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File: ■ Ashwagandha (*Withania somnifera*)
■ Endothelial Function
■ Type 2 Diabetes

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RE: Ashwagandha Improves Endothelial Function in Patients with Type 2 Diabetes

Usharani P, Fatima N, Kumar CU, Kishan PV. Evaluation of a highly standardized *Withania somnifera* extract on endothelial dysfunction and biomarkers of oxidative stress in patients with type 2 diabetes mellitus: a randomized, double blind, placebo controlled study. *Int J Ayur Pharma Research*. 2014;2(3):22-32.

The endothelium (the lining of blood vessels) is a regulator of vascular homeostasis (vessel dilation and contraction). Endothelial dysfunction leads to cardiovascular disease. The oxidative stress caused by reactive oxygen species (ROS) contributes to endothelial dysfunction and the pathogenesis of type 2 diabetes mellitus (T2DM), which explains why many people with T2DM also have cardiovascular disease. Ashwagandha (*Withania somnifera*) has antioxidant effects. The purpose of this randomized, double-blind, placebo-controlled study was to evaluate the effect of ashwagandha on endothelial function in patients with T2DM.

Patients (n = 60, aged 18-65 years) with T2DM participated in this study conducted at the Department of Clinical Pharmacology and Therapeutics, Nizam's Institute of Medical Sciences; Hyderabad, India. Included patients had a fasting plasma glucose of 110-126 mg/dL, a glycosylated hemoglobin (HbA1c) of 6.5-8%, were taking a stable dose of anti-diabetic medication (metformin 1500-2500 mg/day) for 8 weeks prior to the screening visit, and had endothelial dysfunction (defined as ≤ 6% change in reflection index on a post salbutamol challenge test). Excluded patients had severe uncontrolled hyperglycemia, uncontrolled hypertension, cardiac arrhythmia, impaired hepatic or renal function, history of malignancy or stroke, smoked, were chronic alcoholics, had any other serious disease requiring treatment, or were using herbal supplements.

Patients were randomly assigned to receive either 500 mg/day of an aqueous extract of ashwagandha root (Sensoril®; Natreon Inc.; New Brunswick, New Jersey), 1000 mg/day ashwagandha extract, or placebo for 12 weeks. Sensoril contains "not less than 10% withanolide glycosides, not more than 0.5% of Withaferin-A and not less than 32% of oligosaccharides." The primary efficacy measure was the change in reflection index at 12 weeks. Blood was drawn for assessment of secondary efficacy measures: namely, the change from baseline in the oxidative stress markers nitric oxide (NO), glutathione

(GSH), and malondialdehyde (MDA); the inflammatory biomarker high-sensitivity C-reactive protein (hsCRP); and lipid profile at 12 weeks.

There were no significant differences among the groups at baseline. Both doses of ashwagandha significantly increased the reflection index compared to baseline and placebo ($P < 0.001$). There was no significant difference in the reflection index between the 2 dosage groups, although the 1000 mg/day dosage did have a larger effect.

Compared with baseline, 500 mg/day ashwagandha significantly increased NO by 15.29% ($P < 0.05$) and GSH by 14.72% ($P < 0.05$), and significantly decreased MDA by 6.36% ($P < 0.05$) and hsCRP by 41.22% ($P < 0.001$). Likewise, compared with baseline, 1000 mg/day ashwagandha significantly increased NO by 33.75% ($P < 0.001$) and GSH by 31.48% ($P < 0.001$), and significantly decreased MDA by 21.39% ($P < 0.001$) and hsCRP by 57.71% ($P < 0.001$). When comparing the percent change from baseline, both the 500 mg/day and 1000 mg/day dosages significantly changed the levels of NO ($P < 0.01$ and $P < 0.001$, respectively), GSH ($P < 0.001$ for both), and hsCRP ($P < 0.001$ for both) compared with placebo. Only the 1000 mg/day dosage was significantly better than the placebo in reducing MDA ($P < 0.001$). Ashwagandha 1000 mg/day was significantly more effective than 500 mg/day ashwagandha in decreasing MDA ($P < 0.05$), increasing NO ($P < 0.05$), increasing GSH ($P < 0.01$), and decreasing hsCRP ($P < 0.05$).

Analyzing the change from baseline levels, both ashwagandha 500 mg/day and 1000 mg/day significantly reduced the levels of total cholesterol ($P < 0.001$ for both), low-density lipoprotein (LDL) cholesterol ($P < 0.01$ and $P < 0.001$, respectively), and triglycerides ($P < 0.01$ and $P < 0.001$, respectively) compared to placebo. Neither treatment significantly changed very-LDL cholesterol levels. Only the 1000 mg/day dosage significantly increased high-density lipoprotein (HDL) cholesterol compared with baseline and placebo ($P < 0.001$). Also, 1000 mg/day ashwagandha was significantly better than the 500 mg/day dosage in reducing total cholesterol ($P < 0.05$) and increasing HDL ($P < 0.01$).

Both ashwagandha doses were well tolerated. There were no adverse effects reported.

The authors conclude that both 500 mg/day and 1000 mg/day ashwagandha had a beneficial effect on endothelial function after 12 weeks of treatment in patients with T2DM. Also, the significant changes in oxidative and inflammatory biomarkers suggest an improvement in antioxidant status and reduction in inflammation, which could contribute to the improved endothelial function. Limitations of this study were the relatively small population size and the lack of controls for changes in diet and exercise habits which may have affected the outcomes. The authors reported mean body weight and body mass index (BMI) at baseline but not at the end of the study. The authors suggest that the therapeutic role of ashwagandha as an adjunctive diabetes therapy should be further evaluated.

—Heather S. Oliff, PhD

Referenced article can be found at http://ijapr.in/articles/research/231482.pdf.