CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.17443848

https://www.iajps.com/volumes/volume12-october-2025/112-issue-10-october-25/

Available online at: http://www.iajps.com Review Article

FENUGREEK- AN ANTIDIABETIC HERBAL DRUG

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Abstract:

Fenugreek (Trigonella foenum-graecum L.) is an important medicinal herb belonging to the family Fabaceae, widely known for its antidiabetic potential. Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels, primarily due to insulin resistance or deficiency. Fenugreek seeds contain several bioactive compounds such as alkaloids, flavonoids, saponins, and amino acids that contribute to their hypoglycemic activity. Among these, 4-hydroxyisoleucine enhances insulin secretion, while galactomannan delays glucose absorption. The plant also exhibits antioxidant, hypolipidemic, and anti-inflammatory activities that help manage diabetic complications. Traditional systems of medicine, including Ayurveda and Chinese medicine, have long used fenugreek as a natural remedy. Various extraction methods such as Soxhlet and maceration are employed to isolate its active constituents. Pharmacological studies support its role in reducing blood sugar and cholesterol levels. Marketed formulations like capsules, powders, and churnas further confirm its therapeutic importance. Fenugreek is generally safe but should be used cautiously during pregnancy. Overall, it represents a promising herbal alternative for managing Type 2 diabetes mellitus and related metabolic disorders.

Keywords: *Fenugreek, Trigonella foenum-graecum, Antidiabetic activity, Hypoglycemic effect, Herbal medicine, Galactomannan, 4-Hydroxyisoleucine, Saponins, Flavonoids, Type 2 diabetes mellitus, Phytochemical constituents, Traditional medicine.*

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*Please cite this article in press **Rohan R. Munde** et al., **Fenugreek- An Antidiabetic Herbal Drug**, Indo Am. J. P. Sci, 2025; 12(10).*

INTRODUCTION:

Diabetes is one of the leading global health threats after cardiovascular disease and cancer, according to the International Diabetes Federation [1,2]. In 2015, 415 million people were affected, and the number is expected to reach 693 million by 2045 [2]. Based on pathogenesis, diabetes is classified into Type 1, Type 2, gestational, and other specific types, with Type 2 diabetes mellitus (T2DM) being the most common, accounting for over 90% of all cases [3]. It occurs due to an imbalance between insulin secretion and action, leading to improper control of blood glucose levels [4]. Prolonged hyperglycemia can cause cardiovascular injury, kidney disease, diabetic foot, and other complications that affect mental and physical health [5]. Lifelong medication is often necessary, and health care costs are about three times higher for diabetic patients compared to non-diabetics. In 2015, global expenditure for diabetes treatment reached approximately 67.3 billion USD, representing 12% of worldwide health spending [6,7].

Fenugreek (Trigonella foenum-graecum L.) is a plant belonging to the Fabaceae family, native to India and North Africa [8]. It is cultivated widely in China, Australia, North Africa, Europe, and Argentina [9]. Fenugreek has been used as both food and medicine for nearly six thousand years in countries like Iran, India, and China [10]. Pharmacological studies show that fenugreek contains alkaloids, flavonoids, polysaccharides, steroidal saponins, and volatile oils, which possess lipid-lowering and hypoglycemic properties [11–13]. It is used as a natural dietary supplement for diabetes management and has been proven safe and effective [14,15]. Fenugreek-derived alkaloids show β-glucosidase inhibition, antioxidant, anti-inflammatory, anticancer, and cardioprotective effects, while flavonoids, saponins, and polysaccharides help regulate blood glucose levels and treat diabetes-related complications in humans and animals [16,17]. However, the precise mechanism of its action remains unclear.

PLANT MORPHOLOGY OF FENUGREEK:

Fenugreek (Trigonella foenum-graecum L.) is an erect annual herb growing 30–60 cm tall with a strong characteristic odor. It has a taproot system with nodules containing nitrogen-fixing Rhizobium bacteria. The stem is smooth, hollow, green, and cylindrical with distinct nodes and internodes. Leaves are alternate, compound (trifoliate), with three obovate or oblong serrated leaflets that are light to dark green and slightly hairy. The inflorescence is a raceme bearing axillary white or pale-yellow papilionaceous flowers. Each flower is bisexual, zygomorphic, with 5 sepals, 5 petals, 10 stamens (9 fused + 1 free), and a monocarpellary superior ovary. The fruit is a slender, curved yellowish-brown legume (10–15 cm long) containing 10–20 small seeds. Seeds are hard, rhomboidal, yellowish-brown, bitter, and aromatic with mucilaginous endosperm. Flowering occurs 30–40 days after sowing, and fruiting begins after 3–4 months, commonly during the rabi season in India[18].

Botanical Classification[18]

- Kingdom: Plantae
- Division: Magnoliophyta
- Class: Magnoliopsida
- Order: Fabales
- Family: Fabaceae
- Genus: Trigonella
- Species: Trigonella foenum-graecum L.

Soil and Climate Requirements for Fenugreek:

Soil Requirements:- Fenugreek grows best in well-drained loamy or sandy loam soil with a pH of 6.0–7.0. The soil should be rich in organic matter, and the addition of compost or farmyard manure improves yield. Poor drainage or excess moisture causes root rot, while mild salinity is tolerable, making it suitable for semi-arid regions[19].

Climatic Requirements:- The crop thrives in cool and dry climates with an optimal temperature range of 10–25°C. It requires moderate rainfall (30–40 cm annually), and excessive humidity may affect seed development. Fenugreek is mainly cultivated as a winter (rabi) crop in tropical and subtropical regions, sown in October–November. It requires full sunlight and is sensitive to frost during flowering and pod formation stages[19].

PATHOPHYSIOLOGY:

Type 2 diabetes mellitus (T2DM) is a chronic condition characterized by insulin resistance and impaired pancreatic β-cell function. Initially, β-cells produce excess insulin to maintain normal glucose levels, but over time they lose efficiency, leading to hyperglycemia. Most patients with T2DM are overweight, and excess abdominal fat contributes to insulin resistance by releasing free fatty acids and altering adipokine balance. Other contributing factors include physical inactivity, gestational diabetes, hypertension, and abnormal cholesterol levels. Recent studies suggest that disturbances in incretin hormones (like GLP-1), chronic inflammation, elevated glucagon levels, increased renal glucose reabsorption, and gut microbiota imbalance also play a role in disease development. These mechanisms collectively disrupt glucose metabolism and lead to the progression of T2DM[20].

ETIOLOGY:

Type 2 diabetes mellitus develops due to the combined influence of genetic and environmental factors. Unhealthy lifestyle habits such as overeating, lack of exercise, and obesity trigger diabetes in individuals with genetic susceptibility. Glucagon-like peptide-1 (GLP-1) plays a crucial role in both glucose regulation and blood pressure control. Research on animal models has shown that impaired GLP-1 receptor function increases sympathetic nervous activity affecting cardiovascular and metabolic balance. This indicates that GLP-1 not only enhances insulin secretion for glucose control but also helps regulate blood pressure and metabolic health[21].

Major risk factors:

The major risk factors for Type 2 diabetes mellitus include[22]:

1. Age 35 years or older.
2. Overweight or obesity.
3. Prediabetes (A1c 5.7–6.4%, impaired glucose tolerance or fasting glucose).
4. Family history of Type 2 diabetes in a first-degree relative.
5. Hypertension (≥130/80 mmHg or under antihypertensive therapy).
6. Dyslipidemia (HDL <35 mg/dl or triglycerides >250 mg/dl).
7. History of gestational diabetes mellitus.
8. Physical inactivity.

Physical and chemical properties of fenugreek:

Fenugreek seeds of Trigonella foenum-graecum sprout in about three days and grow into 30–60 cm tall annual herbs that enrich the soil through nitrogen fixation. The pods are yellowish-brown, each containing 10–20 small, hard, rhomboidal seeds that are brownish-yellow, bitter, and aromatic. The seeds contain a mucilaginous endosperm rich in fiber and oil, giving them a sticky texture and characteristic odor. Chemically, fenugreek seeds contain 45–60% carbohydrates (mainly galactomannan fiber), 20–30% protein rich in lysine and tryptophan, and 5–10% lipids. Important compounds include alkaloids (trigonelline, gentianine, carpaine), flavonoids (apigenin, quercetin, vitexin, isovitexin), amino acids (4-hydroxyisoleucine, histidine, arginine), and steroidal saponins (diosgenin, yamogenin, tigogenin). They also provide vitamins A, B, C, and minerals such as calcium, iron, and phosphorus. The oils are rich in linoleic, linolenic, and oleic acids[23].

Vitamin profiles of fenugreek:

Fenugreek seeds and leaves are rich sources of essential vitamins that contribute to their nutritional and therapeutic value. The seeds contain ascorbic acid (12–23 mg/100 g), pyridoxine (0.6 mg), niacin (6 mg), retinol (60–100 IU), β-carotene (96 µg), thiamine (340 µg), riboflavin (290 µg), and folic acid (84 µg). The leaves are even richer in certain vitamins, with ascorbic acid (52 mg/100 g), β-carotene (2.3 mg), thiamine (40 µg), and riboflavin (310 µg). These vitamins play vital roles in antioxidant defense, energy metabolism, and overall cellular function, enhancing fenugreek's value as a nutraceutical and functional food ingredient[24].

Chemical constituents of fenugreek:

Fenugreek (Trigonella foenum-graecum L.) seeds contain a wide range of phytochemicals responsible for its pharmacological actions. The major constituents include[19]:

- Alkaloids: Trigonelline, gentianine, carpaine
- Amino acids: 4-hydroxyisoleucine, histidine, lysine, arginine
- Steroidal saponins: Diosgenin, yamogenin, tigogenin, gitogenin
- Flavonoids: Vitexin, isovitexin, orientin, quercetin, luteolin
- Fatty acids: Linoleic, linolenic, oleic, and palmitic acid
- Mucilage and fiber: Galactomannans
- Coumarins: Umbelliferone, scopoletin
- Polyphenols: Gallic acid, caffeic acid
- Vitamins: A, B_1, B_2, B_3, C
- Minerals: Iron, calcium, zinc, magnesium

Chemical structure:

Fenugreek contains several bioactive compounds with distinct chemical structures and pharmacological effects[25]:

4-Hydroxyisoleucine: An amino acid that enhances insulin secretion and exhibits strong antidiabetic activity.

- Trigonelline: An alkaloid known for its hypoglycemic and neuroprotective effects.
- Galactomannan: A polysaccharide responsible for delaying glucose absorption and reducing postprandial hyperglycemia.
- Diosgenin: A steroidal saponin linked to cholesterol-lowering and anti-inflammatory properties.
- Vitexin and Isovitexin: Flavonoid glycosides that act as potent antioxidants and protect against oxidative stress.

Application of fenugreek:

➢ Traditional Uses of Fenugreek

Fenugreek (Trigonella foenum-graecum L.) has been used as a medicinal plant in Central Asia for over 4000

years. Its therapeutic value was mentioned in ancient texts like the Ebers Papyrus. In Ayurveda and Chinese medicine, it is used as an anticonvulsant, lactation stimulant, and laxative. In Egypt, fenugreek seeds were used to enhance milk production and relieve menstrual pain, while also treating skin infections and tuberculosis. During the 19th century, it was included in remedies for menstrual and menopausal discomfort. In Chinese medicine, it is used for kidney disorders and to prevent kidney stone formation. Fenugreek also acts as a detoxifying agent, helping remove toxins and dead cells through the lymphatic system[26-27].

➢ Application of Fenugreek in Food

Fenugreek is rich in proteins and soluble fibers such as galactomannan, which improve food texture and taste. Its gum content is useful in making nutrition bars, yogurts, beverages, and bakery products like bread, cakes, noodles, and tortillas. It also serves as a stabilizer, emulsifier, and adhesive in food processing. The combination of fenugreek gum with soy protein enhances emulsifying and solubility properties, even under varying pH, temperature, and salt conditions. Because of its nutritional and functional qualities, fenugreek is widely used in food formulations to improve health benefits and product stability[28].

Preparation of fenugreek extract [29–31]:

➢ Extraction Process:

Extraction involves using a suitable solvent (menstruum) to isolate active phytochemicals from the plant. The solvent choice depends on the plant part and nature of compounds. Polar solvents like water, methanol, and ethanol extract polar compounds, while nonpolar solvents such as hexane and dichloromethane are used for nonpolar substances.

➢ Preparation of Plant Material:

Mature fenugreek seeds are cleaned, shade-dried, coarsely powdered, and stored in airtight containers until use.

➢ Extraction Methods:

1. Soxhlet Extraction (Hot Continuous Extraction):
   - 25–50 g of powdered seeds are placed in a thimble within a Soxhlet extractor.
   - Ethanol, methanol, or hydroalcoholic mixtures (70:30) are used as solvents.
   - Continuous extraction is carried out for 6–8 hours until the solvent becomes colorless.
   - The extract is concentrated using a rotary evaporator and dried.
2. Maceration (Cold Extraction):
   - 50 g of powder is soaked in 500 mL of solvent (ethanol, methanol, or water) for 3–7 days with occasional shaking.
   - The mixture is filtered, concentrated, and dried to obtain the final extract.

Antidiabetic Activity:

Fenugreek exhibits significant antidiabetic potential through multiple mechanisms. It enhances glucose uptake in hepatic and peripheral tissues by upregulating glucose transporter proteins (GLUT-2 and GLUT-4) [32]. The amino acid 4-hydroxyisoleucine directly stimulates insulin secretion from pancreatic β-cells in a glucose-dependent manner, improving insulin sensitivity and reducing fasting blood sugar and triglyceride levels. The galactomannan fiber present in the seeds forms a viscous gel in the intestine, slowing gastric emptying and carbohydrate absorption, which helps control postprandial glucose levels [33]. Additionally, fenugreek inhibits digestive enzymes such as α-amylase and lipase, reducing starch and fat digestion, thereby lowering glucose spikes after meals [34]. Experimental studies in diabetic animal models have shown that fenugreek seed extracts significantly reduce blood glucose and improve glycogen storage in the liver. Its hypoglycemic action is comparable to insulin and metformin [35]. A pharmacokinetic study further revealed that combining fenugreek extract with metformin enhances the drug's bioavailability and prolongs its therapeutic action by 70% [36].

Other Pharmacological Activities

- Hypolipidemic activity: Fenugreek saponins and fibers lower total cholesterol, LDL, and triglycerides while increasing HDL [37].
- Antioxidant activity: Flavonoids and polyphenols scavenge free radicals, reducing oxidative stress and cellular damage [38].
- Anti-inflammatory activity: Ethanolic extracts inhibit COX and LOX enzymes, reducing prostaglandin and leukotriene formation [39].
- Antimicrobial activity: Active compounds inhibit the growth of E. Coli, Staphylococcus aureus, and Candida albicans [38].
- Anticancer activity: Diosgenin induces apoptosis and suppresses tumor cell proliferation [41].
- Gastroprotective activity: Mucilage forms a protective coating over the gastric mucosa, reducing ulcer formation [42].
- Hepatoprotective activity: Fenugreek reduces ALT and AST levels, minimizing oxidative liver damage [40].
- Cardioprotective activity: Improves cardiac function, lipid metabolism, and reduces atherosclerotic changes [40].

- Galactagogue (Lactation enhancer): Saponins stimulate prolactin secretion, increasing milk production [43].
- Antifertility/Reproductive effects: Alters spermatogenesis and hormonal balance in a dose-dependent manner [37].
- Analgesic and Antipyretic effects: Reduces pain and fever by inhibiting inflammatory mediators [38].
- Wound healing: Enhances collagen synthesis and promotes tissue regeneration [39].
- Neuroprotective/Memory enhancing: Trigonelline and flavonoids protect neurons and improve cognitive function [38].

Toxicity and adverse effects:

Fenugreek is generally recognized as safe when consumed in dietary amounts. However, toxicity may vary depending on dosage and extract concentration. Animal studies show that doses below 1000 mg/kg caused no harmful effects in Wistar rats after 90 days. Mice treated with 0.2–1 g/kg of leaf glycosidic extract for seven days also showed only mild, reversible side effects. Due to its estrogen-like activity, fenugreek is not recommended during pregnancy, as high doses (30% seed diet) affected fetal development in rabbits. Human studies reported no severe adverse effects such as liver or kidney damage, though mild gastrointestinal discomfort may occur. A toxicology assessment (ToxRTool) confirmed standardized fenugreek extracts as non-toxic, with only minor stomach irritation. However, allergic reactions may occur in individuals sensitive to peanuts or legumes due to cross-reactivity. Further long-term clinical studies on diverse populations are needed to confirm its safety profile. Current evidence suggests that fenugreek is a safe and effective natural remedy for Type 2 diabetes[44].

Marketed preparations of fenugreek:

- Himalaya Wellness Fenugreek Capsules [45]: Regulate blood sugar levels, improve digestion, and enhance lactation.
- Organic India Methi Powder [46]: Helps lower glucose, aids weight reduction, and relieves constipation.
- Baidyanath Methi Plus Tablets [47]: Act as an antidiabetic and hypolipidemic agent; also support hormonal balance.
- Jiva Methi Churna [48]: Promotes liver function, controls blood sugar, and supports fat metabolism.
- Nature's Way Fenugreek Capsules [49]: Maintain normal glucose levels, improve lactation, and reduce appetite.

Future perspectives:

Fenugreek (Trigonella foenum-graecum L.) shows great promise as a natural antidiabetic, antioxidant, and lipid-lowering agent. However, more research is needed to standardize its extracts, identify specific bioactive compounds, and clarify its exact mechanism of action. Future studies should focus on large-scale clinical trials, longer treatment durations, and detailed analysis of its pharmacokinetics and safety. Advanced formulation techniques such as nanoparticles or nanoemulsions could improve the absorption, stability, and efficacy of fenugreek extracts. Exploring its interactions with gut microbiota and other drugs will help in understanding its full therapeutic potential. The development of fenugreek-based functional foods and dietary supplements could provide affordable and effective options for preventing and managing diabetes, obesity, and cardiovascular diseases[50].

CONCLUSION:

Fenugreek (Trigonella foenum-graecum L.) is a valuable medicinal plant with proven benefits in managing diabetes and related metabolic disorders. Its key constituents — trigonelline, 4-hydroxyisoleucine, diosgenin, and galactomannan — help reduce blood glucose, cholesterol, and oxidative stress. Studies show that fenugreek enhances insulin secretion, improves glucose tolerance, and lowers lipid levels, making it an effective natural therapy for Type 2 diabetes. It is generally safe for consumption, though further studies are needed to determine long-term safety and optimal dosage. Standardizing fenugreek extracts could ensure consistent therapeutic effects and improve clinical outcomes. Overall, fenugreek holds strong potential as a safe, affordable, and effective herbal medicine for diabetes and metabolic health management.

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