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# A fenugreek seed extract selectively reduces spontaneous fat consumption in healthy volunteers

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## Abstract

**Purpose** Fenugreek seeds (*Trigonella foenum-graecum* L.) are an old herbal remedy used to treat metabolic and nutritive dysfunctions. They have been shown to modulate feeding behaviour in animals, but strong clinical data are lacking. The aim of this study was to investigate the effects of a repeated administration of a fenugreek seed extract on energy intake and eating behaviour in healthy human volunteers.

**Methods** Twelve healthy male volunteers completed a double-blind randomized placebo-controlled three-period cross-over trial of two different doses of a fenugreek seed

extract (588 and 1176 mg). The three 14-day treatment periods were separated by a 14-day washout period. The main endpoints were energy intake, assessed in volunteers under normal ambulatory and free-living conditions by a 3-day detailed dietary record and during a meal test, weight, fasting glucose level, insulin and lipid profile, visual analogue scale scores of appetite/satiety and blood glucose and insulin levels measured repeatedly after a standardized breakfast.

**Results** Daily fat consumption was significantly decreased by the higher dose of fenugreek seed extract [3.73 vs. 4.51 MJ day<sup>-1</sup>, -17.3% vs. placebo, 95% confidence interval (CI) -1.51 to -0.05,  $n=12$ ,  $P=0.038$ ]. This specific reduction tended to lower the total energy intake (9.97 vs. 11.29 MJ day<sup>-1</sup>, -11.7% vs. placebo, 95% CI -2.91 to 0.26,  $n=12$ ,  $P=0.094$ ). No significant effect was observed on the other nutrients or other endpoints.

**Conclusions** The repeated administration of a fenugreek seed extract specifically decreases dietary fat consumption in humans which, given the traditional use of the plant, constitutes a novel result.

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## Introduction

Fenugreek (*Trigonella foenum-graecum* L.) is an herbaceous annual plant from the family of Leguminosae, cultivated in Mediterranean countries and India. Its seeds have long been known as a herbal remedy for various pathological conditions. A number of pharmacological and clinical studies have shown glucose- and lipid-lowering properties of either the seed itself, seed extracts or purified components (see [1] for review). Traditional fenugreek-

based preparations are used in humans to stimulate appetite and promote weight gain [2]. We have previously shown that a repeated administration of a hydro-alcoholic fenugreek seed extract to rats enhanced their motivation to eat and consume food, resulting in a slight weight increase [3]. Appetite and food intake were also increased by the repeated administration of a purified steroid saponin fraction from the seed, and was associated with a modified circadian rhythm of feeding behaviour [4]. In contrast, in a safety study using a dietary supplement of fenugreek seeds in animals [5], no effect was observed on food consumption. A more recent study reported that a fenugreek seed extract reduced the body weight gain induced by a high-fat diet in obese mice [6]. To date, however, there has been no report of an effect of fenugreek seeds on food intake or body weight in humans. Given the inconclusiveness of these data, we conducted a clinical trial with the aim of evaluating the effects of a repeated administration of a fenugreek seed extract on eating behaviour and energy intake in healthy human volunteers.

## Materials and methods

### Study design

The study was a double-blind randomized placebo-controlled three-period cross-over trial of two different doses of a fenugreek seed extract, according to a Latin square design. The three 14-day treatment periods were separated by 14-day washouts.

### Subjects

Twelve healthy male volunteers, aged 19–26 years (mean 22 years), were included in this study. All were of normal and stable weight (mean weight 71.6 kg, range 60.5–80.6, mean body mass index  $22.5 \text{ kg m}^{-2}$ , range 20.0–25.0).

### Ethical aspects

This study was approved by the Ethics Committee “Comité de Protection des Personnes Montpellier-Saint-Eloi” and conducted in accordance with the Helsinki declaration and the ICH guideline for Good Clinical Practice. All the subjects gave written informed consent to participate.

### Test compound

The test compound was a marketed dry hydro-alcoholic seed extract administered three times daily as oral coated tablets in one of two daily doses: a total daily dose of 588 mg (approximately  $8 \text{ mg kg}^{-1}$ ), which is the daily dose

of the extract commonly prescribed in humans, or a double dose 1176 mg (approximately  $16 \text{ mg kg}^{-1}$ ). These doses fall within the range of active doses used in a previous animal study testing the same extract [3] and corresponds to 5–53  $\text{mg kg}^{-1}$  human equivalent doses. The extract contains diosgenine, steroid saponins, 1.38% trigonelline and 1.50% 4-hydroxyisoleucine, as characterized by thin-layer chromatography and high-performance liquid chromatography. Placebo tablets were manufactured using the same excipients, the same process and the same packaging as those used for the active tablets, thereby rendering them indistinguishable from the active tablets. The similarity between the seed extract and the placebo tablets was verified on five criteria (aspect, size, weight, colour and smell).

### Investigations

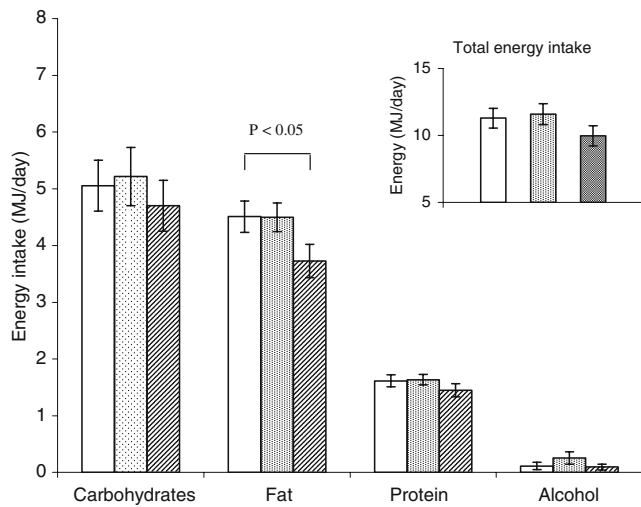
On day 0 and day 14 of each period, the participants came to the centre in a fasting condition. Body weight was recorded with the volunteers dressed in only underclothing and after having urinated; the same balance, accurate to  $\pm 0.1 \text{ g}$ , was used for all measurements. Blood was drawn for determination of the plasma lipid profile. The treatment was taken ambulatory from day 1 to day 14; from day 11 to day 13, the subjects completed a detailed dietary record under free-living conditions. After validation by a dietician, nutrient analysis was performed using IDI software. At 8:00 a.m. on day 14, the time-course of plasma glucose and serum insulin concentrations and the subjective scores of appetite and satiety using visual analogue scales [7, 8] were evaluated before and every 30 min after consumption of a standardized breakfast (750 kcal, 13% proteins, 35% fat and 52% carbohydrates). At 12:30 p.m., a test meal of standardized composition was given ad libitum to evaluate the total energy intake and the type of nutrients preferentially consumed.

### Analytical methods

Plasma glucose was assayed by the glucose oxidase method. Serum insulin was measured by a radioimmunoassay (BI-INSULIN RMA; CIS Bio-international, Gif-sur-Yvette, France). Serum triglycerides, total cholesterol and high-density lipoprotein (HDL)-cholesterol were assayed with an enzymatic method (lipase/glycerokinase, cholesterol oxidase and cholesterol oxidase after separation, respectively).

### Data analysis and statistics

Results are expressed as the mean  $\pm$  standard error of the mean (SEM). The time-courses of postprandial glucose and insulin concentrations, and appetite and satiety scores were integrated in areas under the curves, calculated, including



**Fig. 1** Energy intake (MJ day<sup>-1</sup>) recorded by subjects under free-living conditions during the last 3 days of the 14-day treatment period: placebo (white bars), fenugreek seed extract 588 mg day<sup>-1</sup> (dotted bars), fenugreek seed extract 1176 mg day<sup>-1</sup> (striped bars)

the baseline, by the trapezoidal rule. Means were compared using repeated-measures analysis of variance. 95% Confidence intervals for the differences (95% CI) are given where necessary. Post hoc analyses were performed using the paired *t* test. Calculations and statistical analysis were performed using the Systat ver. 6.0 software for Windows from SPSS (SPSS, Chicago, IL).

**Results**

As shown in Fig. 1, a significant decrease in daily fat consumption, as measured by the 3-day record, was observed in the subjects treated by the higher dose of the fenugreek seed extract (3.73 vs. 4.51 MJ day<sup>-1</sup>, -17.3% vs. placebo, 95% CI -1.51 to -0.05, *n*=12, *P*=0.038). This specific reduction tended to lower the total energy intake (9.97 vs. 11.29 MJ day<sup>-1</sup>, -11.7% vs. placebo, 95% CI -2.91 to 0.26, *n*=12, *P*=0.094). Fasting data on weight,

lipid profile, plasma glucose and serum insulin are summarized in Table 1. No significant alterations were observed for other nutrients, weight, lipid profile or the time-course of serum insulin and plasma glucose concentrations after the standardized breakfast. The scores of appetite and satiety and the food consumed during the meal test were unchanged.

Among the nine non-serious adverse events reported during the three treatment periods, only three may have been related to the treatment: one case of abdominal pain and two cases of a specific urine smell.

**Discussion**

The results of this study reveal for the first time that a 14-day treatment with a fenugreek seed extract reduces daily fat consumption in healthy, normal weight volunteers, with a tendency towards a decrease in total energy intake. We also show that the fenugreek seed extract does not increase appetite or food consumption. This latter result differs from the traditional use of fenugreek-based preparations for appetite stimulation and weight gain [2]. It also contrasts with our previous observations of enhanced food consumption in animals administered the hydro-alcoholic crude extract or a purified steroid saponin fraction [3, 4].

The effect of fenugreek seed extract on fat consumption is specific, without any significant change in the intake of other nutrients and without any alteration of appetite or palatability. It was observed only under free-living conditions, based on a record of all food eaten during a 3-day period, but was not found in the standardized meal test situation. This difference in results is likely related to the lack of sensitivity of a single meal test.

Such a specific effect has already been observed in pharmacological studies undertaken in rats by activation of the hypothalamic serotonin pathway [9], and in human after a methylphenidate challenge activating the brain dopamine pathway by blocking its reuptake [10].

**Table 1** Summary of fasting data of weight, lipid profile, plasma glucose and serum insulin before and after each treatment period

Parameters	Placebo		Fenugreek seed extract: 588mg day <sup>-1</sup>		Fenugreek seed extract: 1176mg day <sup>-1</sup>	
	Baseline (n=12)	Post- treatment (n=12)	Baseline (n=12)	Post- treatment (n=12)	Baseline (n=12)	Post- treatment (n=12)
Weight (kg)	72.5±2.0	72.4±2.0	72.2±1.9	72.2±2.0	72.1±1.9	72.1±2.0
Triglycerides (mmol l <sup>-1</sup> )	1.0±0.1	0.8±0.1	0.9±0.1	0.9±0.1	1.1±0.2	0.8±0.1
Total cholesterol (mmol l <sup>-1</sup> )	4.9±0.2	4.5±0.2	4.7±0.2	4.4±0.2	4.8±0.2	4.4±0.2
High-density lipoprotein-cholesterol (mmol l <sup>-1</sup> )	1.2±0.1	1.1±0.1	1.2±0.1	1.1±0.0	1.1±0.0	1.1±0.1
Fasting plasma glucose (mmol l <sup>-1</sup> )	–	5.0±0.1	–	4.8±0.1	–	4.8±0.1
Fasting serum insulin (mU l <sup>-1</sup> )	–	9.7±1.0	–	8.6±1.4	–	7.3±0.6

The reduction in fat intake observed in our study is in accordance with the recently reported reduction in body weight gain induced by a high-fat diet in obese mice [6]. We were unable to detect any weight modification in our volunteers, which may be explained by the healthy status of the subjects and the short duration of the treatment. It is also worth noting that no significant change in body weight was observed by Sharma et al. [11] in a clinical study in which they evaluated the safety of fenugreek seeds consumed by diabetic patients; however, their study was not designed to assess eating behaviour or weight modifications. Nevertheless, based on these results, it can be suggested that the administration of a fenugreek seed extract may improve the metabolic status and favour a weight reduction in the long term, particularly in some subgroups of overweight or obese patients for whom a low-fat diet is recommended.

The treatment with the fenugreek seed extract did not modify the lipid profile or the glucose tolerance of our volunteers. This result may also be explained by the healthy status of the subjects and the short duration of the treatment.

## Conclusion

Based on the results reported here, the repeated administration of a fenugreek seed extract specifically decreases dietary fat consumption in humans which, given the traditional use of the plant, constitutes a novel result that requires further confirmation. The fenugreek seed's component(s) involved and the mechanism(s) of this effect remain to be elucidated.

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