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Research Article

Exploring the Therapeutic Potential of Fenugreek as an Anti-Diabetic Agent: A Comprehensive Review

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Abstract

Fenugreek (Trigonella foenum-graecum) is a medicinal plant with notable antidiabetic and lipid-lowering properties. Rich in soluble fibers, amino acids, vitamins, and saponins, fenugreek seeds have demonstrated significant efficacy in managing type II diabetes mellitus (T2DM) and associated dyslipidemia. This review synthesizes recent research from 2019 to 2024, highlighting clinical trials and interventional studies. Fenugreek supplementation significantly reduces fasting blood glucose, HbA1c, and improves serum insulin levels, thereby delaying the progression of prediabetes to T2DM. Additionally, fenugreek enhances lipid profiles by lowering triglycerides and LDL cholesterol while increasing HDL cholesterol. These effects are primarily due to fenugreek's high fiber content, which slows carbohydrate absorption and metabolism, and bioactive compounds that stimulate insulin secretion and improve insulin sensitivity. The findings suggest fenugreek as a cost-effective, low-toxicity dietary intervention for managing diabetes and dyslipidemia. Further large-scale clinical trials are recommended to confirm these benefits and explore long-term outcomes.

BACKGROUND

Fenugreek (Trigonella foenum-graecum) is a globally cultivated medicinal plant. It grows erect with trifoliate leaves, white to yellowish flowers, and pods containing 10 20 greenish-brown seeds. Known for their bitterness, the seeds are used as a spice, while the leaves are consumed as vegetables [1]. Fenugreek's mature seeds are rich in various active compounds, including amino acids, fatty acids, vitamins, and saponins such as diosgenin, gitogenin, neogitogenin, homorientin, saponaretin, neogigogenin, and trigogenin. They also contain fibers, flavonoids, polysaccharides, fixed oils, and alkaloids like trigonelline and choline [2].

Type II diabetes mellitus is a metabolic disorder affecting the endocrine system. Hyperglycemia, due to inadequate response of cells to insulin, leads to glucotoxicity and long-term vascular and non-vascular complications. Vascular issues include retinopathy, nephropathy, neuropathy, coronary artery disease, peripheral artery disease, and cerebrovascular disorders [3].

In 1980, the World Health Organization estimated 108 million people had diabetes globally. By 2014, this number had quadrupled. According to the 2018 Diabetes IDF Atlas, 451 million adults (ages 18–99) were living with diabetes, a figure projected to rise to 693 million by 2045 [4]. The second National Diabetes Survey of Pakistan, conducted from February 2016 to August 2017, revealed diabetes had reached epidemic levels. Overall prevalence was 26.3%, with 19.2% previously diagnosed and 7.1% newly diagnosed. Urban prevalence was 28.3%, rural was 25.3%. Pre-diabetes affected 14.4% overall, with 15.5% in urban and 13.9% in rural areas. The risk was higher in those aged 43 and above [5].

Studies have shown Fenugreek seed's role in reduction of blood glucose in diabetics so it may be a safe and affordable, food-based intervention targeting glucose abnormalities [6]. They delay gastric emptying, reduce glucose absorption, and lower glucose uptake in the small intestine due to their high fiber content. Additionally, they slow down carbohydrate metabolism, protect beta cells and elevate serum insulin levels. Fenugreek promotes glycogen synthetase activity, aiding glycogen formation in the liver and muscles. It also reduces proinflammatory cytokines and pancreatic enzymes, supports glycogen replenishment, corrects insulin-sensitive enzyme activities, and improves serum lipid profiles. Furthermore, fenugreek extracts prevent lipid peroxidation, restore antioxidants, enhance insulin sensitivity, and facilitate glucose utilization in peripheral tissues, helping regulate HbA1c levels [7].

METHODOLOGY

To comprehensively explore the antidiabetic properties of Fenugreek (Trigonella foenum-graecum), a systematic search strategy was developed to identify relevant articles published from 2019 to 2024. Major academic databases like Google Scholar, PubMed, Scopus, and Web of Science were systematically searched using a combination of keywords such as "Fenugreek", "diabetes" and "anti-diabetic effects". This approach ensured thorough coverage of the literature.

Inclusion criteria was to use original research articles, including experimental studies, clinical trials, and observational studies, investigating the antidiabetic effects of Fenugreek. Studies involving human subjects and animal models with only English language articles included. For comparison, only original research articles were reviewed. Exclusion criteria included review articles, case reports, letters, and conference abstracts. Additionally, studies published before 2019 were excluded to focus on recent developments.

HISTORY OF FENUGREEK

Fenugreek has been recognized as a versatile medicinal and traditional herb in Iran, India, and China for centuries. Traditionally, fenugreek seeds, widely used across the globe, offer benefits for bone and muscle health, respiratory and gastrointestinal systems, female reproductive health, cardiovascular health, endocrinology, and liver function [8]. It holds a prominent place in Ayurvedic medicine and has been documented for its health benefits since 1500 BC in the Ebers Papyrus, one of the oldest medicinal documents. Known as Methi in Hindi & Urdu, it is commercially cultivated in various countries including India, Pakistan, Afghanistan, Iran, Spain, and Turkey. This ancient medicinal plant has been grown and used for thousands of years across the Indian subcontinent, Middle East, North Africa, Europe, the United States, Australia, and parts of West Asia [9].

BIOACTIVE COMPOUNDS OF FENUGREEK

Fenugreek seeds boast a wealth of nutrients, including fiber, choline, and vitamins A, B1, B2, and C, as well as nicotinic acid, niacin, phospholipids, glycolipids, oleic acid, linolenic acid, and linoleic acid. These seeds are notably rich in lysine and l-tryptophan in their protein content, alongside mucilaginous and gummy fibers [10]. Fenugreek seeds are rich in phenolic compounds, galactomannan, diosgenin, quercetin, trigonelline, and 4-hydroxyisoleucine. They also contain saponins, such as diosgenin, yamogenin and tigogenin comprising 4.8% of the seed composition. Fenugreek's glucose-lowering and antioxidant effects are attributed to its modulation of peroxisome proliferator-activated receptors. It contains around 8000 polyphenolic compounds, including phenolic acids, flavonoids, stilbenes, and lignans, which act as natural defenses against oxidants and pathogens that may offer therapeutic benefits for chronic diseases [11].

Numerous studies have demonstrated the hypoglycemic effects of fenugreek seeds in animals, attributed to their high content of soluble dietary fibers (galactomannan), trigonelline, diosgenin, 4-hydroxyisoleucine, and flavone C-glycosides. Mechanistically, these effects involve delaying gastric emptying of carbohydrate sources, inhibiting digestive enzyme activities, and promoting bowel movements, ultimately leading to reduced blood sugar levels in diabetic subjects [12].

ANTI-DIABETIC EFFECTS OF FENUGREEK THROUGH CLINICAL EVIDENCE

Antidiabetic Effect and Preference of Fenugreek with Dietary Modifications in Patients with Prediabetes

An Interventional Parallel Randomized Study This prospective, randomized, parallel open-labeled study, conducted between January 2018 and August 2020 at a tertiary care hospital, evaluated the antidiabetic effect and patient preference for fenugreek combined with dietary modifications in prediabetic individuals. It included 280 newly diagnosed prediabetic patients aged 20-50, confirmed by OGTT and HbA1c levels. Participants were randomized into two groups: one receiving 10g of fenugreek powder daily with dietary modifications, and the other adhering to dietary modifications alone. Compliance was monitored through monthly phone calls and follow-up visits. Statistical analysis included unpaired t-tests and chi square tests.

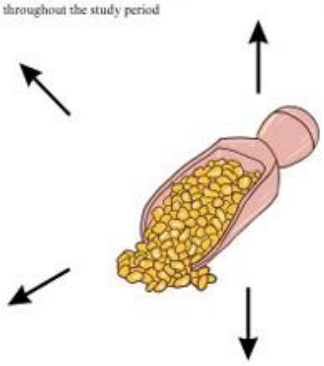
Results showed no significant baseline demographic differences between groups. The fenugreek group had a significant reduction in HbA1c levels at 3, 6, 12, 18, and 24 months, while the control group showed an increasing trend. The incidence of diabetes was lower in the fenugreek group, which also showed improvements in serum insulin levels and HOMA-IR. Compliance with fenugreek treatment was good, with 52.9% to 59.2% adherence, and about one-quarter preferred to continue fenugreek at the study's end. The study concluded that fenugreek supplementation with dietary modifications significantly delays the progression from prediabetes to type 2 diabetes mellitus (T2DM), offering an economical and effective intervention with good acceptability among participants. Despite limitations such as non-blinded design and lack of safety profile assessment, the findings suggest fenugreek as a promising therapy for controlling prediabetic markers [13].

Antidiabetic Effect of Fenugreek Seed Powder Solution (Trigonella foenum graecum L.) on Hyperlipidemia in Diabetic Patient

This study, conducted from May 2015 to January 2016 at Ayder Referral Hospital and Mekelle General Hospital in Mekelle, evaluated the effects of fenugreek seed powder solution on hyperlipidemia in newly diagnosed type II diabetic patients. The study included 114 participants, divided into a treatment group receiving 25 mg of fenugreek seed powder solution twice daily for one month and a control group with no fenugreek or antidiabetic agents but advised on diet and exercise. Data collection covered

Study 1: Among the 280 participants who completed the study, there were no significant differences in baseline demographics. Both groups showed a median HbA1c of 5.7% at baseline, but the dietary modification + Fenugreek group exhibited a significant decrease in HbA1c levels over time. The incidence rate of diabetes mellitus was significantly lower in the dietary modification + Fenugreek group compared to the dietary modification alone group. Serum insulin levels and insulin resistance increased significantly in the Fenugreek group but remained similar in the dietary modification alone group throughout the study period

Study 2: The study evaluated the effects of Trigonella foenum-graecum seed powder solution on blood lipid profiles. Participants had abnormal fasting blood glucose levels and lipid profiles at baseline. After 30 days of treatment, the group receiving the seed powder solution showed significant reductions in total cholesterol (13.6%), triglycerides (23.53%), and low-density lipoprotein cholesterol (23.4%), and a significant increase in high-density lipoprotein cholesterol (21.7%) compared to baseline and the control group. These findings suggest potential beneficial effects of fenugreek seed powder on lipid profiles.



Study 3: The study included 49 type 2 diabetes patients with similar baseline characteristics. Fenugreek supplementation significantly reduced fasting blood glucose levels by 1.83 mmol/L compared to controls, further decreasing to 2.38 mmol/L when adjusting for covariates. Postprandial blood glucose levels were also notably lower in the fenugreek group, with a reduction of 3.65 mmol/L compared to controls, increasing to 4.18 mmol/L when adjusting for covariates. Additionally, fenugreek supplementation led to a 20.83% relative risk reduction among type 2 diabetes patients, with 5 patients no longer classified as diabetic post-study.

Study 4: The study demonstrated a significant reduction in the incremental area under the curve (IAUC) for certain food preparations, indicating a decrease in blood glucose response. Specifically, Fenuflakes reduced IAUC for cooked raw rice and potato paratha by 5% to 35%. Additionally, the addition of Fenuflakes to carbohydrate-containing portions significantly decreased the glycemic index (GI) values of cooked raw rice, idly, and potato paratha ($P < 0.001$), indicating lower blood glucose levels.

Figure 1

sociodemographic, behavioral, and clinical characteristics, with blood samples taken before and after the intervention to measure lipid profiles. Statistical analyses used SPSS, with paired and independent t-tests.

Results showed significant improvements in the treatment group's lipid profile compared to the control group after 30 days: a 13.6% reduction in total cholesterol (TC), a 23.53% decrease in triglycerides (TG), a 21.7% increase in high-density lipoprotein cholesterol (HDL-C), and a 23.4% reduction in low-density lipoprotein cholesterol (LDL C). The control group showed no significant changes. The study concluded that fenugreek seed powder solution significantly improves dyslipidemia in type II diabetic patients, suggesting its potential as a natural treatment option. Further research is recommended to isolate and characterize the bioactive compounds in fenugreek, elucidate their mechanisms of action, and assess long-term outcomes and larger-scale applications [1].

Effect of fenugreek seed supplementation on fasting and postprandial blood glucose level in type 2 diabetic subjects

This randomized controlled trial in Bogura district, Bangladesh, evaluated the impact of fenugreek seed supplementation on blood glucose levels in type 2 diabetic patients over 60 days. The study included 51 participants divided into an experimental group, which consumed 10 grams of fenugreek seed powder soaked in water daily, and a control group with no intervention. Blood glucose levels were measured at baseline and every 15 days. Results showed significant reductions in the experimental group's fasting and postprandial blood glucose levels compared to the control group. Fasting blood glucose decreased by 1.83 mmol/L and postprandial blood glucose by 3.65 mmol/L after 60 days. Additionally, five participants in the fenugreek group achieved non-diabetic status by the study's end. These findings suggest that fenugreek supplementation effectively improves glycemic control in type 2 diabetes patients and highlights the need for further large-scale trials to confirm these results and explore long-term benefits [14].

Glycemic Index Lowering Effects of Defatted Fenugreek Seed Flakes (FenuflakesTM) on some Indian Food Preparations: A Randomized Controlled Clinical Study

This randomized, controlled, open-label clinical study assessed Fenuflakes' impact on the glycemic response of six common Indian foods. The trial, approved by the Madras Diabetes Research Foundation Ethics Committee and registered with the Clinical Trial Registry of India, involved 15 healthy participants (7 females, 8 males) aged 18-45 with a BMI of 18.5-22.9 kg/m^2. Exclusion criteria included diabetes and certain medications.

Participants consumed each food preparation—oats porridge, pressure-cooked plain raw rice, rice idly, semolina

upma, potato sandwich, and potato paratha—with and without 10 g of Fenuflakes, standardized to 50 g of available carbohydrates (25 g for oats). After overnight fasting, baseline measurements were recorded. Participants then consumed a glucose solution (reference), control, and test foods in a randomized crossover order with a two-day washout period. Blood samples were collected at intervals to measure glucose levels, and the incremental area under the curve (IAUC) was calculated for glycemic index (GI) values. The addition of Fenuflakes significantly reduced the IAUC for cooked raw rice by 35% and potato paratha by 27%. Significant GI reductions were observed for cooked raw rice, idly, and potato paratha, attributed to Fenuflakes' high dietary fiber content, which delays carbohydrate absorption. Variations in GI effects were due to procedural and food characteristics. The study concluded that Fenuflakes effectively lower the GI of certain Indian foods, suggesting its potential in managing postprandial glucose levels, with further research recommended to confirm these findings across a wider range of foods [15].

DISCUSSION

The articles highlight the benefits of fenugreek seeds and derivatives like Fenuflakes on glycemic control and lipid profiles, using both animal models and human clinical trials. Addepalli et al. [13], and Khatun et al. [14], showed significant blood glucose reductions in diabetic patients, while Thakurdesai et al. [15], found Fenuflakes lowered the glycemic index of Indian foods. Additionally, 4-hydroxyisoleucine stimulates insulin secretion [16]. Geberemeskel et al. [1], reported improved lipid profiles in diabetic rats, indicating fenugreek's role in managing dyslipidemia [17]. Effective glycemic and lipid management is crucial for reducing diabetes complications [18]. A review of 12 studies found fenugreek significantly lowered fasting and postprandial blood glucose, HbA1c, and total cholesterol, though effects on triglycerides and LDL cholesterol need further study [19,20]. Overall, fenugreek is a promising natural strategy for managing diabetes and dyslipidemia.

CONCLUSION

In conclusion, the consistent findings across these studies emphasize the therapeutic potential of fenugreek in managing both diabetes and dyslipidemia. The hypoglycemic effects are primarily due to its soluble fiber and insulinotropic amino acids, while its lipid-lowering effects are attributed to soluble fiber, saponins, and antioxidant compounds. The use of fenugreek, therefore, represents a promising dietary approach to improving metabolic health and reducing the risk of cardiovascular diseases in diabetic individuals. Further research, especially large-scale clinical trials, would be beneficial to confirm these findings and establish standardized guidelines for fenugreek consumption in diabetes management.

LIMITATIONS

Across the reviewed articles, several limitations were identified that merit consideration. Firstly, several studies, including those in Articles 1 and 4, had relatively small sample sizes, potentially limiting the generalizability of their findings to broader populations. Additionally, the homogeneity of samples in second article might restrict the applicability of results to more diverse demographics. Methodological concerns were also noted, such as the open-label design in second article, which could introduce bias or influence participant behavior. Furthermore, the short duration of interventions in research articles might not fully capture long-term effects or changes in metabolic parameters over time. Another common limitation across the articles was the focus on specific dietary interventions, as seen in third article, which might not fully reflect the impact of fenugreek on diverse dietary patterns or cuisines. Lastly, the lack of blinding in forth article raises concerns about potential bias in outcome assessment. These limitations collectively underscore the need for future research to address these methodological shortcomings and further explore the potential benefits of fenugreek supplementation in the management of diabetes and related conditions.

RECOMMENDATIONS AND FUTURE PROSPECTIVE

Based on the findings and limitations of the reviewed articles, several recommendations can be proposed to guide future research and practice in the field of fenugreek supplementation for managing diabetes and related conditions. Firstly, future studies should prioritize larger sample sizes to enhance statistical power and improve the generalizability of results across diverse populations. This would help address concerns regarding the representativeness of findings, as observed in several of the reviewed articles. Additionally, researchers should consider employing randomized controlled trials (RCTs) with rigorous blinding procedures to minimize bias and ensure the validity of study outcomes, as highlighted in forth article. Moreover, longer intervention durations are warranted to assess the sustained effects of fenugreek supplementation on metabolic parameters and clinical outcomes over time. This would provide valuable insights into the long-term efficacy and safety of fenugreek in the management of diabetes and prediabetes.

Furthermore, future research should explore the potential synergistic effects of fenugreek supplementation with other dietary interventions or pharmacological agents commonly used in the treatment of diabetes. This could help elucidate whether fenugreek complements existing therapies or offers unique benefits when used alone. Moreover, studies investigating the optimal dosage and formulation of fenugreek supplements are needed to guide clinical practice and ensure standardized treatment protocols. Additionally, given the heterogeneity of dietary patterns and cultural practices worldwide, future research should explore the impact of fenugreek supplementation on diverse cuisines and dietary habits beyond those examined in the reviewed articles. This would provide a more comprehensive understanding of fenugreek's role in different dietary contexts and populations. In terms of methodological improvements, future studies could incorporate advanced biomarker assessments, such as measures of insulin sensitivity, inflammation, and

oxidative stress, to elucidate the underlying mechanisms of fenugreek's effects on metabolic health. Moreover, mechanistic studies at the cellular and molecular levels could provide valuable insights into the pathways through which fenugreek exerts its therapeutic effects, paving the way for the development of targeted interventions. Additionally, long-term observational studies and post-marketing surveillance are needed to monitor the safety and tolerability of fenugreek supplementation in real-world settings and assess its impact on clinical outcomes, such as cardiovascular events and mortality.

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