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Effect of FENUGREEK on glucose level and lipid

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Introduction :

FENUGREEK (*Trigonella foenum-graecum*)

Fenugreek is an important and one of the oldest medicinal plants on record, but not one that we are likely to see growing in North America. It is native to the Mediterranean, India, China, Northern Africa and the Ukraine, as well as being widely cultivated in those locales. Cultivated commercial products in the United States come mainly from Morocco, Turkey, India and China.

Fenugreek is an aromatic plant widely grown worldwide. Two distinct types of plants are recognized— the dwarf type grown for culinary (eating) purposes and the tall type grown for medicinal purposes. It has small round leaves sold as vegetables (fresh leaves, sprouts) commonly known as *methi* and long pods that contained seeds known as *menthe*, which are used as such or in powdered form. These seeds are rich in soluble fibers and many phytochemical compounds. In addition to its hypoglycemic effect, the hypolipidemic effect of fenugreek seeds has also been documented. Therefore, fenugreek seeds have a dual role in the management of diabetes. It has been used as a herbal medicine in

the management of glycemia and dyslipidemia since a long time in India.

The leaves and seeds of the fenugreek plant are used as powders and extracts for medicine use. Fenugreek seeds contain 45-60% carbohydrates, most of which is a mucilaginous fiber which is 30% soluble and 20% insoluble fiber. It also contains about 20-30% proteins that are high in lysine and tryptophan, a small amount of oils (5-10%), a small amount of pyridine alkaloids (mostly trigonelline), and a few flavonoids, free amino acids, sapogenins, vitamins and volatile oils. Constituents in fenugreek that are thought to be responsible for its hypoglycemic effects include the testa and endosperm of the defatted seeds called the A subfraction, the

4 -hydroxyisoleucine and the fiber. It is also thought that the saponins in the seeds are transformed in the gastrointestinal tract into sapogenins and this is responsible for the lipid lowering effects

Background about the Effects fenugreek on sugar decreasing and diabetes;

Fenugreek seed powder in the diet reduces blood sugar and urine sugar with concomitant improvement in glucose tolerance and diabetic symptoms in type 2 diabetic patients [15], Too studies [17,18,19], showed hypoglycemic effects of fenugreek seeds type 2 diabetics and [20] conducted a randomized, controlled, crossover trial in 10 patients with type1 diabetes. The hypoglycemic effects of fenugreek have been attributed to several mechanisms. [11] demonstrated in vitro the amino acid

4- hydroxyisolcucine in fenugreek seeds increased glucose-induced insulin release in human and rat pancreatic islet cells, It was observed that 4-hydroxyisoleucine extracted from fenugreek seeds has insulin tropic activity [16]. [11] show This amino acid

appeared to act only on pancreatic beta cells, since the levels of somatostatin and glucagon were not altered. In human studies, fenugreek reduced the area under the plasma glucose curve and increased the number of insulin receptors, although the mechanism for this effect is unclear.
13] In humans, fenugreek seeds exert hypoglycemic effects by stimulating glucose-dependent insulin secretion from pancreatic beta cells, [12] as well as by inhibiting the activities of alpha-amylase and 50ignali, two intestinal enzymes involved in carbohydrate metabolism. According report [14] The hypoglycemic effect of fenugreek is thought to be largely due to its high content of soluble fiber, which acts to decrease the rate of gastric emptying thereby delaying the absorption of glucose from the small intestine.

The cases suggest fenugreek reduced post-prandial hyperglycemia primarily in subjects with diabetes, but less so in subjects without diabetes. This effect might be more pronounced if raw seeds rather than boiled seeds had been used. Fenugreek may aid with insulin secretion, as suggested by animal studies, since typically these patients have little or no endogenous insulin production [3]. Animal tests have proved that galactomannan blocks intestinal absorption of glucose. Water-soluble fiber increases the viscosity inside the intestine and then inhibit absorption of glucose.

Background about the Effects fenugreek on blood lipids decreasing ;
According report [21,7], supplementation of these medicinal plants mixture (fenugreek), decreased in serum triglycerides, total cholesterol, LDL-C,VLDL-C in both raw and cooked form but increased in HDL-C with the increase in supplementation of medicinal plants. Studies reported that diabetic state, resulting from an impaired secretion and sensitivity of insulin may be responsible for high triglycerides level in serum than normal

individuals, as the insulin stimulated the synthesis of adipose tissue by agency of lipoprotein lipase [22]. Similar decrease in triglycerides and total cholesterol level of the diabetics were observed by feeding fenugreek seeds by various workers [19]. Because fenugreek is contain fiber and fiber have effect of dietary fiber on lipoprotein cholesterol is due to its association with absorption and transport of lipids [23]. Too, according reports, Fenugreek seeds also lower serum triglycerides, total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C) [24, 25]. These effects may be due to sapogenins, which increase biliary cholesterol excretion, in turn leading to lowered serum.cholesterol levels. The lipid-lowering effect of fenugreek might also be attributed to its estrogenic constituent, indirectly increasing thyroid hormone [26]. The quality and quantity of protein in the diets have a direct effect on the levels of cholesterol.

Generally plant protein appears to lower cholesterol level [28]. The plant protein in fenugreek is 26%, so it might exert a lipid lowering effect [27]. A study on the extent of degradation of the saponin and/or diosgenin another steroid saponins in the alimentary tract of alloxan diabetic dogs suggested that steroid saponinand sapogenin might have a role in lowering cholesterol [29]. The lipid-lowering potential of diosgenin has been demonstrated by several experimental studies [30]. Diosgenin decreased the elevated cholesterol in serum LDL and HDL fractions in cholesterol-fed rats, and had no effect on serum cholesterol in normo cholesterolemic rats. In addition, diosgenin inhibited cholesterol absorption, and suppressed its uptake in serum and liver, and its accumulation in the liver [31]. Galactomannan influences intestine walls to generate hormones and enzymes and they influence biosynthesis of cholesterol inliver

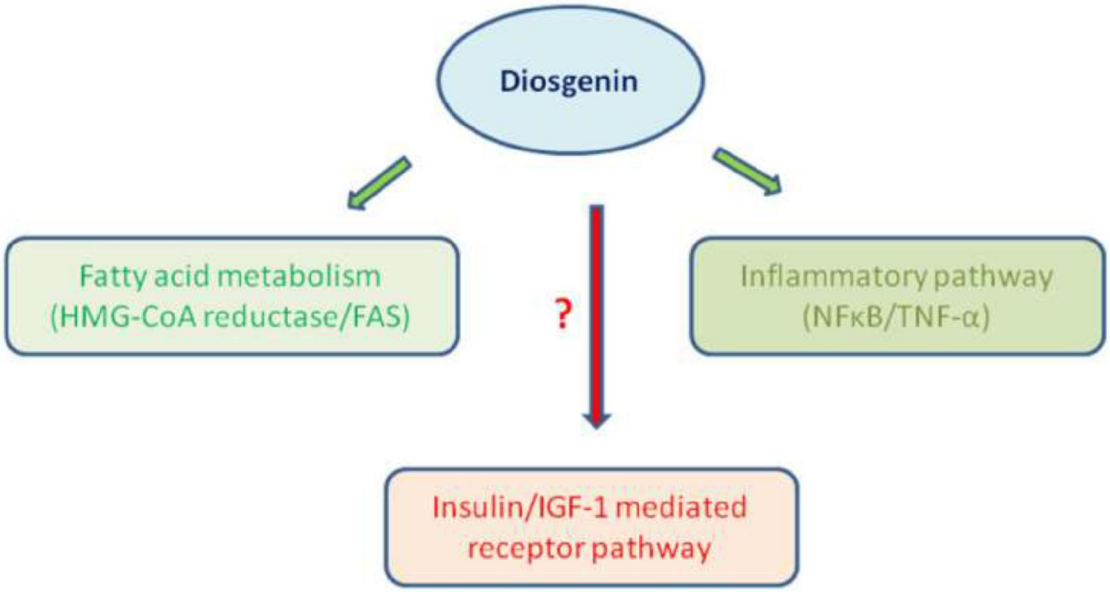

Fig. 4. Schematic representation depicting the molecular mode of action of diosgenin in the control of metabolic
pathway. Diosgenin plausibly regulates signaling molecules in fatty acid metabolism and inflammatory pathway. Insulin and IGF-1 mediated 51ignaling pathways may also be regulated by diosgenin.

Materials and Methods

Design of the study was prospective and was carried out on 50 already diagnosed patients with type 2 DM attending outpatient department of MGM Medical College and LSK Hospital Kishanganj, Bihar. The age of the patients was 40–60 years. All the patients were duly informed about the research work, possible effects, and side effects of fenugreek. They participated with their own interest, and written informed consent was taken from everyone. The

duration of this study was 2 months (8 weeks). Institutional ethics committee approval was obtained before the start of the study.

Inclusion Criteria

1. Subject diagnosed with type 2 DM with dyslipidemia according to criteria of American Diabetes Association
2. Age 40–60 years
3. Fasting blood glucose more than 126 mg/dl
4. HbA1C more than 8%
5. Presence of dyslipidemia (deranged lipid profiles)
6. Glycemia and dyslipidemia not controlled with drugs

Exclusion Criteria

1. Patients on insulin or any hypertensive drugs
2. Subjects having liver diseases, pulmonary tuberculosis, and alcoholism
3. Subjects with any diabetic complications such as neuropathy, nephropathy, or retinopathy
4. Patients with ischemic heart disease
5. Pregnant and lactating women

Patients meeting these inclusion criteria were put on standard diet and exercise for 1 month. Then they were divided into two groups: group 1 patients were given the standard treatment protocol, that is, diet, exercise and 5 g fenugreek seed powder four times a day before meal for 8 weeks. Group 2 patients were given the usual treatment protocol, that is, diet, exercise, and oral hypoglycemic drugs, except fenugreek. Patients were assessed initially and then weekly for blood sugar fasting levels and on the end of eighth week for HbA1C and lipid profiles.

Method of Examination

Blood glucose fasting: by glucose oxidase method with StatFax 3300 (Ark Diagnostic Pvt. Ltd., Bangalore, India).

HbA1C: by DS5 Drew Scientific Machine (ion exchange chromatography; Drew Scientific Ltd., Cumbria, UK)

Lipid Profiles: reference values for plasma total cholesterol were obtained by using auto-analyzer systems to which either the ferric-chloride (sulfuric acid method) or Liebermann–Burchard test was adapted. A fluorometric analysis was used to determine triglyceride reference values. Plasma high-density lipoprotein (HDL) cholesterol determination done by the same procedures used for plasma total cholesterol, after precipitation of Apo-B-containing lipoproteins in whole plasma (low-density lipoprotein (LDL) and very low-density lipoprotein cholesterol) by heparin-manganese chloride. Lipoproteins can be separated by ultracentrifugation, precipitation, and electrophoresis. The quantitative reference method uses precipitation and ultracentrifugation sequentially to determine each lipoprotein component. Usually, measurement of plasma lipid level is sufficient for evaluations of patterns of lipoproteins elevations. Occasionally, paper electrophoresis of plasma is helpful.

Safety Profile

Blood urea, serum bilirubin, liver transaminases (AST, ALT), serum creatinine, and prothrombin time were checked weekly.

At the end of 8 weeks, all the results were collected and analyzed by a statistician. The data for statistical analysis were assessed using SPSS, version 16 (SPSS Inc., Chicago, IL). Numerical variables were recorded as mean±SD. Statistical significance was computed by unpaired *t*-test. The level of significance was fixed at 5% ($p < 0.05$).

Results:

In this study, 50 patients of known cases of type 2 DM were enrolled. They were divided into two groups before the study. One group was considered as cases (group 1) and other group as controls (group 2) (Figure 1). From the group 1 four subjects and from group 2 one subject withdrew themselves from the study. Results of this study have been shown in Tables 1–3.

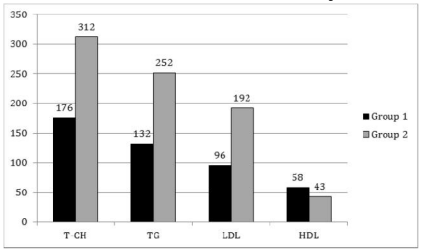

Table 1: Comparison of blood sugar profile (F) in weeks in groups 1 and 2

	Initial	2	4	6	8	*t*-Value	*p*-Value	Significance
Group 1 mean± SD	178±72.4	159±55.8	142±52.2	126±56.1	104±28.2	4.36	<0.0001	ES
Group 2 mean± SD	149±46.4	138±52.4	134±78.3	129±46.3	122±52.6	1.88	0.065	NS

Table 2: Comparison of HbA1 c levels in groups 1 and 2

	Initial mean± SD	Final mean± SD	*t*-Value	*p*-Value	Significance
Group 1	12±3.2	10.6±3.7	1.31	0.197	NS
Group 2	9.25±2.8	8.45±1.8	1.16	0.248	NS

Table 3: Comparison of lipid profiles in groups 1 and 2

	Initial mean±SD	Final mean±SD	*t*-Value	*p*-Value	Significance
Group 1					
T-CH	350±20.6	176±17.2	29.71	<0.0001	ES
TG	280±18.2	132±16.8	27.38	<0.0001	ES
LDL	220±21.4	96±14.2	22.12	<0.0001	ES
HDL	27±13.4	58±32.2	4.07	<0.0002	ES
Group-2					
T-CH	322±23.2	312±26.4	1.39	0.170	NS
TG	261±17.8	252±21.2	1.59	0.118	NS
LDL	204±16.7	192±18.2	1.19	0.24	NS
HDL	32±18.4	43±19.8	1.99	0.052	NS

Discussion

It is a well-known fact that attainment of good glycemic control in patients with type 2 DM is not always adequate and may require some additional/alternative approach. This study was undertaken to evaluate the efficacy of fenugreek seeds for controlling glycemia and dyslipidemia in patients with type 2 DM. Various studies have been conducted to see the effect of high-fiber diet, fenugreek, and other herbal agents in the management of diabetes. In our study, intake of fenugreek seeds resulted in significant reduction in blood glucose (F), T-CH, LDL and triglycerides (TG) with significant increase in HDL. Although there was a beneficial effect on HbA1C, but statistically, it was not significant. This fact was also supported by the research study by Neelakantan et al.[8] The results of a study conducted by Zargar et al.[9] are very similar to that of this study. ICMR (Indian Council of Medical Research) in its bulletin described the alkaloids of fenugreek and also reported the antidiabetic action of fenugreek seeds.[10] Similar results were also obtained by some other studies.[11–13] Italian herbalists frequently suggested fenugreek for glycemic control.[14] Studies in animals such as diabetic dogs and rats also showed that fenugreek seed intake increased insulin sensitivity and reduced blood glucose levels.[15–17] Lipid-lowering effect of fenugreek may be an additional benefit in patients with type 2 DM with dyslipidemia.[18–20]

El-Soud et al.[21] found in albino rats with experimental diabetes induced by streptozotocin that during diabetes liver shows decrease in weight due to enhanced catabolic processes such as glycogenolysis, lipolysis, and proteolysis, which is the outcome of lack of insulin and/or cellular glucose in liver cells. There is, however, an increase in kidney weight due to glucose excess and subsequent enhancement in glycogen synthesis, protein

synthesis, and lipogenesis.[22] These changes may lead to serious microvascular renal complications involving a series of metabolic changes in the pathogenesis of diabetic nephropathy.[23] Studies indicated treatment of diabetic rats with fenugreek alkaloids significantly prevented the alteration in liver and kidney weight and pathology with return to their normal texture. The principal hypoglycemic alkaloid in fenugreek seed is trigonelline (0.2–0.36%). However one study has shown that the purified hypoglycemic principle of fenugreek seeds is different from that of alkaloid trigonelline based on UV and IR absorption spectra, thin-layer chromatography, and high-performance liquid chromatography criteria. This highly active hypoglycemic principle isolated from fenugreek seed increases glucose-induced serum insulin levels and improves glucose tolerance after treatment with a dose of 100 mg/kg in alloxan-induced diabetic rabbits. There was an improvement in glycosylated hemoglobin and serum lipid profile. There was
an increase in the activity of the key enzymes of glycolysis in muscle but not in the liver. Slight inhibition in the activity of gluconeogenic enzymes was also noticed, proving thereby that the active compound acts at both pancreatic and extrapancreatic sites.[25] Thus, our studies in humans confirm that crude fenugreek seeds including trigonelline and others do have a good overall effect on DM and its complications

Conclusion

We show that fenugreek seeds may be a promising additional option for management of diabetes as these are widely available at low cost in poor countries like India but certain things should kept be in mind before prescribing fenugreek seeds to diabetic patients:

1. It must be standardized and tested for its composition
2. It should be consumed 20 min before intake of food every time (breakfast, lunch, dinner, and snacks)
3. The amount should be same even if small meal or snack (i.e., 5 g) is taken
4. If on current oral medications, use of this herbs should be at least 2 h before or after these drugs because fenugreek fiber has the potential to interfere with the absorption of oral medication due to its mucilaginous contents (which gives it a moist and sticky texture)
5. Fenugreek use in pregnancy is not recommended as it has the potential to induce labor
6. Fenugreek seeds DO NOT cure diabetes but helps in blood sugar control

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