, dose-response study was designed to assess the safety and tolerability of escalating doses of ashwagandha in healthy subjects, as measured by vital signs and hematological and biochemical parameters. Secondary endpoints were the percentage of body fat, lean body weight, muscle strength, and exercise tolerance. It was a single-arm study with no placebo control group.

Included participants were males or females who were 18-30 years of age with a body mass index (BMI) of 19-30 kg/m^2 who did not take any medications, supplements, or adhere to an exercise regimen within the prior month. Those that had taken or donated blood within 3 months of the study were excluded. Potential participants underwent a physical exam, an assessment of organ function, a chest X-ray, and an electrocardiogram (ECG).

A total of 18 subjects were enrolled in the study. At baseline, the mean age of the subjects was 24.33 ± 2.14 years, the mean height was 165.94 ± 7.43 cm, the mean weight was 66.65 ± 8.79 kg, and the mean BMI was 24.28 ± 2.70 kg/m^2. None of the subjects smoked or used tobacco or alcohol.

For a 30-day period, doses of an ashwagandha aqueous extract were increased in 10-day intervals, starting at 250 mg in the morning and 500 mg in the evening on days 1 to 10 (750 mg/day). From days 11 to 20, 500 mg was taken in the morning and 500 mg was taken in the

evening (1,000 mg/day). The dosage on days 21 to 30 was 500 mg in the morning and 750 mg in the evening (1,250 mg/day).

The test material was a gelatin capsule, containing 250 mg or 500 mg of 8:1 pulverized ashwagandha root aqueous extract. Neither the source, preparation process/standardization, nor the manufacturer of the ashwagandha extract used in this study is disclosed.

Vital signs, body weight, BMI, ECG, exercise tolerance, muscle strength, and blood panels were assessed at baseline and on days 11, 21, and 31. The blood panels included hematological (erythrocyte sedimentation rate, platelet, hemoglobin, differential, red, and white cell counts), organ and metabolic function (serum bilirubin, protein, albumin, alanine transaminase, aspartate transaminase, alkaline phosphatase, uric acid, and fasting blood glucose), and lipid (total cholesterol, high-density lipoprotein [HDL], low-density lipoprotein [LDL], and very-low-density lipoprotein [VLDL]) parameters. Exercise tolerance was measured by cycle ergometer, and muscle strength was assessed by hand grip, quadriceps, and back extensor force. Body fat percentage and lean body weight were measured by skin fold thickness at the biceps, triceps, and subscapular and suprailiac areas.

There were no significant changes in vital signs (body temperature, pulse, blood pressure, and respiration rate), body weight, or hematological parameters during the study. Measures of organ function such as the serum bilirubin, protein, albumin, alanine transaminase, aspartate transaminase, and alkaline phosphatase remained within the normal range, as did uric acid and fasting blood glucose levels. No significant changes in appetite, bladder or bowel habits, or sleep duration were reported; although 6 (33%) of the subjects voluntarily reported improved sleep quality. The authors note that "Needrajaran" or sleep induction is an important clinical application of ashwagandha in Ayurvedic medicine.

Muscle force significantly increased in both the quadriceps (28.02 ± 8.23 kg vs. 34.05 ± 8.10 kg, $P<0.05$) and the back extensor (26 ± 8.83 kg vs. 30.02 ± 8.10 kg, $P<0.05$) as compared to baseline. Increasing trends were reported in handgrip strength and exercise tolerance. The authors suggest that in accordance with the traditional usage of ashwagandha, these results together with the observed increase in serum creatinine (0.85 ± 0.14 mg/dl vs. 0.95 ± 0.13 mg/dl, $P<0.05$) indicate muscle mass promotion activity, rather than adverse renal function, since there was a significant concomitant drop in urea nitrogen (10.93 ± 3.62 mg/dl vs. 9.78 ± 3.38 mg/dl, $P<0.05$).

These findings were further supported by a trend towards decreasing body fat percentage and increasing lean body weight, although body weight and BMI did not significantly change. Total cholesterol significantly decreased (175.9 ± 24.62 mg/dl vs. 159.6 ± 17.22 mg/dl, $P<0.05$), and decreasing trends were also seen in triglycerides, LDL cholesterol, fasting blood sugar, and BMI.

With the exception of 1 subject, this study reports the good safety profile of daily ashwagandha supplementation up to 1,250 mg. No changes were seen in vital bodily functions or appetite, gastrointestinal habits, or sleep. It is mentioned that the adverse side effects reported in the withdrawn subject may be due to previously cited impacts of ashwagandha on the central nervous system and libido. These potentially serious adverse side effects warrant further study. However, the formulation was found to be safe in terms of hematological and biochemical parameters; and it improved sleep quality, strengthened muscles, and lowered lipids in healthy subjects. These positive results support the use of ashwagandha to potentially aid in promoting strength and general health. Future directions for ashwagandha clinical research include further

evidence of quality-of-life benefits for perimenopausal women, and ashwagandha's potential efficacy in the treatment of sarcopenia.

—Amy C. Keller, PhD

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