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The Postprandial Hypoglycemic Activity of Fenugreek Seed and Seeds' Extract in Type 2 Diabetics: A Pilot Study

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ABSTRACT

Trigonella foenum-graecum L. is directly related to the traditional use. *Trigonella foenum-graecum* L. have been reported to be beneficial for treating type 2 diabetes (T2D). The study was conducted to investigate the postprandial hypoglycemic effect of fenugreek seeds on patients with T2D. Pretest - posttest control group design was used to test the hypothesis that fenugreek may have a hypoglycemic effect on blood sugar. One hundred sixty-six D2T patients were assigned into three groups: FG0 (control group: placebo drink), FG2.5 (2.5g of fenugreek), and FG5 (5g of fenugreek). Participants were instructed to drink the extract and chew the seeds. Postprandial plasma glucose level was measured before and 2-hours after the administration of the treatment. Accounting for gender, age, education, physical activity, body mass index, glycemic control, and medication, patients in FG5 group showed the greatest decrease in postprandial glucose with a pretest-posttest difference (D) of -41 ± 6.1 mg/dl. Two-hour plasma glucose dropped for patients in FG2.5, however, the drop was not statistically different from that noticed in the placebo group ($D = -24.8 \pm 4.9$ mg/dl vs. -9.8 ± 2.2 mg/dl respectively). Fenugreek seeds appear to have a significant hypoglycemic activity in T2D patients.

KEYWORDS: Type 2 diabetes (T2D); *Trigonella foenum-graecum* L.; Postprandial Period; Hyperglycemia; Hypoglycemia.

INTRODUCTION

Type 2 diabetes (D2T) is one of the primary threats to human health due to its increasing prevalence, chronic course and disabling complications. Diabetes and diabetes-associated complications such as atherosclerosis, and cardiovascular disease are becoming major causes of mortality. According to the World Health Organization (WHO) there were 150 million people over 20 years of age living with diabetes in 2000 and they project that by 2025 there will be 300 million people living with this condition. The increase is expected to be 42% in developed countries and 70% in developing countries (1). In Jordan, diabetes affects a much higher proportion of people during their prime working years. Male deaths during middle age could create a significant cohort of widows, which increases the likelihood that women will live out their final years in poverty. In both humanitarian and economic terms,

diabetes is one of the most costly diseases (2). The problem of diabetes becomes more complex by the fact that diabetes mellitus is not a single disease but occurs in several forms and has complications that can affect every system in the body (3)

Currently, there is an arsenal of synthetic hypoglycemic drugs available; however, these drugs normally cause side effects prompting the patients to stop taking the medication and T2D progresses with further acute and chronic complications and even death. For this reason, a phytomedicine capable of treating the disease at early stages, but with fewer side effects and less expensive, will be of great help to the diabetic patients specially due to the extended belief that natural treatments cause less harm to the organism (4). There is an interest among health care providers, nutritionists, regulatory agencies, diabetic

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patients, and the general public to investigate the potentials of functional foods against both types of diabetes. The uniqueness of fenugreek seeds lies in its content of several highly desirable biologically active compounds having considerable potentials for the use in the food and pharmaceutical industries, particularly relative to newer developments in the area of functional foods or nutraceuticals (5). Fenugreek, *Trigonella foenum-graecum* L (Leguminosae), is a medicinal plant of Mediterranean origin, used by ancient Egyptians and cultivated worldwide. Some researchers have studied two fractions of the seed, precisely the lipid extract, and the defatted seed material which contains fibers (6). The researcher concluded that the active component was in the defatted portion of the seeds not in the lipid extract. Ribes et al (1986) further divided the defatted portion into two sub fractions namely, subfraction 'a' which comprised of the testa and endosperm, this subfraction is rich in fiber (79.6%) and associated with the hypoglycemic effects of fenugreek. Whereas, subfraction 'b' consisted of cotyledons and axles and is rich in proteins (52.8%) (3). Numerous beneficial effects of fenugreek has been reported including the use of fenugreek as an antioxidant (7-8), anti-carcinogenic (9-10), anti-microbial (11-12), anti-ulcer (13), anti-obesity (14), and hypocholesterolemic (15-17). Other desirable actions of the extracts of fenugreek include protection against hyperglycemia in patients with diabetes (18-22-19). Many studies have addressed the potential effect of fenugreek seeds on hyperglycemia, however, only a few have been subjected to studying this effect in humans. In this study, we intended to investigate the hypoglycemic activity of fenugreek seed along with the aqueous extract in patients with D2T.

MATERIALS AND METHODS

Plant Material and Extract Preparation:

The fenugreek seeds (*Trigonella foenum graecum*) were purchased from a local market. The identity of the plant species was verified by a professional taxonomist using live specimens. Voucher specimens of these herbs were stored at the faculty herbarium.

Control group received a solution of 0.8 g of dextrose dissolved in 25 ml of warm water. Treatment groups (FG2.5 and FG5 groups) received fenugreek seeds soaked in dextrose solution a ratio of 1:5 (wt:vol). Fenugreek amounts used were 2.5 g and 5 g, for FG2.5 and FG5 groups respectively. After cooling down, participants were asked to drink the extract and chew the seeds.

Study Protocol

The study was conducted according to the principles stated by Declaration of Helsinki and approved by the deanship of research at Jordan University of Science and Technology (JUST).

Information about the objectives of the study and the procedure were provided in the consent form and were explained to the participants. The patients were informed about the benefits and possible risks of the study; they could withdraw at any time during the study for any personal reason, or if he or she developed an adverse reaction to the treatments. Participants were asked to sign a consent form if they agreed to participate. Upon consenting, each participant was interviewed, asked to recall food items and preparation type eaten at breakfast.

Selection Criteria

Inclusion criteria: Outpatients from either sex with diagnosis of type 2 diabetes (40-70 years old) were selected. All patients must be under medical treatment, showing either a Poor (HbA1C >8.5) or Fair control (HbA1C ≤8.5).

Exclusion criteria: Patients affected by diabetic complications or with clinical and biochemical data of nephropathy were not enrolled. Also excluded were pregnant women, patients with diagnosis of gestational diabetes, insulin-dependent or type 1 diabetics, people who needed to travel frequently, and hospitalized patients.

Study Design

One Hundred Sixty-six patients from both genders (females= 91, males =75) suffer from T2D were recruited from different towns in northern Jordan. Height and weight were measured to calculate body mass index (BMI). Data regarding last glycosylated test (HbA_{1c}) as an indicator of glycemic control, level of physical activity, education, age, and medications used to manage diabetes, were also obtained. Pretest - posttest control group design (23) was selected to test the hypothesis that patients consuming fenugreek may have lower postprandial blood glucose level. Participants were assigned randomly into three groups in such a way that it will allow best possible matching in gender, age, education, physical activity, glycemic control, type of medication used to manage diabetes, and body mass index. The groups were as follow:

- 1st group :FG0 group (n=50; participants received a placebo drink),
- 2nd group: FG2.5 group (n= 61; participants ingested 2.5 g of fenugreek),

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- 3rd group: FG5 group (n=55; participants ingested 5 g of fenugreek).

Participants were visited at their residences before lunch time (typical lunch time in Jordan is 2:00 p.m.). This time was chosen to catch participants in postprandial state. The rationale for selecting postprandial state not a fasting state, taking a risk of increasing variability between groups, is that we wanted to minimize the risk of developing hypoglycemia after ingesting the fenugreek. Participants in the untreated control FG0 group were directed to drink the prepared solution. Participant under the two treatments groups (FG2.5 and FG5), were asked to drink the extract and chew the seeds. The assessed endpoint was proposed to be the blood glucose level 24. Blood glucose levels were measured for all participants before dose ingestion (pretest) and two hours later (posttest), using blood glucose meter (Super Glucocard II). The differences between the pretest and the posttest (D) was calculated and tested against zero.

Statistical analysis:

The distribution of the confounding variables between groups was studied using Chi-square test. Means of SD were subjected to ANOVA for a completely randomized design using the general linear procedure of SAS (SAS Institute, 1991. Version 6.0). Means comparison were analyzed using the LSD procedure of SAS. Unless otherwise stated, significance was declared at $p < 0.05$.

RESULTS

Table 1 indicates that participants from both genders, different level of physical activity, different levels education, and from different therapeutic approaches were distributed evenly in the groups. Chi -square showed no differences between the observed frequencies and the expected ones. There were no mean differences in age, and the last HbA_{1c} reading ($P > 0.05$). As shown in Figure 1, there was a dose dependant reduction in the postprandial blood glucose level such, that the higher the fenugreek dose the lower blood glucose level.

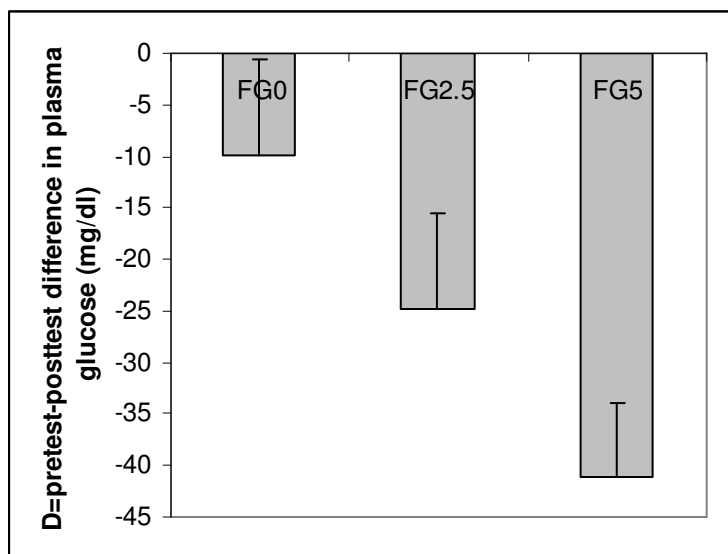
Table 1 Distribution of demographic and health related variables between the control and the experimental groups.

VARIABLE	FG0 (N=50)	FG 2.5 (N=61)	FG5 (N=55)	CHI SQUARE, F (P- VALUE)
Gender: n (%)				
Males	22 (56 %)	31 (51%)	22 (40%)	2.8 (0.24)
Females	28 (44%)	30 (49%)	33 (60%)	2.8 (0.24)
Age (Mean years $\pm$ S.E*)	58.20 $\pm$ 1.9	59.7 $\pm$ 1.7	53.3 $\pm$ 1.8	0.5 (0.58)
Education: n (%)				
Illiterate	6 (24%)	24 (39 %)	16 (29 %)	3.0 (0.21)
High school	22 (44%)	27 (44%)	24 (44%)	0.0 (1.0)
College degree	16 (32%)	10 (17%)	15 (27%)	3.5 (0.17)
Physical Activity: n (%)				
Active (leisure physical activity)	10 (20%)	7 (11%)	12 (23%)	3.1 (0.20)
Sedentary (activities of typical day-to-day life)	40 (80%)	54 (89%)	43 (77%)	3.1 (0.20)
BMI: n (%)				
Underweight (<18.5)	0 (0)%	0 (0)%	2 (1%)	1.1 (0.60)
Normal (18.5-24.9)	16 (32%)	12 (20%)	10 (18%)	3.4 (0.18)
Overweight (25-29.9)	24 (48%)	31 (50%)	23 (42%)	0.8 (0.67)
Obese (> 30)	10 (20)%	18 (29%)	20 (36%)	3.3 (0.19)
Medication: n (%)				
None	7 (14%)	5 (8%)	5 (9%)	1.2 (0.55)
Insulin	18 (36%)	20 (33%)	21 (38%)	0.3 (0.85)
Oral hypoglycemic drugs	19 (38%)	32 (52%)	28 (51%)	2.6 (0.27)
Combination therapy	6 (12%)	4 (7%)	1 (2%)	4.1 (0.13)
Glycemic control				
Poor (HbA _{1c} >8.5)	29 (58%)	36 (59%)	35 (64%)	0.5 (0.8)
Fair control (HbA _{1c} $\leq$ 8.5)	21(42%)	25 (41%)	20 (36%)	0.5 (0.8)

*S.E. = standard error

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Figure 1 Change in plasma glucose before and 2-hours after the ingestion of fenugreek in control and experimental groups *.



* Error bars represent the standard error of the mean; bars with different letters are significantly different ($p < 0.05$)

DISCUSSION AND CONCLUSION

Patients with T2D, in most cases, have problem with insulin sensitivity rather than insulin secretion. This may explain the decrease in the pre- and post-test (D) in the placebo group. The ingestion of 2.5 g of fenugreek seeds with their aqueous extract does not seem to have significant effect. The D value observed for FG2.5 ($D = -24.8 \pm 9.3$) was not statistically different from that observed for the FG0 ($D = -9.8 \pm 2.2$ mg/dl) group. However, administration of 5 g of fenugreek seems to be effective in achieving a greater statistically significant drop in blood glucose levels ($D = -41.1 \pm 7.2$).

Fenugreek seeds have been known for a long time for their anti-diabetic action (25-26). The prevalence of diabetes is becoming increasingly alarming and is projected to increase substantially over the next decades. Hence, there is an interest among health care providers to investigate the potentials of medicinal plants and functional foods against both types of diabetes. The uniqueness of fenugreek seeds lies in its content of several highly desirable biologically active compounds having considerable potentials for the use in the food and pharmaceutical industries. Xue and coworkers reported that oral administration of fenugreek extract for Streptozotocin-induced diabetic resulted in lower blood glucose and glycosylated hemoglobin (27). This effect of fenugreek was also observed when normal mice were used (28). A number of investigations have been conducted to

identify the factors responsible for the antidiabetic activity of fenugreek and the mechanisms involved in this effect. Fenugreek seeds contain high amount of fiber (30% soluble fiber and 20% insoluble fiber). The role of fiber in reduction blood glucose of diabetic patient has been extensively studied and well established. Therefore, another mechanism by which fenugreek seeds lower blood glucose level is due to its high content of soluble fiber which would delay the gastric emptying and interfere with glucose absorption (29).

In conclusion this study revealed that fenugreek with such low and short treatment course, possesses a significant hypoglycemic activity. However, further investigations for long-term use are needed to support these findings.

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