Original Communication

Effect of Fenugreek Seeds on Blood Glucose and Lipid Profiles in Type 2 Diabetic Patients

Nazila Kassaian[1], Leila Azadbakht[2], Badrolmolook Forghani[3], Masud Amini[3]

[1]Infectious Diseases Research Center. Isfahan University of Medical Sciences, Isfahan, Iran.
[2] Department of Nutrition, School of Health, Isfahan University of Medical Sciences, Isfahan, Iran.
[3] Endocrine and Metabolism Research Center. Isfahan University of Medical Sciences, Isfahan, Iran

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Abstract: *Background:* Recently use of herbal medicines, have been considered as an alternative for therapeutic usage. So, this study was undertaken to evaluate the hypoglycemic and hypolipidemic effects of fenugreek seeds in type 2 diabetic patients.
Methods: In a clinical trial study, 24 type 2 diabetic patients were placed on 10 grams/day powdered fenugreek seeds mixed with yoghurt or soaked in hot water for 8 weeks. Weight, FBS, HbA_1C, total cholesterol, LDL, HDL and food record were measured before and after the study. The differences observed in food records, BMI and serum variables were analyzed using paired-t-test and t-student and $P \leq 0.05$ was considered as significant.
Results: After exclusion of 6 cases for changing in medication or personal problems, the results of 18 patients (11consumed fenugreek in hot water and 7 in yoghurt)were studied. Findings showed that FBS, TG and VLDL-C decreased significantly (25 %, 30 % and 30.6 % respectively) after taking fenugreek seed soaked in hot water whereas there were no significantly changes in lab parameters in cases consumed it mixed with yoghurt. BMI, Energy, Carbohydrate, Protein and fat intake remained unchanged during study.
Conclusion: This study shows that fenugreek seeds can be used as an adjuvant in the control of type 2 diabetes mellitus in the form of soaked in hot water.

Key words: Fenugreek Seed, Diabetes Mellitus, Glycosylated Hemoglobin, Blood Sugar, Serum Lipids.

Introduction

Diabetes mellitus is one of the major metabolic disorders, afflicting a large proportion of the population all over the world. It is recognized for sever complications, which include diabetic nephropathy, neuropathy and retinopathy (1). Type 2 diabetes may account for 90 % to 95 % of all diagnosed case of diabetes. The primary goals for persons with type 2 diabetes are to achieve and maintain normal blood glucose and lipid levels (2). In any form of management of diabetes with insulin or drug, diet is a common factor. With respect to diet, plants and foods of medicinal value have proved to be very useful which one of them is fenugreek seed (3, 4).

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Fenugreek (Trigonella foenum graecum) is an annual herb belonging to the family Leguminosae, widely grown in India, Egypt and Middle Eastern countries (5). Fenugreek seeds are used as a traditional remedy for the treatment of diabetes and hypercholesterolemia in Ayurvedic (Indian), Unani (Arabic) and Chinese medicine
(6, 7). In some of studies of animals and humans with both diabetes and high cholesterol levels, fenugreek appeared not only to regulate blood sugar levels but also lower levels of harmful cholesterol. However, in studies of those who did not have diabetes, a similar effect was not reported (8). It has been said that he seeds are rich in protein and contain a unique major free amino acid 4-hydroxisoleicine (4-OH-IIe), which has been characterized as one of the active ingredients in fenugreek seeds. The effect of 4-OH-ILe is both dose and glucose dependent and has been shown to stimulate insulin secretion and improve glucose tolerance in normal and diabetic animals as the result of direct β-cell stimulation (9, 10). It is said that fenugreek, reveals a potential benefit in diabetes either in a mixture of water or milk products or in cooking (11). In limited of the alternative references it is prescribed in the form of mixed with yoghurt and in others, in the form of soaked in hot water (12) but, the most effective form has not been established approved.

In the other hand, the potential effects of this herb has not been approved yet and due the lack of sufficient clinical studies, it is premature to actively recommend use (13, 14). In Iran, the use of medicinal herbs ie. Fenugreek among diabetic patients is common. Therefore, it is essential to increase the level of awareness among diabetic patients and health care providers regarding the efficacy of this medicinal herb using more clinical studies.

Fenugreek natural extractives, oleoresins and essential oils are generally recognized as safe (GRAS) approved (21 CFR 182.20), included by the Council of Europe in the list of substances granted Approval (COE No.460) and GRAS by the Flavor and Extract Manufacture's Association (FEMA No. 2485) (5). Thus, the present study was conducted to evaluate the beneficial effect of fenugreek seed powder on diabetic status **in different formulations** in type 2 diabetic patients.

Methods and Materials

In a before and after clinical-trial study, 24 type 2 diabetic patients (diagnosed by ADA protocol) referred to Isfahan Endocrine and Metabolism Research Center in 2005 who had no gastrointestinal problems after giving constant entered in to study. They were both male and female over 30 years old and either used no hypoglycemic or hypolipidemic agents or theirs might be unchanged during study. Also, they were prescribed to have the diet and physical activity as they had before during the study. The patients were divided into two equal groups (A, B): Group A in took 5 grams fenugreek seed powder into 250 g yoghurt and group B used the same amounts into one quart hot water before lunch and dinner (10grams per day) for two months.

Fasting blood glucose, serum triglyceride, LDL and HDL cholesterol (Enzymatic, Colorimetric method: Zistchimi-Tehran-Iran), HbA_1C (Colorimetric method: Mahsayaran-Tehran-Iran), 3-days food record, weight and height were obtained and LDL-C/HDL-C, TCHOL/HDL-C, VLDL (TG/5), intake of daily energy, charbohydrate, protein, fat and BMI were calculated before and after study.

Data observed before and after fenugreek seed consumption in each group and between two groups, were compared via paired t-test and t-student in SPSS-11 software and $P \leq 0.05$ was considered statistically significant.

Results

Six subjects were excluded because of changes in their medication or personal problems. The remains were 7 in group A and 11 in group B. They were 14 women and 4 men with mean of age 52.8±9 and duration of diabetes: 7.69±5.34 years. 8 ones didn't receive any medication and were on diet alone and the other 6 were on hypoglycemic agents who 2 were on hypolipidemic agents as well which remained unchanged during the study. Their mean of BMI was 27.4±3.6 kg/m^2 which remained unchanged during the study. Also the amounts of energy, carbohydrate, protein, fat intake were unchanged during the study (Table I). There was no statistically significant changes in lab parameters in group A (Table II) but in group B, fenugreek seed, as it seen in Table III, reduced FBS (25%), TG (30%) and VLDL (30.6%) significantly.

Total cholesterol and FBS were significantly decreased in group 2 compaired with group 1 (Table IV).

Table I: Body mass index and the amount of nutrients intake among the type 2 diabetic patients (n=18)

Parameter	Initial	Final	P-Value [1]
BMI (kg/m^2)	27.4 ± 3.6 [2]	27.3 ± 3.6	0.18
Energy (kcal)	1411 ± 446	1325 ± 409	0.2
Carbohydrate (g)	200 ±54	190 ±36	0.5
Protein (g)	66 ±10	63 ±8	0.5
Fat (g)	38 ±12	31 ±15	0.09

[1] P-Values were calculated by independent t-test
[2] Values of mean ± SD

Table II: Effect of fenugreek seed powder soaked in yoghurt on lab parameters in type 2 diabetic patients (n=7)

Lab parameter	Initial	Final	P-Value[1]
Total cholesterol (mg/dl)	206.8 ± 46[2]	228.4± 42	0.17
FBS (mg/dl)	142.6 ± 24.8	152.6 ± 24	0.28
HbA_1 C(%)	9.6 ± 1	9 ± 1	0.54
HDL-C (mg/dl)	41.2 ± 9	40.7 ± 13	0.94
LDL-C (mg/dl)	124± 54	155 ± 37	0.2
TG (mg/dl)	201.4± 37	182.8 ± 56	0.28
LDL-C /HDL-C(mg/dl)	3.96± 0.8	3.9 ± 1	0.92
TC/HDL-C (mg/dl)	5.7± 1.6	5.9 ± 1.3	0.9
VLDL-C (mg/dl)	42.5± 10	39.7± 12.7	0.2

[1] P-Values were calculated by independent t-test
[2] Values of mean ± SD

Table III: Effect of fenugreek seed powder in hot water on lab parameters in type 2 diabetic patients (n=11)

Lab parameter	Initial	Final	P-Value[1]
Total cholesterol (mg/dl)	230.3 ± 50.8[2]	208.5± 29.5	0.1
FBS (mg/dl)	182 ± 58	136 ± 25	0.01 *
HbA_1 C(%)	9.8 ± 1.6	9.6 ± 0.9	0.58
HDL-C (mg/dl)	41.9 ± 6.9	42.7 ± 6.6	0.7
LDL-C (mg/dl)	134.4± 49	122 ± 27	0.25
TG (mg/dl)	245.4± 131	172 ± 84	0.04*
LDL-C /HDL-C(mg/dl)	3.5± 1.6	2.9 ± 1	0.1
TC/HDL-C (mg/dl)	5.6± 1.8	4.8 ± 1.1	0.06
VLDL-C (mg/dl)	49± 26	34± 16	0.04*

[1] P-Values were calculated by independent t-test
[2] Values of mean ± SD
* Significant differences (P-Value ≤0.05)

Table IV: The comparison of laboratory parameters between 2 groups

Lab parameter	Differences In Group 1* n= 7	Differences In Group 2** n= 11	P-Value
Total cholesterol (mg/dl)	***22 ± 26	22 ± 43	0.02†
FBS (mg/dl)	10 ± 30	46.3± 51.5	0.01†
HbA_1 C (%)	0.6 ± 1.4	0.2 ± 1.5	0.9
HDL-C (mg/dl)	0.7 ± 3.2	0.8 ± 9.1	0.5
LDL-C (mg/dl)	0.06± 1	0.6 ± 7.2	0.6
TG (mg/dl)	18± 45	12 ± 30	0.1
VLDL-C (mg/dl)	2.8± 5.4	15± 20.7	0.1

*Group 1: consuming fenugreek seeds with yoghurt.
**Group 2: consuming fenugreek seeds soaked in hot water.
***The mean ±SD of Before-after study amounts.
† Statistically significant

Discussion

In this study, improvement in fasting blood sugar, triglyceride and VLDL levels were observed after fenugreek seed soaked in hot water consumption.

Also, HbA_1C, total cholesterol and LDL-C levels tended to be lower and HDL-C to be higher but without a statistical difference. These results were similar to those by Basch et al (6), Boca et al (8, 9), Khosla et al (12) and Kumar et al (1) who reported hypoglycemic effects of fenugreek seed and differ from those by Whorter (16), Stark et al (16) and LU et al (17), who indicated fenugreek seed can improve serum cholesterol and glycated hemoglobin in diabetic patients or animals. Recent study, also indicated that fenugreek seed powder consumed with yoghurt had no role neither on hypoglycemic nor hypolipidemic status in type 2 diabetic subjects. In group who consumed fenugreek seeds in hot water, FBS, total cholesterol, glycated hemoglobine, triglyceride and LDL-C decreased and HDL-C increased during study whereas in group who added it in yoghurt, total cholesterol and FBS increased and the other parameters de4cresed. Total cholesterol and Fasting blood sugar were significantly decreased following fenugreek seed consumption soaked in hot water compare with in yoghurt. So, it seems that it is better to use this herbal medicine in the form of soaked in hot water. In the most studies, anti-diabetes effects of fenugreek seed in water were under assessment (18). It may be because that fenugreek seed contains a substantial amount of mucilaginous fiber which is cause of the most beneficial effects of it. The mucilage found in fenugreek, does not dissolve but instead swells when mixed with fluids like water (10) and for better digestion, it is preferred to soaked in hot water. Purported hypoglycemic mechanisms of fenugreek seed include delay of gastric emptying, slowing carbohydrate absorption and inhibition of glucose transport from the fiber content, as well as increased erythrocyte insulin receptors and modulation of peripheral glucose utilization (18,19).

Additionally, studies indicate that 4-hydroxyisoleucine found in fenugreek seed, may induce or promote the production of insulin when blood sugar levels are elevated. This amino acid appeared to act only on pancreatic beta cells, since the levels of somatostatin and glucagons were not altered (9, 10).

In a study by Mohammad et al (20) in India, alloxan-diabetic animals have been taken and the administration of fenugreek seed powder was assessed for its effect on the expression of pyruvate kinase (PK) and phosphoenolpyruvate carboxykinase (PEPCK) in liver and corrected the alteration in distribution of glucose transporter (GLUT4) in the skeletal muscle.

PK and PEPCK are 2 enzymes of glycolysis and gluconeogenesis respectively and play a crucial role in glucose homeostasis along with skeletal muscle glucose transporter. In the diabetic state, this balance is disturbed owing to the absence of insulin, the principal factor controlling this regulation.

In fenugreek, various components of the seeds have varying activities. For example, the component called fenugreekine, a steroidal sapogenin peptide ester, may exert hypoglycemic properties. Trigonelline, another component, may exert hypoglycemic

effects in healthy patients without diabetes, but other studies have shown that fenugreek has no effect on fasting or postprandial blood glucose levels in non-diabetic subjects.

In Preet et al (21) study, fenugreek seed powder added to diabetic rat diets for 60 days, improved polyol pathway enzymes aldose reductase and sorbitol dehyrogenase and modulated the activities of hexokinase, glucose-6-phosphate dehyrogenase, glutathione peroxidase and glutathione reductase in the rat lens to control values. The authors concluded that fenugreek seed may be considered as promising approaches for the prevention of diabetic retinopathy and other ocular disorders. Another studies showed that fenugreek seeds can improve glucose metabolism and normalized creatinine kinase activity in heart, skeletal muscle and liver of diabetic rate. It also reduced hepatic and renal glucose 6-phosphatase and fructose 1, 6-biphosphatase activity and has antioxidant properties (22).

It is possible fenugreek lowers lipids because it contains saponins that are transformed in the gastrointestinal tract into sapogenins. Fenugreek seeds contain
50-percent fiber (30-percent soluble fiber and 20-percent insoluble fiber). This may be a secondary mechanism for its hypolipidemic effect.

The lipid-lowered effect of fenugreek might also be attributed to its estrogenic constituent, indirectly increasing thyroid hormone T_4 (6). Experiments in vitro employing the averted-sac technique showed that the ethanol extract of fenugreek seed, had the ability to inhibit taurocholate and deoxycholate absorption in a
dose-dependent manner and so, the hypocholesterolaemic effect. Most of studies indicate that the hypolipidemic effects of fenugreek seed are in defatted type. It may be the reason that in recent study, serum cholesterol, LDL and HDL-C remained unchanged. It may also because of the dose of fenugreek seed given in this study which is differ from other studies. The significant decrease in triglyceride and VLDL observed in this study, might be because of fenugreek seed's effects on glycemic control or polyol pathway.

In conclusion, this study shows that fenugreek seeds can be used as an adjuvant in the control of type 2 diabetes mellitus. More well defined clinical trials are warranted in this area.

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Nazila Kassaian

Infectious Diseases Research Center
Isfahan University of Medical Sciences
Isfahan, Iran
E-mail: Arbabnia_mn@Yahoo.com