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Effects of a Fenugreek Seed Extract on Feeding Behaviour in the Rat: Metabolic–Endocrine Correlates

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PETIT, P., Y. SAUVAIRE, G. PONSIN, M. MANTEGHETTI, A. FAVE AND G. RIBES. *Effects of a fenugreek seed extract on feeding behaviour in the rat: Metabolic–endocrine correlates.* PHARMACOL BIOCHEM BEHAV **45**(2) 369–374, 1993.—Fenugreek seeds (*Trigonella foenum graecum L.*) are assumed to have restorative and nutritive properties. The present work was designed to investigate the effects of a fenugreek seed extract on feeding behaviour. Experiments were performed to determine food consumption and motivation to eat as well as metabolic–endocrine changes in chronically treated animals. Male Wistar rats were given the seed extract orally (10 and 100 mg/day per 300 g body weight), mixed together with food, and control animals were monitored in parallel. The results show that chronic oral administration of the fenugreek extract significantly increases food intake and the motivation to eat. The treatment, however, does not prevent the anorexia nor the decreased motivation to eat induced by *d*-fenfluramine (2 mg/kg, IP). An increase in plasma insulin and a decrease in total cholesterol and very low-density lipoprotein (VLDL)-low-density lipoprotein (LDL) total cholesterol were also observed. In conclusion, chronic administration of a fenugreek seed extract enhances food consumption and motivation to eat in rats and also induces hyperinsulinemia as well as hypocholesterolemia.

Fenugreek seed Feeding behaviour Blood glucose Plasma insulin Plasma cholesterol Plasma triglycerids Rat

FENUGREEK (*Trigonella foenum graecum L.*) is an annual plant from the family of *Leguminosae,* cultivated in South Europe, Northern Africa, and India. Over the past few years, fenugreek seeds have been shown to have hypocholesterolemic activity (25,26,29) due to the defatted part (34) and implicating saponin-rich subfractions (21,23). In addition, the seeds and some of their fractions display a hypoglycemic effect in experimental diabetes (15,19,20,24) as well as in diabetic patients (27,28).

Being known from earliest times as a traditional medicine, fenugreek seeds are assumed to have restorative and nutritive properties (18,30) and stimulate the digestive process (7). They are known to be an important constituent of a traditional food (Methipak) consumed during pregnancy and lactation in India (17). Moreover, fenugreek seeds are well known for their pungent aromatic properties (16); as a spice, they are a component of many curry preparations and are often used to flavour food and stimulate appetite. The present work was designed to investigate the effects of a fenugreek seed extract on feeding behaviour. Experiments were performed in chronically treated rats to determine food consumption and food motivation to eat, as well as metabolic–endocrine changes under the influence of the seed extract.

METHOD

Plant Material and Animals

The fenugreek seed extract was from Monal Laboratories (Palaiseau, France). It was obtained by extraction in a mixture of ethylalcohol/water. The extract was concentrated under vacuum, at temperature below 50°C, and dried. It was without protein and lipids and contained 12.5% steroid saponins,

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4.8% free amino acids, and 0.002% 3-hydroxy-4,5-dimethyl-2(5*H*)-furanone (HDMF), the characteristic aromatic compound of fenugreek (10).

Male Wistar rats with an initial weight of 280–300 g were individually housed in metabolic cages under conditions of constant temperature (20–22°C) and 12 L : 12 D cycle (dark period beginning at 1900 h). Every day, a dish containing 50 g powdered food (UAR powder P 2.5; Villemoisson, Epinay-sur-Orge, France) was placed in each cage at 10 h, which provided ad lib access to food. Food and water intake was measured daily before and during chronic oral treatment with the fenugreek seed extract. Spilled food was collected and correction was made accordingly in the calculation of food consumption. Two measurements of food intake during the light phase were performed: before and during the second week of the treatment. The dry extract was incorporated into the powdered food. Considering the low dose of fenugreek administered (see below), no correction was made as regards the calorie content of the diet. Control animals receiving diet alone were monitored in parallel. Animals were randomly assigned to treated and control groups.

Runway Apparatus and Training and Test Procedures

Motivation to eat was evaluated as running speed in the food-rewarded runway behaviour procedure (13,32).

The runway apparatus consisted of a wooden 1.8-m long straight alley, separating a start box and a goal box, each measuring 35 × 16 cm. The alley (internal width and height: 16 cm) and the start box were painted matt black, while the goal box was painted pale yellow. The roof was of Plexiglas, allowing animals to be clearly observed while minimizing external stimuli. Access to the alley from the start box was controlled by a hand-operated plastic guillotine gate. The food containing dish was placed in the goal area. The time interval from the start of the animal after opening the gate until reaching the food was measured using a hand-held stopwatch by an independent observer unaware of the treatment received by each rat. The running speed (m/s) in the runway could then be calculated.

Once habituated to the apparatus after a period of free access to all of its components, including food, rats were given a daily trial that consisted of placing the rat in the start box for 10–15 s before opening the gate. They were then allowed to run in the alley toward their own dish of food, which had been renewed just before the test. Once the animal had reached the food, it was allowed 30 s to stay free in the goal box. After 5 days, rats were found to have stable running speeds.

Thereafter, each rat was tested once daily according to a similar procedure; the scores analyzed in the results are the means of three consecutive tests.

Experimental Designs

In the first experimental design, three parallel groups of eight rats were followed during 21 days. The first group (control animals) received only food, while the second received a chronic treatment from day 8 onward. The fenugreek extract (10 mg/day per 300 g body weight) was administered orally, mixed with the food. The daily dose was calculated according to the weight on day 7 and corrected for the second week according to the weight on day 14. Food and water consumption, as well as weight, were measured daily in each animal. At the end of the treatment period, animals were sacrificed to investigate metabolic and endocrine modifications. The third group of animals was treated with a 10-fold higher dose of the fenugreek extract (100 mg/day per 300 g body weight) and monitored similarly regarding food intake and weight gain.

In the second experimental design, animals were treated as previously indicated during 8 days (10 mg/day per 300 g b.w.), from day 8 onward. Food intake as well as running speed in the runway were daily monitored in treated and control animals. In addition, to test the potential role of the olfactive properties of the seed extract a third group received the same food as the controls but in the presence, although out of reach, of the fenugreek extract (a similar amount of the extract was placed inaccessible in a slot of the dish). Thus, these animals were fed the control diet both in their home cages and in the test situation and had access to the scent in both situations. Moreover, at the end of the treatment period and after 24-h fast a group of animals received an acute administration of *d*-fenfluramine (2 mg/kg, IP) to investigate whether the chronic treatment with fenugreek could prevent the anorectic effect of the drug (*d*-fenfluramine was kindly supplied by Servier, Courbevoie, France).

Metabolic Studies and Assays

At the end of the first experimental protocol (14 days of chronic treatment with the fenugreek extract), all rats in non fasting state were killed by decapitation and blood was collected to evaluate glycemia, plasma insulin, glucagon, and lipid levels.

Blood glucose levels were immediately determined using the Technicon method (1); then, plasma samples were frozen for hormone radioimmunoassays. Plasma insulin levels were measured by the method of Herbert et al. (12) using an antibody supplied by Miles Laboratories (Paris). ^{125}I-insulin was obtained from International CIS (Gif-sur-Yvette, France); the standard used was pure rat insulin (Novo, Copenhagen, Denmark) whose biological activity was 22.3 μU/ng. The intra- and interassay coefficients of variations were, respectively, 9 and 13.5%. The analytic sensitivity was 0.1 ng/ml. Plasma glucagon levels were measured by the method of Unger et al. (33) using the BR124 glucagon antiserum from the Institut de Biochimie Clinique (Centre Médical Universitaire, Geneva, Switzerland). The intra- and interassay coefficients of variations were 10 and 15%, respectively. The sensitivity was 15 pg/ml.

Triglycerides as well as total and free cholesterol were determined using commercial kits (Biomérieux, Lyon, France). Esterified cholesterol was calculated from the difference between total and free cholesterol. High-density lipoprotein (HDL) fraction was obtained after precipitation of very low-density lipoprotein (VLDL) and low-density lipoprotein (LDL) by phosphotungstate/magnesium chloride (14).

Expression and Statistical Analysis of Results

Results are expressed as means ± SEMs. All data were submitted to Student's *t*-test or to analysis of variance followed by the multiple comparison test of Newman-Keuls (35).

RESULTS

Food Intake and Water Consumption

Daily food intake (g/24 h) became rapidly stable during the first 7 days of experiment. At the end of the baseline period (day 7), it was similar in control and test animals, 32.0 ± 0.8 and 31.8 ± 1.0 g/24 h, respectively (Fig. 1). Addition

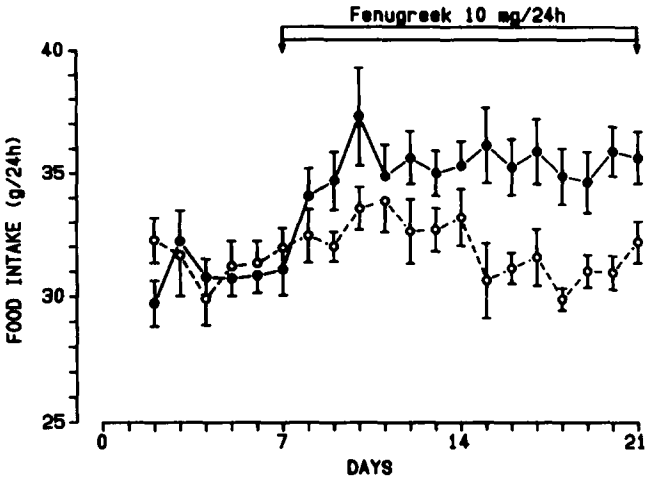

FIG. 1. Effect of the fenugreek seed extract (10 mg/day per 300 g body weight) on food intake. (●), treated rats; (○), control rats. Eight animals were used in each set of experiments.

of the fenugreek extract (10 mg/24 h per 300 g body weight) resulted in a clear increase in daily food intake. This effect was observed from the first day of treatment onward and reached a maximum after 3 days (37.3 ± 1.9 g/24 h, food intake increased by about 20% vs. baseline); it was sustained and significant throughout the treatment ($p < 0.01$). Further, the treatment significantly increased food intake even during the light phase (16.4 ± 0.9 g/8 h on day 16 vs. 3.5 ± 0.4, baseline, or 5.4 ± 0.6, control group on the same day, $p < 0.001$).

On day 7, water consumption averaged 39.4 ± 1.7 and 38.7 ± 1.2 ml/24 h in control and test animals, respectively. Water consumption was not modified by the fenugreek treatment: On day 21, water intake averaged 43.1 ± 2.8 and 39.4 ± 1.7 ml/24 h in control and treated animals, respectively.

Administration of a 10-fold higher dose of the fenugreek extract (100 mg/day per 300 g body weight) also induced a rapid increase in food intake (35.8 ± 2.8 g/24 h on day 3 of treatment vs. 30.7 ± 0.5 g/24 h at the end of the baseline period); this effect, however, was not enhanced as compared with the lower dose.

Weight Gain

At the end of the baseline period (day 7), control rats weighed 336 ± 8 g and those designed to be treated 332 ± 5 g. The weight increase during the first week of treatment (10 mg/24 h per 300 g body weight) was similar in both groups. In contrast, the weight increase was significantly higher in the treated group than in the control during the second week of treatment (+10.1 ± 1.0% vs. +7.0 ± 0.7%, $p < 0.05$).

When the higher dose of the extract was administered (100 mg/24 h per 300 g body weight), the effect on weight gain was not enhanced as compared with the lower dose (not shown).

Food Motivation

Running speed toward food was significantly increased during the treatment (10 mg/300 g b.w., daily). This effect occurred from the beginning of treatment and paralleled the increase in food consumption (Fig. 2). While the mean running speed remained stable in control animals, it significantly

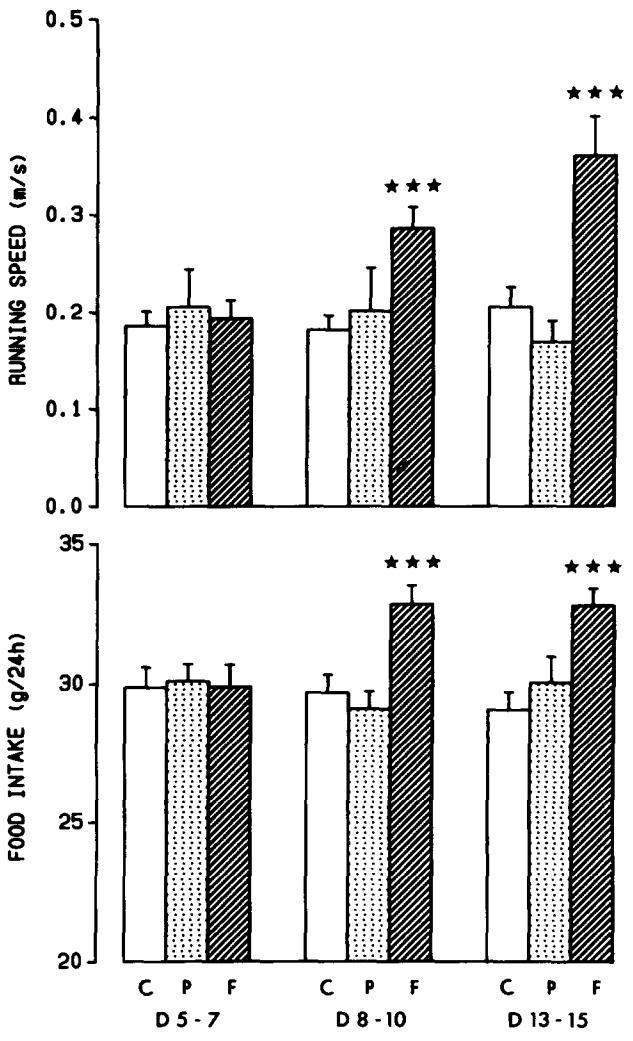

FIG. 2. Effects of the fenugreek seed extract (10 mg/day per 300 g body weight) on running speed (upper panel) and food intake (lower panel). Fenugreek-treated rats: F; fenugreek out of reach: P; control rats: C. Each bar represents the mean of three consecutive tests. Eight animals were used in each set of experiments. ***$p < 0.001$.

and progressively increased in treated animals as compared with the baseline values: 0.29 ± 0.02 m/s (days 8–10, $p < 0.01$) and 0.36 ± 0.04 m/s (days 13–15, $p < 0.001$) vs. 0.19 ± 0.02 m/s (baseline).

When the fenugreek extract was present in the same amount as in treated animals but out of reach, there was no alteration in food intake and running speed (P in Fig. 2). In addition, the effect of fenugreek on food intake disappeared 3–5 days after stopping the treatment (not shown).

Experimentally Induced Anorexia (Fig. 3)

A diminished motivation to run for food was induced by IP injection of *d*-fenfluramine (2 mg/kg) to 24-h-fasted animals. After 20 min, animals were evaluated for food motivation in the food-rewarded runway testing and food intake during the next 24 h. Administration of *d*-fenfluramine resulted in a significant reduction of running speed ($p < 0.02$) and food intake ($p < 0.001$). However, in these experimental

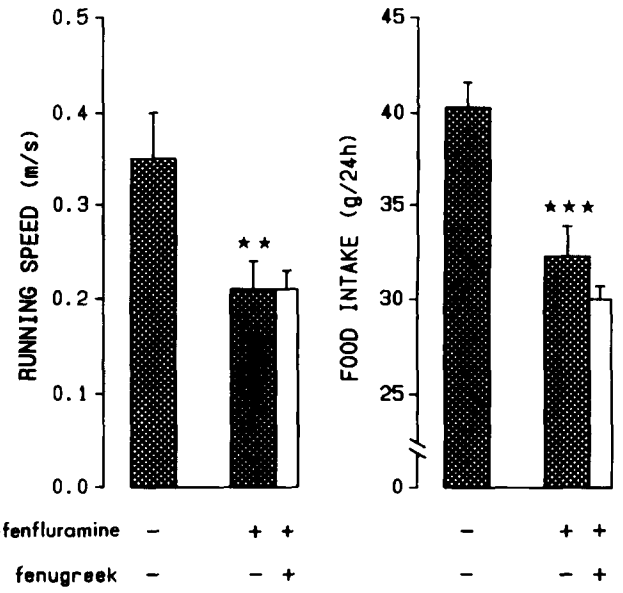

FIG. 3. Experimental anorexia induced by *d*-fenfluramine (2 mg/kg. IP). Effects of the fenugreek seed extract (10 mg/kg per 300 g body weight) on running speed (left panel) and food intake (right panel). Eight animals were used in each set of experiments. $^{**}p < 0.01$, $^{***}p < 0.001$.

conditions the chronic treatment with the fenugreek extract did not prevent the action of *d*-fenfluramine.

Metabolic and Endocrine Effects (Table 1)

The fenugreek-treated group had a significantly higher plasma insulin than the control group (5.91 ± 0.87 vs. 3.72 ± 0.35 ng/ml, $p < 0.01$), whereas plasma glucagon and blood glucose levels were not significantly different.

As regards plasma lipid compounds, the results show a significant decrease in plasma total cholesterol (1.49 ± 0.08 vs. 1.72 ± 0.04 mmol/l, $p < 0.05$), in HDL free cholesterol (0.17 ± 0.01 vs. 0.25 ± 0.02 mmol/l, $p < 0.05$), and in VLDL-LDL total cholesterol (0.64 ± 0.06 vs. 0.85 ± 0.08 mmol/l, $p < 0.05$).

DISCUSSION

The present results clearly show that a chronic oral administration of the fenugreek seed extract increases food consumption in the rat. This effect is not accompanied by an increase in water intake, as it is the case with morphine in freely feeding animals (22), or with most of the typical benzodiazepines (5). Thus, the fenugreek extract does not share the properties of such compounds that enhance the overall ingestional responses in animals. The runway performance has been regarded as a measurement of the motivation of the animal for food, with the running speed being related to the motivational level (6). In these experiments, the fenugreek extract appeared to increase the motivation to eat. The effects of fenugreek on food intake and motivation occurred rapidly and persisted throughout the treatment. When rats are maintained under conditions of a 12 L : 12 D cycle, they eat 80–90% of their food intake during the dark phase (31). The fenugreek treatment significantly increased food intake during the light phase, thus modifying the circadian rhythm of feeding pattern. Finally, food intake increased from the beginning of treatment, whereas the weight gain became significantly higher only during the second week. There was only a minimal difference in weight gain between treated and control animals and, just like the effects on food consumption, the effect on weight gain was not enhanced when a 10-fold higher dose of the fenugreek extract was administered.

Eating behaviour appears to be controlled by hypothalamic structures that also receive inputs from metabolic, hormonal, and other factors (4). The hypothalamus modulates eating behaviour by a balance among several mechanisms involving neurotransmitters such as serotonin (3). Whether one of the numerous components of the fenugreek extract could interfere with central serotoninergic transmission has been investigated using *d*-fenfluramine, an anorectic drug that has been shown to exert its effects on feeding by interacting specifically with brain serotonergic mechanisms (8). Under our experimental conditions, treatment with the fenugreek extract failed to interact with fenfluramine-induced anorexia, suggesting that serotonergic mechanisms do not play a fundamental role in the orexigen effect observed. In addition to physiological signals such as modifications of neurotransmitter functions within the CNS, feeding behaviour is influenced by perceptual cues and depends largely upon palatability. Thus, the effects of fenugreek on food intake and motivation to eat might be related to the well-known aromatic properties of the seeds (9). The participation of the smell in the occurrence of these effects has been ruled out because feeding behaviour was not modified when only the smell of the seed was associated with food, which does not, however, exclude the influence of other components of palatability.

The increase in insulin plasma levels may be due either to a direct stimulatory effect on the B cell of one of the extract components or to an indirect effect related to the palatability and the flavour-enhancer properties of the extract. Thus, using freely moving Wistar rats Berthoud et al. (2) have shown that the sweet taste of a saccharin solution triggered a rapid cephalic phase of insulin response in the absence of any significant change in glycemia. Further, the increase in plasma glucagon level, in counteracting the effect of insulin, may participate in the stability of glycemia.

On the other hand, the present results show a decrease in total cholesterol without any significant changes in HDL cholesterol. These results are in agreement with previous observations in alloxan-diabetic dogs (21) or in type I diabetic patients (27). The present work brings further indications as to the influence of the fenugreek extract treatment on plasma lipoproteins. Thus, in HDL cholesterol the decrease of free cholesterol without change in total cholesterol necessarily implies an increase in cholesterol-esters, which could be explained by an increase in the activity of lecithin cholesterol acyl transferase (11). As regards VLDL-LDL, the decrease in total cholesterol without change in free cholesterol indicates a diminution of cholesterol esters. The VLDL concentration is probably not modified because the triglycerides are stable. Sharma (26) also showed that fenugreek powder did not induce any significant change in triglyceride levels in hypercholesterolemic rats. It can therefore be suggested that treatment with fenugreek extract induces a decrease in LDL.

In conclusion, a chronic administration of the fenugreek seed extract increases food intake and motivation to eat in rats. Moreover, this extract appears to induce hyperinsulinemia as well as hypocholesterolemia.

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TABLE 1

METABOLIC PARAMETERS RECORDED IN NORMAL FED RATS AFTER A DAILY INTAKE OF THE FENUGREEK SEED EXTRACT (10 mg/24 h PER 300 g b.w.)

Animals	Blood Glucose (mg/dl)	Plasma Insulin (ng/ml)	Plasma Glucagon (pg/ml)	Plasma TC (mmol/l)	Plasma FC (mmol/l)	Plasma TG (mmol/l)	HDL TC (mmol/l)	HDL FC (mmol/l)	VLDL-LDL TC (mmol/l)	VLDL-LDL FC (mmol/l)
Control (8)	85 ± 2	3.72 ± 0.35	123 ± 11	1.72 ± 0.04	0.65 ± 0.02	1.80 ± 0.06	0.79 ± 0.06	0.25 ± 0.02	0.85 ± 0.08	0.32 ± 0.04
Treated (8)	90 ± 4	5.91 ± 0.87*	178 ± 36	1.49 ± 0.08†	0.58 ± 0.03	1.81 ± 0.06	0.82 ± 0.05	0.17 ± 0.01†	0.64 ± 0.06†	0.31 ± 0.02

The number of animals is indicated in parentheses. TC, total cholesterol; FC, free cholesterol; TG, triglycerides.
*$p < 0.01$.
†$p < 0.05$.

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