

Review Article**Phytochemical and Pharmacological Activity of *Trigonella Foenum Graceum*: A Comprehensive Review****Mahesh Kumar Sharma¹, Dr. Pankaj Kumar Sharma², Dr. Jaya Sharma³**¹PhD. Research Scholar, School of Pharmacy, Apex University, Jaipur²Professor, and Dean, School of Pharmacy, Apex University, Jaipur³Professor, School of Pharmacy, Apex University, Jaipur**Corresponding Author: Mahesh Kumar Sharma****Abstract**

Trigonella Foenum Graceum (Menugreek) is a rich source of various essential compounds and such ingredients play an important role in treating diseases through their anti-diabetic, anti-inflammatory, hepatoprotective, cardioprotective, neuroprotective, immunomodulatory, nephroprotective and antimicrobial activity. Furthermore, fenugreek seeds are a rich source of antioxidants and such ability prevents the pathogenesis of diseases through free radical scavenging activity. This review comprehensively summarizes the role of fenugreek seeds in health management with a special emphasis on modulating various physical and biochemical activities as well as in vitro and in vivo studies.

Keywords: nephroprotective and antimicrobial activity

Introduction

In the ancient Indian traditional system of medicine, Ayurveda, fenugreek has been suggested as an important medicine to treat a variety of digestive and mucosal conditions. [1, 2] The fenugreek seed has traditionally been used as a carminative, demulcent, expectorant, laxative and stomachic agent. The mature fenugreek seed has many other active components such as amino acids, fatty acids, vitamins and saponins such as disogenin, gitogenin, neogitogenin, homorientin saponaretin, neogigogenin and trigogenin, fibers, flavonoids, polysaccharides, fixed oils and some identified alkaloids, that is, trigonelline and choline. [3] The plant has also been employed against diseases such as bronchitis, fever, sore throat, wound, swollen glands, skin irritation, diabetes and ulcers. Recently, due to the widespread use and beneficial properties of fenugreek, many studies have been undertaken to investigate its potential application in health and many common disorders. Such experimental studies examined the effects of various extracts of fenugreek seed in experimental animals in the early to late 1960s. [4] A huge number of studies have returned positive findings, indicating the efficacy of fenugreek seed as a functional food that can be beneficial in health and disease. Fenugreek is well known for its multiple pharmacological properties including antidiabetic, antioxidative, hypocholesterolemic, antineoplastic, anti-inflammatory, antiulcerogenic, antipyretic, immunomodulatory and antitumor. [5] Different active components of fenugreek seeds have been identified and isolated such as polyphenolic flavonoids which exhibit most common properties, that is, hypoglycemic, hypocholesterolemic, hypotriglyceridemic and antiperoxidative [6], steroid saponins exhibiting anti-inflammatory and uterus and lactation-stimulating properties, polysaccharides such as galactomannans contains antidiabetic effects and an amino acid 4-hydroxyisoleucine has been shown to possess insulin-mimetic properties.

[7] Here, we provide a review of recent findings showing effects of *Trigonella* in different diseases in the experimental studies.

TRIGONELLA FOENUM GRACEUM

Plant Description

Trigonella foenum-graecum is an erect, annual, aromatic herb, up to 30-45cm high, leaves are pinnately compound, trifoliate attenuated towards the base and with toothed margins. Leaves are light green in color and petiolated. The first trifoliate leaf appears 5-8 days after germination. The size of leaves is approx. 20-50× 8-17mm. Flowers are small, triangular, axillary and sessile. Flowers are hermaphrodite and pollination takes place through insects. The pollen grains may be oval or circular. White and yellow colored flowers arise from the leaf axils and are arranged singly or in little groups of twos. Fruits are narrow, long and oblong. Size of pod is 80-150×2-4 mm and it ends with an elongated beak. Fruits ripen in summer and harvested in autumn. Pods contain 10-20 small seeds. Seeds are smooth, hard, elongated and flat. Seeds are yellow brown in colour. It has pungent and aromatic seeds. Seeds are quadrangular and a groove in central part divides each seed into 2 parts: larger 2-5 cm long and smaller 15-3.5 cm. The pod shape gives the name “goat’s horn” to the plant. [8, 9]

Table 1: Taxonomy of Fenugreek [10]	
Kingdom	Plant
Family	Fabaceae
Genus	<i>Trigonella</i>
Species	<i>foenum-graecum</i>
General name	Fenugreek
English name	Fenugreek
Arabic name	Hhulbah, Hhelbah
French name	Trigonelle, Senegrain, Foingrec
German name	Gemeiner, Hornklee, Bockshornklee
Indian name	Sagmethi, Methi, Kasurimethi



Figure1: Fenugreek leaves



Figure 2: Fenugreek seeds

Origin and Distribution.

It originated in central Asia ~ 4000 B.C. It is native to southern Europe, Mediterranean region and Western Asia. Its geographical distribution is Middle East, India, China, Central and Southern Europe, Mediterranean region, North Africa, United states. [8]

Cultivation

Fenugreek is best grown as an annual crop from seeds which are sown following the line sowing method. The land should be prepared for ploughing. The irrigation channels are made along the alternate rows of bed. The seeds should be treated with rhizobium culture before sowing. Seeds are pre-soaked for 12 hours prior to sowing. Low humidity is required. Seeds are sown during mid-late spring. The seeds germinate within 6-8 days after sowing. The optimum soil temperature at planting > 10 0C. It grows well in well drained loamy soil. The soil pH should ranges from 5.3 -8.2. Plants are frost tolerant (vegetative stage only). Harvesting is done in 30-40 days for herb and 105-140 days for seeds. Plucking (hand harvesting) is done for herb and machine is used for harvesting the seed. Seeds should be stored below 12% moisture and under dry and cool conditions. [9]

PLANT CHEMISTRY

The main ingredients of the seed contain steroidal saponins, alkaloids, mucilage, and fibers (50%). [10]

Steroidal Saponins: The most important steroidal saponins (0.1% to 2.2%) are diosgenin and yamogenin. Other sapogenins include tigogenin, gitogenin, sarsapogenin, yuccagenin, and smilagenin. The seeds also contain a sapogenin peptide ester named fenugreekine.

Alkaloids: Trigonelline is the alkaloid of this plant that up to 36% concentration of it has been extracted. Other alkaloids of the seed include gentanin and carpaine choline.

Oils: Fenugreek seeds contain fixed oil containing golden yellow and odorless unsaturated fatty acids (6% to 10%). Oil is easily dissolved in ether, benzene, sulfur, and petroleum ether. Fenugreek oil has antimicrobial activity.

Mucilage: Mucilage compounds exist in endosperm of the seed that produce mannose and galactose following hydrolysis. Fenugreek is neutral and contains galactomannan and a xylene. Fenugreek seeds have laxative property and this effect is because of mucilage presence. Mucilage of fenugreek has water-holding capacity against sodium alginate. Also its emulsifying and suspending effect is satisfactory. [11]

Protein Compounds: The amount of protein in this plant is high (22% to 25%), and its protein is rich in lysine, arginine, tryptophan, and to some extent, histidine. It contains low levels of sulfur-containing amino acids, threonine, valin, methionine and high levels of lysine, arginine, and gelicin.

Carbohydrates: The amount of carbohydrates of this plant is about 8%. The seeds of fenugreek also contain proteinase inhibiting compounds. They are also reported to contain minerals such as iron, phosphate, calcium, and vitamins such as nicotinic acid, B1, C, A, and D.

Flavonoids: The main flavonoids identified in this plant include glycoside, orientin, isoorientin, vitexin, epigenin, and quercetin.

Aromatic Ingredients of Seeds: The aromatic ingredients of seeds, including n-alkenes, sesquiterpenes, and some oxygenized compounds like hexanol have been reported in this plant.

Coumarins: Coumarins available in this plant are lactone orthodihydroxy cinnamic acid and the presence of a coumarin named scopoletin in fenugreek has also been reported. Other substances like tannins and carotenoid compounds have been reported in seeds. [12]

PHARMACOLOGICAL ACTIONS OF FENUGREEK

Anti-diabetic activity

The harmful side effects of synthetic drugs, the enormous cost and the inability of existing modern therapies to control all pathological aspects and the poor advance therapies for many rural populations in developing countries are the major drawback of synthetic drugs, to overcome these issues the plant compounds are used now a days, fenugreek plays a vital role in treating several diseases. Postprandial blood glucose response has reduced by soluble fiber, Galactomannan, it is isolated from Canadian grown fenugreek seeds. In vitro studies were conducted to identify the effect of galactomannan on intestinal glucose uptake in genetically determined lean and obese rats. The viscosity of different combinations of galactomannan solutions was prepared. The galactomannan as of the viscous property it has potential to reduce intestinal absorption of low or high concentration of glucose and; therefore for the benefit of blood glucose control. [13]

The anti-diabetic properties of a Soluble Dietary Fibre [SDF] fraction of *Trigonella foenum-graecum* were evaluated, they demonstrated that SDF fraction of *Trigonella foenum-graecum* significantly improved glucose homeostasis in type I and type II diabetes by delaying carbohydrate digestion and absorption, and enhancing or mimicking insulin action. After oral sucrose ingestion in non-diabetic and type 2 diabetic rats, SDF fraction suppressed the elevation of blood glucose. Glucose transport in 3T3-L1 adipocytes and insulin action was increased by *Trigonella foenum-graecum*. They indicated that the SDF fraction of *Trigonella foenum-graecum* seeds applies anti diabetic effects mediated during inhibition of absorption and carbohydrate digestion, and enhancement of peripheral insulin action. [14]

The effect of oral administration of Fenugreek whole seed powder [5% in the diet] for 21 days in alloxan-induced diabetic Wistar rats were studied, the altered enzyme activities were restored to control values in both the liver and kidney after fenugreek seed powder treatment. The biochemical effects exerted by fenugreek seeds make it a potential new curative effect in

type-1 diabetes. The anti-diabetic actions of fenugreek seeds in part have been considered as to the presence of steroid, saponins and fibre content in the seeds. [15]

Pharmacological experiments performed in vivo in normal and streptozotocin induced diabetic rats resulted in increased food intake and consequent progressive weight gain in the diabetic rats treated with the furostanol saponins, in contrast to the untreated diabetic rats. [16] It was identified that Trigonella seed powder treatment to diabetic rats affects key glycolytic, gluconeogenic and NADH-linked lipogenic enzymes. The change in the activities of enzymes effected by Trigonella seed powder treatment as elucidated in this study suggest that a normal glucose metabolism, in peripheral tissues such as liver and kidneys, is critical in achieving normoglycemia. Intermit therapy is possible with the potent product GII of fenugreek which is of great benefit in diabetes induced rabbits. [17]

The fenugreek saponin fraction significantly modulated the disaccharidase and glycogen enzyme activities in the intestine; it increased the hepatic glycogen content, suppressed the increase of blood glucose level and improved results in the Oral Glucose Tolerance Test [OGTT]. The fenugreek saponin extract also efficiently protected the hepatic function, which was by the significant increases of superoxide dismutase [SOD], catalase [CAT], glutathion peroxidase [GPX], aspartate transaminase [AST], alanine transaminase [ALT] and lactate dehydrogenase [LDH] enzyme activities. Fenugreek saponins reveal attractive properties and can be considered as capable candidates for potential purpose as therapeutic agents in biotechnological with bioprocess based technologies, mainly those related to the improvement of anti-diabetic, hepatoprotective and hypolipidemic drugs. [18]

Lipid profile

The effect of fenugreek on blood lipids, blood sugar, platelet aggregation, fibrinogen and fibrinolytic activity were assessed. Healthy individuals, patient of Coronary Artery Disease [CAD], and patients with Non-insulin Dependent Diabetes Mellitus [NiDDM], who either had CAD or were without CAD. Fenugreek given in a dose of 2.5g twice daily for 3 month to healthy individuals does not change the blood lipids and blood sugar [fasting and post prandial]. Though, administered in the same daily dose for some duration to CAD patients also with NiDDM, fenugreek significantly reduce the blood lipids without affecting the HDL-C while administered in the same daily dose to NiDDM patient [mild cases], fenugreek reduced the blood sugar. In severe NiDDM cases, the blood sugar was only slightly reduced; fenugreek did not affect platelet aggregation, fibrinolytic activity and fibrinogen. [19]

The hypocholesterolemic properties of ethanol extract from defatted fenugreek seeds were studied. Purification of the crude extracts by dialysis produced an isolated component with hemolytic characteristics. The dialysate wasal so found to include saponins shown by thin-layer chromatography. In two separate feeding trials, hypercholesterolaemic rats were supplied on 30 or 50 g ethanol extract/kg for a 4-week time. Reductions in plasma cholesterol levels ranged from 18 to 26%, and a tendency for lower concentrations of liver cholesterol was examined. The ethanol extract from fenugreek seeds contained hypocholesterolemic components that look to be, saponins that interact with bile salts in the digestive tract. The focus on the contribution of an ethanol [EtOH] extracts obtained from ground fenugreek seeds in reducing cholesterol levels in hypercholesterolemic rats. Hence, fenugreek contains biologically-active components which do not directly, interact with cholesterol. [20, 21]

Rats were fed with mucilage at a dose of 4 mg/100 g body weight per day for 8 weeks, and changes in the levels of total cholesterol and triacylglycerols in serum, liver and aorta were

analysed. A greater lipid-lowering effect was shown by mannans like Glucomannan and galactomannan than arabinogalactan. The hypolipidemic effect of this mucilage appears to be due to a decrease in the synthesis and secretion of VLDL by hepatocytes. A reduction in production of VLDL can be due to a reduction in the synthesis of apoB as well as lipids associated with VLDL. [22] Polyphenols present in fenugreek seeds play a significant role in mitigating lipid abnormalities and maintaining collagen content and properties during alcohol-induced liver damage. Besides the prevention of collagen cross linking, the benefits of fenugreek might be related to anti-inflammatory activity and effects on IL-6, TNF- α , and enzyme systems responsible for collagen synthesis and degradation. [23] The impact of a novel fibre mix of fenugreek seed powder, guar gum and wheat bran [Fibernat] on LDL oxidation was evaluated, Fibernat administration thus prevented the oxidative modification of LDL; the LDL + VLDL fraction also displayed a resistance to oxidative modification. Plasma antioxidant status with respect to GSH was enhanced. In general, these studies imply that Fibernat intake could reduce the risk for atherosclerosis and other disorders of lipid metabolism in rats. [24]

Immunomodulatory and anti-toxic activity

Trigonella foenum graecum showed stimulatory effects on macrophages. Phagocytosis of microorganisms by macrophages of against *Trigonella foenum graecum* has immune stimulatory. [25]

Cypermethrin [CM] is an important type II pyrethroid pesticide used widely in pest control and is to cause hepatic and renal toxicity. Oxidative stress and lipid peroxidation [LPO] have been involved in the toxicology of pyrethroids. The protective power of aqueous extract of germinated fenugreek seeds in CM-induced hepatic and renal toxicity were studied. CM treatment has caused increases thiobarbituric acid reactive substances [TBARS], depletion in glutathione [GSH] and decrease in the activities of superoxide dismutase [SOD], catalase [CAT], glutathione peroxidase [GPx] and glutathione-S-transferase [GST] in the liver and kidneys. The activities of tissue antioxidants SOD, CAT, GPx and GST, decreased significantly [$p < .05$] in CM-treated rats while the CM and germinated fenugreek seed extract treated rats displayed a notable increase [$p < .05$] in all the tissue antioxidants when compared with the CM-treated rats. Aqueous extract of fenugreek was reported to ameliorate additive urotoxicity of buthionine, sulfoximine and cyclophosphamide by restoring the anti-oxidant status and reversing the cyclophosphamide-induced apoptosis in free radical-mediated LPO in the urinary bladder. [26] Fenugreek in the diet showed a marked reduction in diabetes-induced polydipsia, hyperglycemia, polyuria, urine sugar, renal hypertrophy and glomerular filtration rate. [27] Numerous useful physiological properties and strong antioxidant potential and its widespread availability, the nutraceutical value of fenugreek makes it an ideal candidate to protect against pesticide-induced toxicity and the inhibition of fenvalerate toxicity in vitro by fenugreek seeds in blood samples of healthy human volunteers [22-26 years]. [28]

Anti-cataract Activity

The anti-cataract potential of *Trigonella foenum-graecum* L seeds [fenugreek] in selenite-induced in vitro and in vivo cataract was evaluated. In vitro enucleated rat lenses were maintained in organ culture containing Dulbecco's modified Eagles medium [DMEM] alone or in addition with 100 μ M selenite and served as standard and control groups, respectively. For the test group, the medium was supplemented with selenite and *Trigonella foenum-graecum* aqueous extract. The lenses were incubated for 24 h at 37°C. After incubation, the lenses were processed for the estimation of reduced glutathione [GSH], lipid peroxidation product [malondialdehyde], and the antioxidant enzymes. A fall in GSH and a rise in malondialdehyde

levels were seen in control as compared to standard lenses. Trigonella foenum-graecum protects against the experimental cataract by virtue of its anti-oxidant properties. GSH level in the normal group was found to be $1.19 \pm 0.24 \mu\text{mol/g}$. There was a significant reduction, in GSH level, in the presence of selenite stress, and the level was found to be $0.11 \pm 0.05 \mu\text{mol/g}$ of lens in the control group. Fenugreek supplemented group significantly restored the GSH level in a dose-dependent manner. It was observed that, in the presence of selenite stress, antioxidant enzymes were reduced as compared with the average group. [29]

Anti-oxidant activity

Ethanollic extract of fenugreek seeds was shown highest anti-oxidant activity [% DPPH scavenging activity]. The anti-oxidant activity could be associated with the polyphenolic components present in the extract. [30]

Fenugreek seeds could modulate the activity of glyoxalase system SOD, catalase and GST. Fenugreek seeds seem to have a dual effect on the tissues as is visible from the enhanced anti-oxidant state at lower doses and prooxidant effect at higher doses. Anti-diabetic and hypoglycemic properties could be connected, to its ability to increase the activity of gly I and anti-oxidant potential. [31] An aqueous extract of; fenugreek seeds were examined for its anti-radical and in vitro anti-oxidant activity in different model systems. The radical activity could be correlated with the polyphenolic compound present in the extract, and the result of this process provides some important factors responsible for antioxidant potentials of fenugreek seeds. [32, 33]

The functional food quality of fenugreek seeds were assessed by determining the lipid peroxidation [LPO] and cyclooxygenase enzyme [COX] inhibitory activities in hexane, ethyl acetate, methanolic and water extracts using MTT, LPO, COX-1 and COX-2 enzyme inhibitory assays. The extracts inhibited LPO by 55–95%, COX-1 by 6–87% and COX-2 by 36–70%, respectively, at 250 g/ml. Bioassay-guided purification of these extracts yielded triglycerides, fatty acids, saccharides and flavonoid-C glycosides. The antioxidant and anti-inflammatory activities exhibited by the isolated compounds from fenugreek seeds support its anecdotal health applications. [34]

Other medicinal uses

The fenugreek seeds are important in keeping a healthy digestive system; thus the continue, and daily use of this spice may increase the digestibility of eaten food, which may further promote good absorbing capacity of food constituents in blood for best metabolic use in the body cells. Fenugreek seeds have restorative and nutritive properties.

The daily use of fenugreek seeds as the dietary supplement is safe. It has good beneficial effects to increase blood Hg by natural means. This might extra help avoid and cure anemia and have good healthy life for longer duration in females of child bearing age. [35] Modulatory effect of fenugreek seeds on 1, 2- dimethylhydrazine-induced hepatic oxidative stress during colon carcinogenesis was studied in male wistar rats. [36]

It was identified that in pulverized seed of fenugreek in the diet of DMH treated rats reduced the colon incidence up to 16.6%. Acetyl cholinesterase inhibitors [AChEI] give a significant relief to some of the clinical signs of the disease. They studied to regulate the extract of fenugreek with trigonelline by HPTLC method and determine the in vitro AChE inhibitory activity of fenugreek and its components using galantamine as a reference. From this, they

showed that the fractions and trigonelline fenugreek seed has a potential AChE inhibitory activity and could be used for the cure of Alzheimer's disease. [37]

Conclusion

The present review highlights the importance of the various pharmacological activities of *Trigonella foenum-graecum*. A lot of studies were done for this plant. However, this study briefly discusses novel treatment activities. Thus anti-diabetic's effect, anti-toxic potential, the anticancer effect of this plant is an important pharmacological activity, which should be more focused in the future.

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