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UNLOCKING FENUGREEK'S POWER IN PCOS AND DIABETES

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ABSTRACT

Polycystic Ovary Syndrome (PCOS) and Diabetes Mellitus are two prevalent endocrine and metabolic disorders that share common pathophysiological features, particularly insulin resistance, hormonal imbalance, and oxidative stress. These conditions not only affect metabolic homeostasis but also contribute to reproductive dysfunction and long-term cardiovascular risks. Conventional pharmacological treatments, though effective, often come with side effects and limited long-term compliance, prompting interest in natural therapeutic alternatives. Fenugreek (Trigonella foenum-graecum), a traditional medicinal herb, has gained scientific recognition for its significant role in managing metabolic and endocrine disorders. Its bioactive constituents- such as galactomannan, 4-hydroxyisoleucine, diosgenin, and trigonelline- demonstrate insulin-sensitizing, hypoglycemic, lipid-lowering, and hormonal regulatory effects. Data from randomized controlled trials and open-label studies were collected and analyzed together. Additionally, it effectively reduces fasting blood glucose, cholesterol, and oxidative stress markers in diabetic individuals. Overall, fenugreek represents a safe, affordable, and evidence-based herbal approach to managing PCOS and Diabetes Mellitus. Continued research into its molecular mechanisms, dosage optimization, and pharmacokinetic interactions could further establish its role as a reliable phytotherapeutic agent in integrative healthcare.

KEYWORDS: Fenugreek, Polycystic ovary syndrome, Diabetes mellitus, Insulin sensitivity, phytochemical constituents, Phytotherapy.

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is an ovarian disorder, most common endocrine disorders affecting women of reproductive age, with a global prevalence estimated between 6 % and 13 %.[1] It is characterized by irregular menstrual cycles, hyperandrogenism, and polycystic ovarian morphology, often accompanied by metabolic abnormalities such as insulin resistance and dyslipidemia. Beyond its reproductive implications, PCOS represents a complex metabolic condition that significantly increases the risk of developing type 2 diabetes mellitus and cardiovascular diseases.[1] Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Insulin, a hormone produced by the pancreas, plays a crucial role in regulating blood glucose levels by facilitating glucose uptake in cells. Impaired insulin production or insulin resistance leads to elevated blood glucose concentrations, a hallmark of diabetes.[2] Both PCOS and Diabetes represent significant global health challenges, with Diabetes alone affecting over 10.5% of the world's population, leading to severe health complications and substantial economic burdens.[3] The overlap between PCOS and Diabetes is increasingly recognized. Insulin resistances serve as a common pathophysiological denominator, linking hyperinsulinemia to both hyperandrogenism in PCOS and hyperglycemia in Diabetes. Up to 70% women with PCOS exhibit some degree of insulin resistance, independent of body mass index (BMI).[4] The bioactive constituents of fenugreek exhibit a synergistic effect on reducing blood glucose levels by upregulating glucose transporter type 2 (GLUT-2) receptor expression and sterol regulatory element-binding protein 1c (SREBP-1c) mRNA levels.[5] The traditional uses of fenugreek across diverse pharmacopeias, including Ayurvedic, Chinese, Arabic, Greek and Latin systems, further highlight its historical recognition for various medicinal properties, such as being a laxative, demulcent, galactagogue, and carminative.[6]

Supplementation with fenugreek has been shown to have beneficial effects on lipid profiles, contributing to decreased cholesterol levels and a reduced risk of cardiovascular disease, which in turn lowers the risk of developing type 2 diabetes mellitus.[7] The global prevalence of diabetes mellitus has undergone a significant increase, rising from 108 million cases in 1980 to 422 million in 2014, with a further escalation to 463 million cases in 2020.[8]

According to the literature survey journey "Unlocking Fenugreek's Power in PCOS and iabetes", this article highlights the bioactive constituents of fenugreek, its mechanism of

action, and its role as a complementary intervention alongside conventional therapies.

FENUGREEK: BOTANICAL AND PHYTO CONSTITUTIONS

Biological Source

Fenugreek seeds are obtained from Trigonella foenum-graecum L., a member of the Fabaceae (Leguminosae) family. The spices are indigenous to the Mediterranean, southern Europe, and western Asia, and are now extensively cultivated globally, with major production in India, North Africa, and the Middle East.[9]

MORPHOLOGY

Fenugreek (Trigonella foenum-graecum) is an annual herb valued for its notable culinary and medicinal uses. The plant generally reaches a height of 0.3 to 0.8 meters and is characterized by trifoliate leaves, meaning each leaf is divided into three smaller leaflets. Fenugreek provides small flowers that are either white or yellow, which later develop into long, slender pods. These pods, upon maturing, turn from yellow to brown and contain hard, brown seeds- the primary part of the plant used for both medicinal purposes and cooking. The seeds are commonly ground into a powder and employed in managing digestive disorders, diabetes and inflammation. Nutritionally, fenugreek seeds are rich in protein, fiber and essential nutrients. The leaves of fenugreek, whether fresh or dried, have a strong, distinctive flavor and are widely used in cooking, particularly across the Indian subcontinent. Fresh leaves can be consumed as a vegetable, while dried leaves are referred to as kasurimethi, adding a unique, slightly bitter and aromatic taste to many traditional dishes. Due to its wide range of applications in medicine and cuisine, fenugreek holds significant importance in traditional practices.[10] The flowers of fenugreek (Trigonella foenum-graecum) are small, solitary, and range in color from pale yellow to white. They are papilionaceous, exhibiting the characteristic butterfly-like structure of the Fabaceae family, consisting of five petals: a single standard (vexillum), two lateral wings, and a pair of fused keels.[9]

Taxonomy of Fenugreek

The genus Trigonella L. belongs to the sub tribe Trifoliate within the Fabaceae family, which also includes the genera Medicago, Trifolium, and Melilotus. This sub tribe forms a monophyletic group within the “vicioid clade” and is characterized by trifoliate leaves with stipules that are attached to the stem but do not completely cover it. Among the genera of this sub tribe, Trigonella is the largest and most economically important. Key morphological features of Trigonella species include campanulate or tubular sepals with two prominent

upper lobes and three smaller lower lobes, diadelphous stamens with persistent anthers, a terminal stigma, and an ovary containing numerous ovules. These species are primarily adapted to arid and semi-arid regions across the Mediterranean, West Asia, Europe, North and South Africa, North America, and South Australia. The exact number of Trigonella species remains uncertain due to unresolved taxonomic issues, synonymies, and variation in species concepts. While Linnaeus initially described 260 species, later studies have recognized between 62 and 128 species. Recent research, including studies by small, suggests that the genus currently comprises 62 species. According to the plant list, 98 taxa are accepted, alongside 97 unresolved names, three misapplied names, and 27 accepted synonyms. Among these, Trigonella foenum-graecum holds significant economic and medicinal value, including cholesterol-lowering properties, making it a focus of pharmaceutical and natural health research. These characteristics underscore the importance of Trigonella species as both nutritional sources for livestock and potential medicinal applications.[11]

Table 1: Taxonomical classification.[12]

Kingdom	Planate
Division	Magnoliophyta
Class	Magnoliopsida
Order	Fabales
Family	Fabaceae
Genus	Trigonella
Species	T. foenum-graecum
Binomial Name	Trigonella foenum-graecum L.

Phytochemical Composition

The therapeutic potential of fenugreek seeds depends on the bioactive components. These include alkaloids such as trigonelline, proteins, amino acids, flavonoids, steroidal saponins, coumarin, lipids, vitamins, minerals, and galactomannan fiber. There is substantial clinical and pharmacological data supporting the use of fenugreek seeds as a medication for diabetes and PCOS. The structures of Phytochemicals are shown below in Fig.1.

Medicinal and Nutritional Significance

Fenugreek seeds have a protein level of between 22 and 26%, plus 58% carbohydrates, a rate of 25% fiber, and 0.9% fat. The amounts of fiber, protein, and carbohydrates in fenugreek leaves are 1.1%, 4.4%, and 6%, respectively.[13]

Polysaccharides and Fibers: Polysaccharides and, in particular, galactomannan, which make up 25–45% of the dry weight of the seeds, are the most prevalent primary metabolites found in fenugreek seeds. Its stabilizing, thickening, and emulsifying qualities make it useful not only in the pharmaceutical and medical sectors but also in the nutraceutical sector. Various milk and meat products, soups, baked dishes, and a variety of powdered or gel-formed products are all made with it. The unique physicochemical properties of fenugreek galactomannan are responsible for these diverse uses in a range of industries. The endosperm is dominated by galactomannan, a soluble fiber comprising a β-(1→4) mannose backbone with α-(1→6) galactose substitutions. Present at 25-45% of seed mass, galactomannan increases viscosity, slows glucose absorption, and binds bile acids, thereby influencing glycemic and lipid profiles.[14]

Proteins and Amino Acids: Fenugreek proteins (20-30%) are notable for high lysine and tryptophan content. At alkaline pH, the protein in fenugreek is more soluble. A distinctive component, 4-hydroxyisoleucine, enhances glucose-dependent insulin secretion and improves insulin sensitivity.[15]

Lipids: Lipids are present in fenugreek seeds at a concentration of 100 g/kg. Diglycerides, glycolipids, phospholipids, and triglycerides make up approximately 6.3%, 5.4%, 10.5%, and 86.1% of the total composition, respectively, making them the main lipids. Monoglycerides, free fatty acids, and sterols are present in trace levels in fenugreek seeds.[13]

Saponins and Sapogenins: Steroidal saponins, particularly diosgenin, yamogenin, and tigogenin, contribute to hypocholesterolemia and insulin-sensitizing effects. Diosgenin is well-studied for its role in glucose and lipid regulation.[16]

Alkaloids: Trigonelline, a pyridine alkaloid, exhibits ant diabetic, insulin-sensitizing, and neuroprotective actions in experimental models.[17]

Polyphenols and Antioxidants: Antioxidant activity (AOA) may help shield cells from aging and reduce the risk of chronic diseases because fenugreek seeds are high in antioxidants, such as polyphenols and flavonoids, which fight oxidative stress (OS) and lessen the harm caused by free radicals.[13]

Iron: Fenugreek's nutritional value is enhanced by the fact that it is a good source of iron, with approximately 33 mg of iron per 100 g of dry weight. Because of the combination of

these components, fenugreek is a valuable plant that has potential therapeutic effects (because of its alkaloids, saponins and polyphenols) as well as nutritional benefits (because of its protein and iron content).[18]

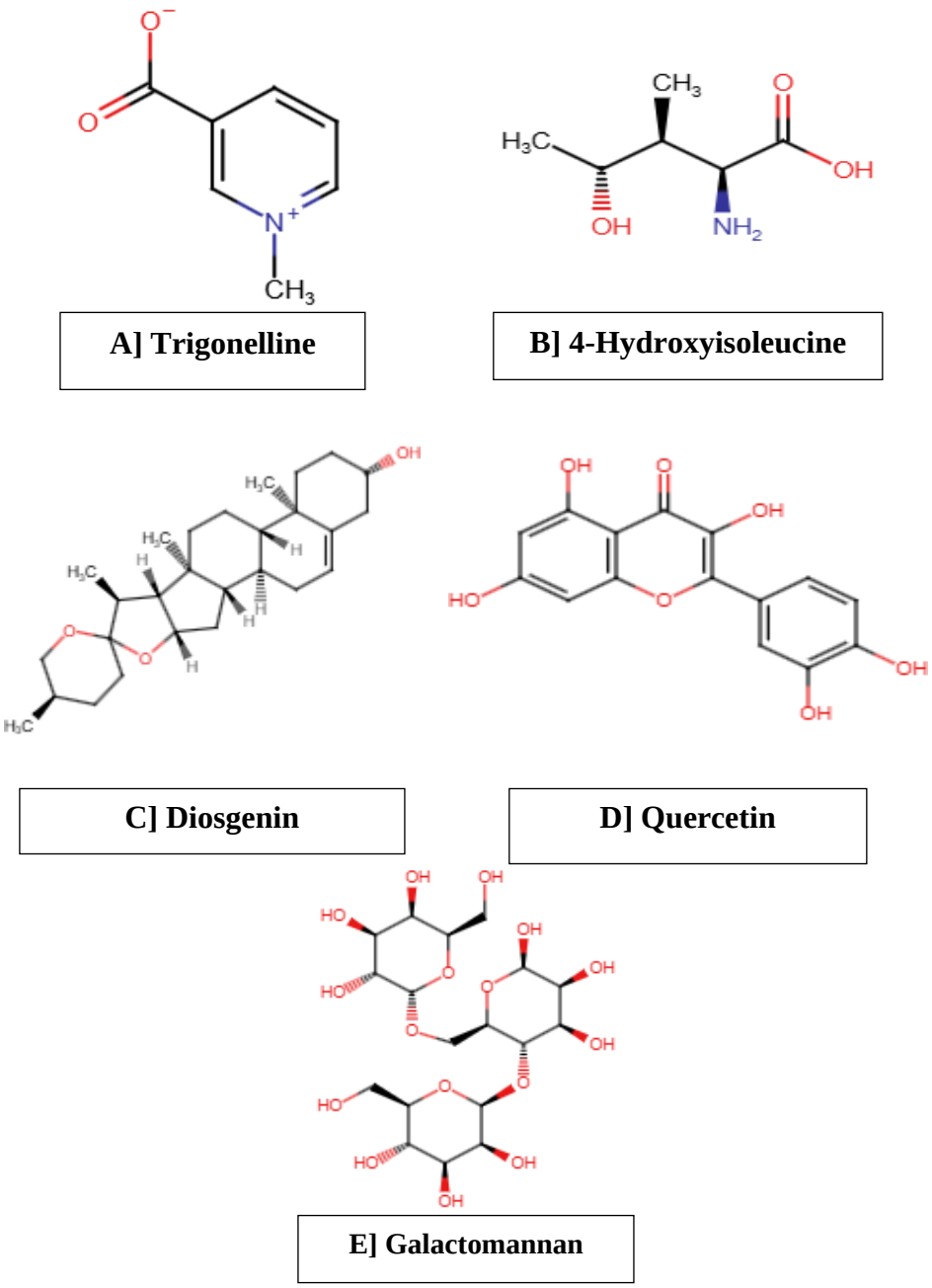

Figure 1: Phytochemical Structures of Fenugreek Seeds.

TRADITIONAL USES OF FENUGREEK IN MEDICINE

Fenugreek (Trigonella foenum-graecum) has a long history of use in traditional medicine systems across Asia, the Middle East, and Europe. In Chinese and Middle Eastern herbal practices, the plant has been prescribed for kidney ailments, male reproductive disorders, and as a uterine stimulant to ease labor pains. Folk medicine also records its application for

menstrual cramps, gastrointestinal disturbances, and as an aid in childbirth.[19] Culinary, Fenugreek seeds are valued both as a flavoring and preservative, added to pickles, chutneys, bakery items, dairy and meat products, condiments, beverages, and confectionery. The seeds are also given as a nutritive tonic during convalescence, anorexia, or fever, with some sources comparing their antipyretic effect to quinine. Pharmacologically, fenugreek exhibits multiple therapeutic properties. Its mucilaginous content provides a demulcent action that soothes inflamed mucosa in gastritis, peptic ulcers, colitis, and irritable bowel conditions. The soaked seed water and sprouts have been used to alleviate constipation, respiratory congestion, and mucus accumulation in asthma, bronchitis, sinusitis, and influenza. Additionally, its antioxidant and lymphatic cleansing actions contribute to detoxification, improved circulation, and enhanced immunity. Ethnomedical reports highlight its diverse applications: as a breath freshener, skin emollient, and agent for restoring appetite and taste; as a galactagogue to stimulate lactation within 24-72 hours due to its phytoestrogenic activity; and in folk oncology, where seeds have been used intravaginally in China for cervical conditions. Experimental studies further support its nephroprotective role, showing reduced calcium oxalate deposition in rat models of kidney stones, thereby validating its traditional use in renal disorders.[20] Collectively, fenugreek is regarded as a multipurpose herb with gastrointestinal, respiratory, metabolic, reproductive, and immunomodulatory benefits, making it one of the most versatile botanicals in both traditional and modern therapeutic contexts.[19]

FENUGREEK IN PCOS MANAGEMENT

Mechanism of Action

Three major bioactive substances may account for the potential positive benefits of fenugreek seeds on inflammation and oxidative stress. A steroidal saponin called diosgenin can lower lipid peroxidation levels, limit inflammatory mediators produced by macrophages, and restore the antioxidant state. A new branched-chain amino acid found in fenugreek, 4-hydroxyisoleucine (4-OH-Ile), exhibits potent suppression of the generation of reactive oxygen species (ROS) and associated inflammation. Additionally, it has been shown that fenugreek fiber increases glutathione and α-tocopherol while decreasing homocysteine and serum LDL oxidation. Furthermore, by lowering the amounts of glycerophospholipid metabolites and downregulating the catabolic route of histidine to urocanic acid, galactomannan may inhibit oxidative stress and inflammation, which further helps to improve insulin sensitivity.[21]

Fenugreek treatment showed a significant restoration in all of the measured sex hormones in EV-induced rats. It also determined that fenugreek had an infertile impact on healthy female mice by demonstrating that its extract reduced FSH and LH while also reducing folliculogenesis in the ovaries. In women with PCOS, it was also demonstrated that fenugreek improved menstrual cycles, decreased the amount of ovarian cysts, and decreased the LH/FSH ratio. Some of these women managed to conceive. Since dehydroepiandrosterone (DHEA), which is mostly formed from cholesterol, is the primary component of androgen, it is crucial to note that fenugreek has a lipid-lowering impact that may aid in androgen reduction.[22]

These key findings suggest that fenugreek supports metabolic homeostasis and reproductive restoration in PCOS women. These dual actions contribute to the improvements of insulin sensitivity, lipid profiles, and menstrual regularity, marking fenugreek as a valuable adjunct in integrative PCOS therapy.

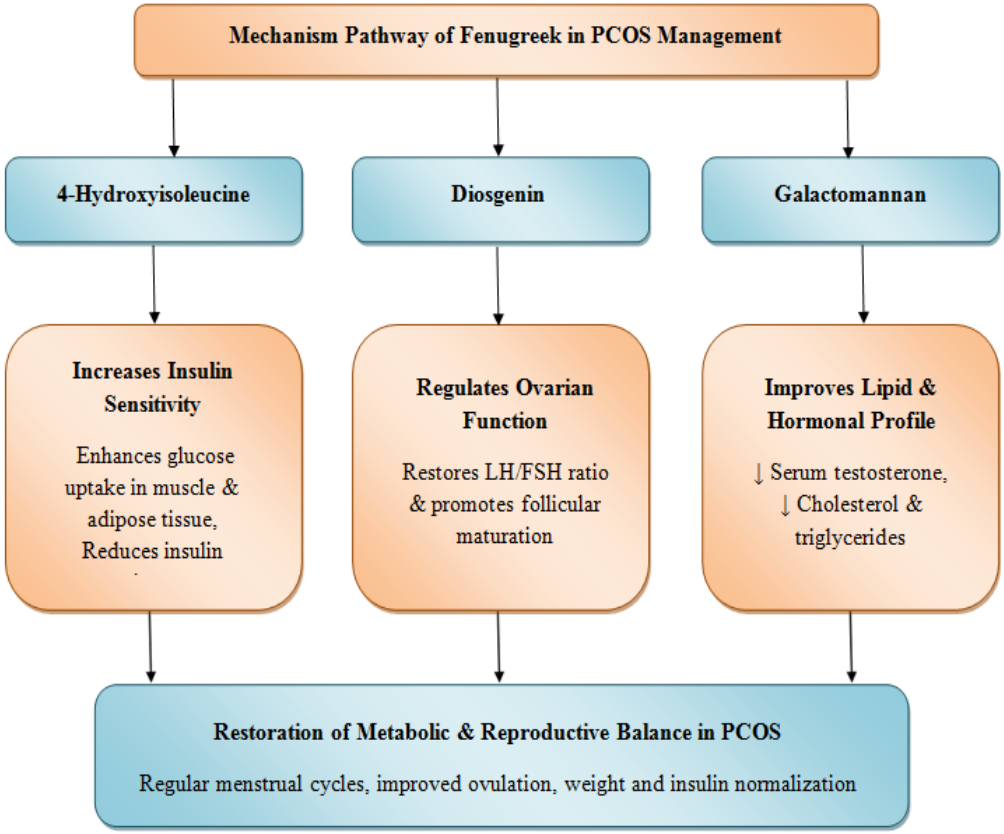

Figure 2: Overall mechanism pathway of fenugreek in PCOS management.

FENUGREEK IN DIABETES MANAGEMENT

Clinical investigations have substantiated the hypoglycemic efficacy of Trigonella foenum-

graecum (fenugreek) in individuals afflicted with type 2 diabetes mellitus. A randomized controlled trial conducted by Kassaian revealed that supplementation with 10 g/day of powdered fenugreek seeds for an 8-week period resulted in a significant reduction (approximately 25%) in fasting blood glucose (FBG) concentrations when the seeds were subjected to hot water immersion. Conversely, concomitant consumption of fenugreek with yoghurt failed to elicit significant alterations in FBG or HbA1c levels. The hypoglycemic effect of fenugreek is ascribed to its high soluble fiber content, which retards carbohydrate absorption and gastric emptying, as well as the presence of the amino acid 4-hydroxyisoleucine, which potentiates insulin secretion and enhances glucose tolerance. These findings imply that fenugreek seed, particularly when prepared via hot water immersion, may constitute a valuable adjunctive therapeutic strategy in the management of type 2 diabetes.[23]

Fenugreek (Trigonella foenum-graecum) seeds and their extracts, particularly Fenfuro™, have shown beneficial effects on insulin sensitivity and secretion in patients with type 2 diabetes mellitus (T2DM). Fenfuro contains around 40% furostanolic saponins, which are believed to enhance insulin action and glucose utilization. Clinical findings from Verma et al. (2016) reported that supplementation with Fenfuro (500 mg twice daily for 90 days) significantly reduced fasting and postprandial blood glucose levels. Furthermore, both fasting and postprandial C-peptide levels—biomarkers of pancreatic β-cell function—showed significant increases from baseline values, suggesting improved insulin secretion. However, the difference between the treatment and placebo groups for C-peptide levels was not statistically significant, indicating that Fenfuro may primarily enhance insulin sensitivity rather than directly stimulate excessive insulin release. The improved glycemic control, coupled with elevated C-peptide levels and decreased dependency on conventional anti-diabetic medications, suggests that fenugreek may support β-cell activity and peripheral insulin responsiveness. These outcomes are likely attributed to the combined effects of furostanolic saponins and soluble dietary fibers, which modulate carbohydrate metabolism, slow glucose absorption, and improve tissue glucose uptake. Overall, Fenfuro demonstrates potential as a safe, plant-based adjunct therapy that improves insulin sensitivity and supports insulin secretion in T2DM management.[24]

Preclinical and Clinical Evaluation of Fenugreek

Table 2.

Sr No.	Research Title	Research Type	Intervention	Population and Sample Size	Key Findings
1.	Efficacy studies of Fenugreek Seeds against Polycystic Ovary Syndrome[25]	Randomized Controlled Trial, Single-blind, active control trial in 3 parallel groups.	Two groups Treatment & control group, treatment period of 90 days	Population: Premenopausal women diagnosed with Polycystic Ovarian Syndrome (PCOS) Sample size: 90 participants	Prolonged intake of raw fenugreek seed powder for three months showed significant improvement in: Menstrual cycle regularity, egg maturation, reduction in ovarian volume, and improvement in fertility outcomes
2.	Efficacy of Novel Fenugreek Seed Extract (Trigonella foenum-graecum, Furocyst®) in PCOS[26]	Open-label, single-arm, Non-randomized, post-marketing surveillance study	Furocyst® 2 capsules of 500mg Each day treatment period of 90 days	Population: Premenopausal women aged 18–45 years, BMI < 42, diagnosed with PCOS Sample size: 50 participants	46% showed a reduction in ovarian cyst size 36% had complete dissolution of cysts 71% regained regular menstrual cycles 12% became pregnant after treatment 94% of patients benefited overall. Significant increase in LH and FSH levels Significant reduction in ovarian volume and cyst number. No significant adverse effects, confirming the broad-spectrum safety of Furocyst
3.	The effect of Fenugreek Seeds (Trigonella foenum-graecum) supplementation on glycemic status, Specifically, in letrozole induced PCOS rat model[27]	Experimental animal study (preclinical study)	Oral administration of aqueous Fenugreek Seed extract for 21 days on letrozole Induced PCOS rat	Population: Female Wistar rats Sample size: 40 rats total Control group: 10 rats (received saline) PCOS control group: 30 rats (received letrozole 1 mg/kg to induce PCOS, then subdivided for treatment)	Letrozole induced PCOS-like changes: ↑ testosterone, ↑ insulin, ↑ glucose, ↑ cholesterol, and ovarian cyst formation Fenugreek-treated rats showed: Normalization of estrous cycle Restoration of normal ovarian structure Significant reduction in testosterone, insulin, glucose, and cholesterol levels (P<0.001)

					Improvement similar to or better than metformin treatment
4.	Immunomodulatory Effects of Fenugreek (Trigonella foenum-graecum L.) Extract in mice.[28]	Preclinical Experimental in-vivo study controlled dose dependent laboratory experiment.	Fenugreek seed extract administered Orally at doses of 50,100, & 200 mg/kg Body weight/day for 15 days.	Population: Male Swiss albino mice Sample size: Not explicitly mentioned in the paragraph (multiple groups treated at different doses)	Thymus weight increased significantly at 50 and 100 mg/kg; liver weight increased at 100 and 250 mg/kg without adverse liver enzyme changes. Delayed-type hypersensitivity (DTH) response significantly increased at 50 and 100 mg/kg ($p < 0.001$). Plaque-forming cell (PFC) assay showed elevated antibody response at 100 mg/kg. Phagocytic activity and phagocytic capacity of macrophages were significantly enhanced. Lymphoproliferation response was mild but positive.
5.	Effect of Fenugreek Seeds on Blood Glucose and Lipid Profiles in Type 2 Diabetic Patients[23]	Clinical trial study	Administration of 10 grams/day of powdered fenugreek seeds Consumed either soaked in hot water or mixed with yoghurt Duration: 8 weeks	Population: Patients with Type 2 Diabetes Mellitus Initial sample size: 24 patients Final sample size (after exclusions): 18 patients 11 consumed fenugreek soaked in hot water 7 consumed fenugreek mixed with yoghurt	Significant reduction in: Fasting Blood Sugar (FBS) ↓ 25% Triglycerides (TG) ↓ 30% VLDL-C ↓ 30.6% No significant changes in BMI, energy intake, carbohydrate, protein, or fat intake Fenugreek soaked in hot water was more effective than fenugreek mixed with yoghurt
6.	Antidiabetic Effects of Subfractions from Fenugreek Seeds in Diabetic Dogs.[29]	Experimental study (in vivo)	Subfraction “a” (rich in fibers) and Subfraction “b” (rich in saponins/proteins) from defatted fenugreek	Population: Alloxan-diabetic dogs (animal model for diabetes) Sample size: Not explicitly stated, but	The addition of subfraction “a” to insulin treatment resulted in a clear decrease in hyperglycemia and glycosuria.

			seeds.	multiple dogs were used in the experiment.	
7.	Role of Fenugreek in the prevention of type 2 diabetes mellitus in prediabetes. [30]	Randomized, controlled, parallel study (clinical trial)	Fenugreek powder, 5 grams twice daily before meals (total 10 g/day) Duration: 3 years	Population: Men and women aged 30–70 years with prediabetes Sample size: Fenugreek group: 66 participants Control group: 74 participants Total: 140 participants	A significant reduction in the cumulative incidence of diabetes in the Fenugreek group compared to controls. Decreased fasting plasma glucose (FPG), postprandial plasma glucose (PPPG), and LDL cholesterol. Increased serum insulin levels and decreased insulin resistance (HOMA-IR). The control group had 4.2 times higher risk of developing diabetes compared to the Fenugreek group. No adverse effects were observed
8.	Hypolipidemic Effect of Fenugreek Seeds: A Chronic Study in Non-Insulin Dependent Diabetic Patients.[31]	Chronic Clinical Study	25 g fenugreek seed powder mixed with an isocaloric diet	60 non-insulin dependent diabetic subjects	Ingestion resulted in a significant reduction of total cholesterol, LDL, VLDL cholesterol and triglyceride levels, indicating a beneficial hypolipidemic effect in diabetic subjects.
9.	Fenugreek seeds as a natural source of L-arginine-encapsulated lipid nanoparticles against diabetes.[3]	Experimental in-vitro and in-silico study (includes molecular docking, nanoparticle formulation, and laboratory characterization)	L-arginine-encapsulated lipid nanoparticles synthesized from fenugreek seed oil	Population: Not human or animal subjects — laboratory-based (computational and experimental) study Sample size: Not applicable (in-vitro and in-silico analyses conducted)	Docking results: L-arginine showed strong binding with diabetes-related genes (CYP1A2, CYP2C19, NFKB) with binding energies between −7.2 to −8.9 kcal/mol Nanoparticle characteristics: Average size: 100.2 nm Zeta potential: −9.37 mV (neutral stability) UV–Vis peaks: 415 nm (plain nanoparticles) and 521 nm (L-arginine-loaded).

10.	Soluble dietary fibre fraction of Trigonella foenum-graecum (fenugreek) seed improves glucose homeostasis in animal models of type 1 and type 2 diabetes by delaying carbohydrate digestion and absorption.[32]	Experimental animal study (preclinical study)	Soluble Dietary Fibre (SDF) fraction of Trigonella foenum-graecum (fenugreek) seeds Dose: 0.5 g/kg body weight Duration: 28 days (daily oral administration).	Population: Normal, type 1 diabetic, and type 2 diabetic rats Sample size: Not specified in the paragraph (experimental groups of rats)	Improved oral glucose tolerance in normal, type 1, and type 2 diabetic rats. Increased unabsorbed sucrose in the gastrointestinal tract indicates reduced carbohydrate absorption. Decreased intestinal disaccharidase activity and reduced glucose absorption. Increased gastrointestinal motility. Reduced serum glucose and increased liver glycogen levels after 28 days. Enhanced total antioxidant status without altering serum insulin levels. Improved peripheral glucose transport and insulin action in adipocytes (3T3-L1 cells)

SYNERGISTIC EFFECTS OF FENUGREEK WITH CONVENTIONAL TREATMENTS

The acute hypoglycemic properties of fenugreek seeds and their extract have been assessed in both diabetic and non-diabetic individuals. Whole raw fenugreek seeds, powdered extracts, cooked seeds (25 g), and gum isolate from the seeds (5 g) have been found to lower postprandial glucose levels, while degummed seeds (25 g) exhibited minimal impact. These results indicate that the immediate effects of fenugreek seeds are primarily attributable to the gum component, although they do not rule out the potential long-term influence of other constituents of fenugreek on blood sugar levels. Animal studies also show that the soluble fiber component of fenugreek seeds slows down the rate of enzymatic breakdown and glucose absorption in the gastrointestinal system. Trigonelline consumption decreased blood glucose levels and improved insulin sensitivity in diabetic rats. Furthermore, in isolated rat and human pancreatic islet cells, 4-hydroxyisoleucine, a new amino acid derivative derived from fenugreek seeds, promoted glucose-dependent insulin secretion. Therefore, through

enhanced insulin secretion and glucose absorption, fenugreek optimizes metabolic regulation.[33] The following schematic (Fig. 2) illustrates the integrated mechanism through which fenugreek amplifies therapeutic efficacy and supports metabolic and reproductive balance.

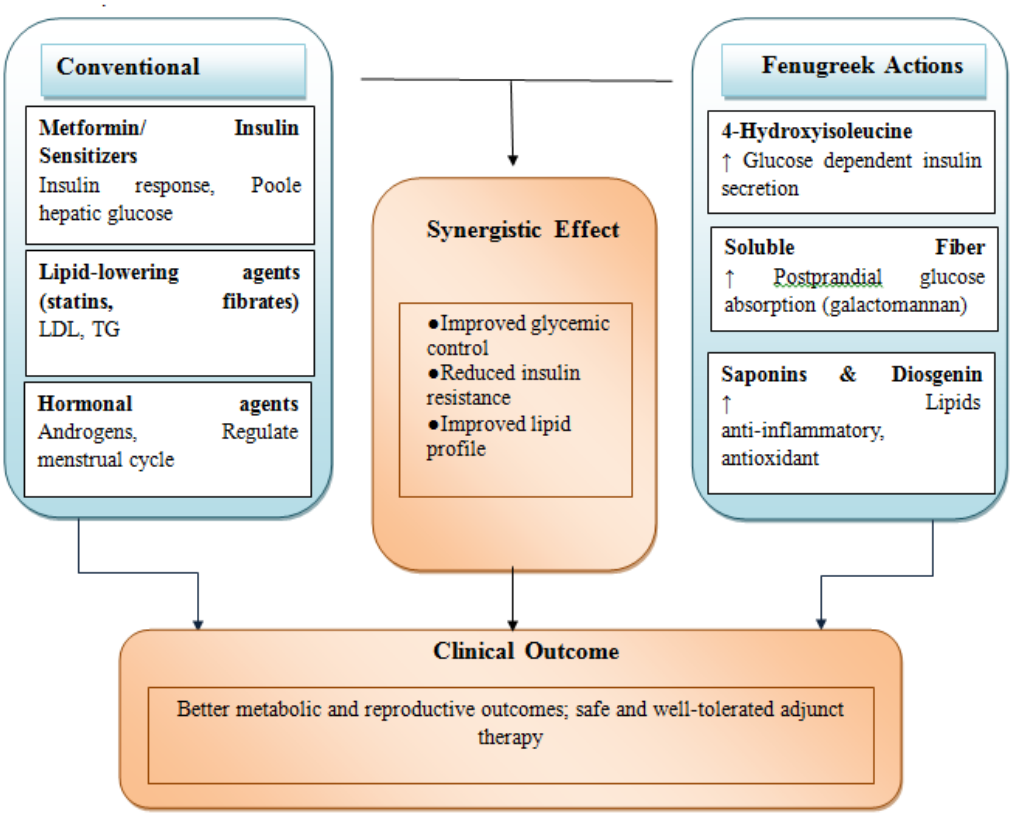

Figure 3: Integrated Mechanism of Fenugreek Action.

SAFETY AND DOSAGE CONSIDERATIONS

Fenugreek is generally well-tolerated when consumed within recommended doses. However, careful monitoring is required when used with other hypoglycemic drugs due to potential additive effects.[34] Fenugreek extracts, oleoresins, and oils have been designated as Generally Recognized as Safe (GRAS) by the US Food and Drug Administration for use as a seasoning or flavoring agent.[35] The existing literature suggests that fenugreek consumption is typically associated with minor or no adverse effects. Reported human adverse effects are primarily limited to temporary gastrointestinal disturbances and discomfort.[36][37]

Notably, long-term administration of gram quantities of fenugreek seed in patients with diabetes has not been linked to any clinically significant hepatic or renal abnormalities.[38] Given the absence of genotoxicity concerns, fenugreek is likely to be safe for consumption at

doses commonly used to modulate blood glucose and lipid levels, as supported by various studies.[39] Rodents tolerated a dietary fenugreek seed concentration of 2.5% w/w without adverse reactions, and even elevated levels (20% w/w) administered over a 90-day period yielded no toxicological findings.[40] Acute and sub-chronic toxicity assessments of debitterized fenugreek seed powder in murine and rat models revealed no notable toxicity at doses reaching 5 g/kg.[41] Furthermore, comprehensive in vivo evaluations of fenugreek-derived test materials failed to detect any adverse effects or safety concerns.[42] A noteworthy outcome of fenugreek ingestion is the presence of sotolon, a lactone derivative inherent in the seeds, which possesses a distinctive aroma and may induce a maple syrup-like olfactory characteristic in the sweat and urine of individuals consuming fenugreek.[43] The typical consumption patterns of Fenugreek for traditional and culinary purposes have not been extensively documented or quantified. Limited data suggest that a standard serving size (100 g) of ethnic foods containing fenugreek may provide approximately 1.2 g of the botanical ingredient.[44] In India, the average daily consumption of fenugreek seed has been reported to range from 0.3 to 0.6 g per adult. While high doses of fenugreek-containing supplements have been reported to reach up to 100 g per day, typical daily intake is generally in the range of 1 to 5 g.[45] One report[46] recommended a daily intake limit of 21 g of fenugreek per 60-kg adult has been proposed to mitigate the risk of accidental overdose via oral administration.

FUTURE PROSPECTIVES

The potential benefits of fenugreek in managing diabetes and polycystic ovary syndrome (PCOS) warrant further investigation. Future research directions should prioritize[34]:

1. **Validation Studies**: Large-scale, multicenter, and long-duration clinical trials are essential to establish dose-response relationships, safety profiles, and long-term benefits of fenugreek therapy. These trials will provide critical evidence for the efficacy and safety of fenugreek in diverse patient populations.
2. **Molecular Investigation**: Further studies should investigate the molecular mechanisms underlying fenugreek's effects on glucose metabolism and insulin signaling pathways. Particular focus should be placed on gene-level regulation and signaling pathways involving insulin receptors, GLUT-4, and inflammatory mediators.
3. **Precision Herbalism**: Advances in nutrigenomics and metabolomics may enable the development of personalized herbal formulations tailored to individual metabolic profiles and disease phenotypes. This approach could optimize the therapeutic benefits of fenugreek while minimizing potential side effects.

4. **Standardization and Regulatory Compliance Guidelines**: Standardization of fenugreek extracts with defined chemical markers and validated bioactivities is crucial for ensuring reproducibility, safety, and efficacy. Regulatory frameworks should be established to govern the use of fenugreek in dietary supplements and pharmaceutical applications.
5. **Bioactive Food Components and Nutraceuticals**: Incorporating fenugreek into daily diets through fortified foods, teas, or functional snacks represents a practical and culturally accepted approach to chronic disease prevention. This approach may improve patient compliance and provide a sustainable solution for managing diabetes and PCOS.

   By addressing these research directions, we can unlock the full potential of fenugreek as a therapeutic agent for diabetes and PCOS management.

CONCLUSION

Fenugreek, a leguminous herb with a rich history in traditional medicine, emerges as a promising adjunctive therapy for managing Polycystic Ovary Syndrome (PCOS) and Diabetes Mellitus, owing to its multifaceted pharmacological properties. The herb's bioactive compounds, including galactomannan, 4-hydroxyisoleucine, and diosgenin, collectively contribute to its beneficial effects on insulin sensitivity, glucose metabolism, hormonal regulation, and oxidative stress. Clinical studies demonstrate that fenugreek supplementation improves glycemic control, reduces insulin resistance, and alleviates symptoms of PCOS, such as menstrual irregularity and hyperandrogenism. Moreover, fenugreek's favorable safety profile, affordability, and accessibility position it as a viable option for integrative management, particularly in resource-limited settings. However, further research is needed to establish standardized dosing, long-term efficacy, and potential interactions with conventional medications, thereby facilitating the integration of fenugreek into evidence-based clinical practice.

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