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# HerbClip™



**File: ■ Fenugreek (*Trigonella foenum-graecum*, Fabaceae)**
**■ Menopause**
**■ FenuSMART™**

**HC 101651-556**

**Date: November 15, 2016**

**RE: Proprietary Fenugreek Extract Alleviates Postmenopausal Symptoms and Increases Estradiol Levels**

Shamshad Begum S, Jayalakshmi HK, Vidyavathi HG, et al. A novel extract of fenugreek husk (FenuSMART™) alleviates postmenopausal symptoms and helps to establish the hormonal balance: A randomized, double-blind, placebo-controlled study. *Phytother Res*. July 13, 2016; [epub ahead of print]. doi: 10.1002/ptr.5680.

The physiological, psychological, and sociocultural discomforts associated with menopause are attributed to a decrease in estrogen levels. Phytoestrogens from plants may help alleviate menopausal symptoms. The seeds of fenugreek (*Trigonella foenum-graecum*, Fabaceae) are used as a culinary spice and are generally recognized as safe (GRAS) by the US Food and Drug Administration. Fenugreek seeds are a rich source of phytoestrogens and clinical trials have found that fenugreek seed extract reduced the severity of menopausal symptoms. The purpose of this randomized, double-blind, placebo-controlled study was to evaluate the safety and efficacy of a proprietary fenugreek seed husk extract for the treatment of postmenopausal symptoms.

Purposive sampling was used to select natural menopausal female patients (n = 130), aged between 45 and 58 years, for this study conducted at M/S Sri Jayadeva Institute of Cardiovascular Sciences and Research; Bangalore, India. Included patients did not have menses for ≥ 12 months, had their last menses ≤ 3 years previously, had moderate to severe postmenopausal discomforts as assessed by a score of ≥ 25 on the Greene Climacteric Scale (GCS), and had ≥ 3 hot flashes/day during the last 3-5 weeks. Excluded patients used hormone replacement therapy previously, had a family history of breast cancer, had a personal history of malignant neoplasm, were hospitalized during the previous 3 months, had any cardiac risk factors, or were taking any medication or dietary supplement.

A total of 88 women gave informed consent and were randomly assigned to receive either placebo (cellulose) or fenugreek (FenuSMART™; M/S Akay Flavours & Aromatics Pvt. Ltd.; Cochin, India) at 500 mg/day for 1 week, and then 1000 mg/day for another 12 weeks. The fenugreek product was a proprietary hydroethanolic extract of fenugreek seed husks (FHE) rich in protodioscin, trigonelline, and 4-hydroxyisoleucine. The FHE

had a "drug extract ratio of 18:1 (w/w [per weight]) with respect to fenugreek husks (1 kg FHE was equivalent to 24 kg of dried fenugreek seeds) … ." The FHE was characterized by a high-performance liquid chromatography fingerprint profile and met the quality requirement of the US Pharmacopeia.

At baseline, day 45, and day 90 (study end), quality of life was assessed with the Short Form-36 (SF-36) Health Survey, and the severity of postmenopausal symptoms was evaluated with the GCS. Anthropometric data were collected, blood pressure was measured, and blood was drawn at baseline and study end. The blood samples were analyzed to determine total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, very-low-density lipoprotein cholesterol, estradiol, and calcium levels.

At baseline, there were no significant differences between groups in terms of demographic variables, laboratory parameters, or GCS scores. The dropout rate was 27.3% in the placebo group and 13.6% in the treatment group, "mainly because of their difficulty to appear for follow-ups and strictly adhere to the conditions of the treatment regime." None of the dropouts were due to adverse events or intolerance of the FHE. Treatment compliance (measured by pill counts) was > 95% for both groups.

The FHE group had a significant improvement in GCS total score compared with baseline ($P < 0.001$) and placebo ($P < 0.001$). Scores for the 4 GCS domains (psychological, vasomotor, physical, and libido) also were significantly lower in the FHE group compared with the placebo group ($P < 0.001$ for all). The greatest reductions were observed in the scores for insomnia (decreased 75%), mood swings (68%), irritability (65%), night sweats (57%), headache (54%), and hot flashes (47.8%). Approximately 32% of the FHE group reported no hot flashes at study end. Based on SF-36 scores, 73% of the FHE group had a significant improvement in quality of life compared with placebo ($P < 0.001$). Compared to baseline, the FHE group had significant improvements in physical/mental fatigue, enhanced interest in daily work, general well-being, and mental health ($P < 0.05$ for all), while a similar increase was not observed for the placebo group.

Plasma estradiol increased 120% in the FHE group compared with < 5% in the placebo group ($P < 0.01$). Patients who had high levels of estradiol at baseline had relatively lower increases in estradiol over the course of the study and vice versa (i.e., those with the lowest baseline levels experienced the greatest increase in estradiol). Calcium increased 2% in the FHE group compared to a decrease of 0.8% in the placebo group ($P < 0.01$). Patients in the FHE group with hypercholesterolemia at baseline had significant decreases in total cholesterol, LDL, and triglyceride levels ($P < 0.05$ for all), while those with a normal lipid profile at baseline maintained healthy cholesterol levels with no decrease in HDL. There were no significant changes in anthropometric measures, although there was a trend towards improvement in body weight ($P < 0.06$) and hip circumference ($P < 0.08$). No adverse events were reported.

In summary, supplementation with FenuSMART for 90 days significantly alleviated symptoms of menopause, improved quality of life, and increased serum levels of estradiol in postmenopausal women. The FHE also had beneficial effects on lipid profiles and serum calcium levels, and did not cause any adverse reactions. The authors conclude that FHE is a safe and effective treatment for the management of postmenopausal symptoms. This study was well designed and reported. Acknowledged

limitations of the study include the purposive sampling procedure, small sample size, absence of endometrial surveillance, and lack of measurements of other key hormones (androgens and estrogens), bone density, and bone calcium levels. Financial support for the study was provided by M/S Akay Flavours & Aromatics Pvt. Ltd., the manufacturer of FenuSMART; 4 of the authors (Gopakumar, Abin, Balu, and Krishnakumar) are employed by the company.

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Referenced article can be accessed at http://onlinelibrary.wiley.com/doi/10.1002/ptr.5680/full.