Effects of Fenugreek Seed Extract in Obese Mice Fed a High-Fat Diet

Toshiaki HANDA,1 Kohji YAMAGUCHI,1 Yoshikatsu SONO,2 and Kazunaga YAZAWA1,†

1Laboratory of Nutraceuticals and Functional Foods Science, Graduate School of Marine Science and Technology, Tokyo University of Marine Science and Technology, 4-5-7 Konan, Minato-ku, Tokyo 108-8477, Japan
2Technical Sourcing International, Inc., 2-8-2 Nihonbashi Honcho, Chuo-ku, Tokyo 103-8448, Japan

Received October 14, 2004; Accepted March 11, 2005

It was found that fenugreek seed extract reduced the body weight gain induced by a high-fat diet in obese mice. The extract decreased plasma triglyceride gain induced by oil administration. The major component of the extract, 4-hydroxyisoleucine, also decreased plasma triglyceride gain. Consequently, fenugreek seed extract is expected to prevent the obesity induced by a high-fat diet.

Key words: fenugreek; 4-hydroxyisoleucine; high-fat diet; triglyceride; obesity

Obesity is an abnormal condition accumulating lipid in adipose tissue. It is known that it is caused by various environmental and genetic factors.1) One of the main environmental factors causing obesity is the high-fat diet which has come into wide use today. Obesity can be a risk factor for disease, including diabetes, hyperlipemia, and hypertension. Hence it is very important to prevent obesity for a healthy life.

During in vivo screening for anti-obesity foods, an extract of fenugreek seed was found to have a potent suppressive effect on obesity in mice on a high-fat diet. Fenugreek (Trigonella foenum graecum L) is a leguminous plant extensively cultivated in India, the Mediterranean, and Africa. It is traditionally used as a medical herb and a spice. Previously, a fenugreek extract has been reported to have an effect in improving diabetes2) and hypercholesterolemia.3)

Fenugreek seed was extracted with ethanoal and the solution was evaporated. The extract significantly reduced the body weight gain induced by a high-fat diet (Fig. 1). These obese model mice were fed a high-fat diet containing 30% casein, 40% beef tallow (w/w), 11% cornstarch, 5% cellulose, 9% sucrose, 1% vitamins, and 4% minerals. Female ddY mice (4 weeks old) were used. Animal studies were done according to the 1980 guideline entitled Notification No. 6 of the Prime Minister’s Office of Japan. Fenugreek seed extract administrated groups were fed a high-fat diet containing 0.3% and 1% fenugreek seed extract in place of 0.3% and 1% casein, because it is known that a small change in casein content does not affect body weight gain.4) A low-fat diet contained 30% casein, 5% beef tallow (w/w), 11% cornstarch, 40% cellulose, 9% sucrose, 1% vitamins, and 4% minerals. The fenugreek seed extract did not affect food intake.

As shown in Table 1, feeding the high-fat diet markedly increased tissue weight in adipose tissue compared to the low-fat diet. The fenugreek seed extract (1% and 0.3%) significantly reduced adipose tissue weights. Liver weight was also decreased by it (1%). Although the extract did not affect solid liver weight excepting lipids, liver triglycerides decreased. These results suggest that fenugreek seed extract decreased

---

† To whom correspondence should be addressed. Fax: +81-3-5463-0417; E-mail: yazawa@s.kaiyodai.ac.jp

---

Fig. 1. Effect of Fenugreek Seed Extract on Body Weight in Obese Model Mice.
Mice (5 weeks old, female) were fed a high-fat diet (□, n = 8) and a low-fat diet (●, n = 7). Fenugreek seed extract was mixed into a high-fat diet at concentrations of 0.3% (●, n = 7) and 1% (△, n = 8). The mice were fed these diets for 22 d. Body weight was measured twice a week. Data are expressed as the mean ± S.E. and were analyzed by one-way ANOVA and Scheffe’s test; *p < 0.05, **p < 0.01, ***p < 0.005, vs. the high-fat diet group.
lipid accumulation in the liver induced by a high-fat diet. On the other hand, the extract did not affect the tissue weights of the kidney and spleen. It affected lipidic tissue selectively. These results indicate that the body weight reduction was caused by inhibition of fat accumulation but not by the toxicity of the extract. The safety of fenugreek was also shown in rats by P. U. Rao et al.5)

For the purpose of clarifying the mechanism of the body weight reduction, the effect of the fenugreek seed extract on absorption of triglyceride in the intestines was investigated by a lipid-loading test. Female ddY mice (7 weeks old) were used. After fasting for 24 h, the mice were administrated 0.2 ml of corn oil with the extract solution or vehicle (distilled water). The fenugreek seed extract decreased the plasma triglyceride gain caused by corn oil administration (Fig. 2).

The extract used in this study contained about 20% 4-hydroxyisoleucine. Hence 4-hydroxyisoleucine was also investigated using the same experiments, as described above. 4-Hydroxyisoleucine decreased the plasma triglyceride gain caused by corn oil administration, but not the only one. It has been reported that fenugreek seed contains some bioactive compounds, for example, amino acids, galactomannan, flavonoids, and saponins. It is necessary to isolate active compounds in the fenugreek seed extract. The study of active compounds is now being pursued in our laboratory. Furthermore, these results suggest that inhibition of lipid absorption is not enough to prevent obesity. This suggests the hypothesis that prevention of obesity by fenugreek seed extract is caused not only by inhibition of lipid absorption but also in other ways.

The effective doses of fenugreek seed extract in the lipid-loading test and the high-fat diet feeding test were 750 mg/kg and about 350 mg/kg/d respectively. The dose of 350 mg/kg/d was calculated from the amount of food intake in the group fed the high-fat diet containing 0.3% fenugreek seed extract. These doses are perhaps too high for a dietary supplement or a drug. But high doses were necessary to prevent the undesirable effects of the large amount of lipid that was used to obtain clear results. The doses of lipid in the lipid-loading test and the high-fat diet feeding test were 6,000 mg/kg and about 53,000 mg/kg/d respectively. These great amounts of lipid are impossible to intake in our usual diet. Since the average intake of lipid in Japan is about 53,000 mg/kg/d respectively. These great amounts of lipid are impossible to intake in our usual diet. Since the average intake of lipid in Japan is 55.3 g/d,8 the daily dose of a man of 60 kg body weight is under 1,000 mg/kg/d. Since the daily dose of lipid in humans is much lower than the doses in these experiments, the undesirable effects of lipid in our usual diet ought to be prevented by a smaller dose of fenugreek seed extract than in these experiments. On the other hand, there is rich experience in eating of fenugreek. These results suggest that fenugreek seed extract ought

### Table 1. Effect of Fenugreek Seed Extract on Tissue Weight in Obese Model Mice

<table>
<thead>
<tr>
<th></th>
<th>Low-fat diet (mean ± S.E.)</th>
<th>High-fat diet (mean ± S.E.)</th>
<th>High-fat diet + fenugreek (mean ± S.E.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adipose tissue (g/100 g body weight)</td>
<td>1.5 ± 0.7^b</td>
<td>4.9 ± 1.2</td>
<td>3.4 ± 0.9^b</td>
</tr>
<tr>
<td>Liver (g/100 g body weight)</td>
<td>4.8 ± 1.9^c</td>
<td>12.1 ± 3.2</td>
<td>10.3 ± 2.3</td>
</tr>
<tr>
<td>Liver triglyceride (mg/g liver weight)</td>
<td>11.5 ± 1.6^d</td>
<td>65.8 ± 6.8</td>
<td>31.8 ± 2.8^e</td>
</tr>
<tr>
<td>Solid liver weight (g/100 g body weight)</td>
<td>4.7 ± 0.1</td>
<td>4.6 ± 0.1</td>
<td>4.7 ± 0.2</td>
</tr>
<tr>
<td>Kidney (g/100 g body weight)</td>
<td>1.5 ± 0.1^b</td>
<td>1.2 ± 0.1</td>
<td>1.3 ± 0.1</td>
</tr>
<tr>
<td>Spleen (g/100 g body weight)</td>
<td>0.4 ± 0.1</td>
<td>0.4 ± 0.1</td>
<td>0.4 ± 0.1</td>
</tr>
</tbody>
</table>

Mice (5 weeks old, female) were fed a high-fat diet (n = 8) and a low-fat diet (n = 7). Fenugreek seed extract was mixed into a high-fat diet at concentrations of 0.3% (n = 7) and 1% (n = 8). The mice were fed these diets for 22 d, and then wet tissue weights were measured. Data are expressed as the mean ± S.E., and were analyzed by one-way ANOVA and Scheffe’s test; ^p < 0.05, ^p < 0.005, vs. the high-fat diet group.

![Fig. 2. Effect of Fenugreek Seed Extract on Plasma Triglyceride Concentration in Lipid-Loading Test.](image-url)

Mice (8 weeks old, female, n = 9) were administrated 0.2 ml of corn oil after fasting for 24 h with oil, 750 mg/kg; △, 1500 mg/kg) or without (■) fenugreek seed extract. Plasma triglyceride concentration were measured from 0 to 6h. Data are expressed as the mean ± S.E., and were analyzed by one-way ANOVA and Scheffe’s test; *p < 0.05, ***p < 0.005, vs. the control group.
to be accepted as a useful anti-obesity food. More experiments, including in humans, are required.

References


