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Pharmacological and Therapeutic Properties of Fenugreek (*Trigonella foenum-graecum*) Seed: A Review

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ABSTRACT

Fenugreek, scientifically known as *Trigonella foenum-graecum*, is a versatile annual leguminous plant belonging to the Fabaceae family. It is cultivated worldwide and serves numerous purposes as a spice, herb, food, and medicine. Fenugreek is resilient and can thrive in various environments, including those with drought conditions. The plant is abundant in active constituents such as saponins, flavonoids, alkaloids, and steroids. Additionally, it is an excellent source of dietary fiber, protein, linoleic acid, linolenic acid, and vitamins A, B1, B2, and C. Fenugreek has a rich history in traditional medicine, particularly in Ayurveda, Unani, and Tibetan medicine. Studies have shown that it possesses antimicrobial, antioxidant, antidiabetic, antihyperlipidemic, antiobesity, anticancer, anti-inflammatory, carminative, aphrodisiac, and emollient properties. Moreover, its seed polysaccharide content has made it useful in the food industry as a stabilizer, adhesive, and emulsifying agent. This article provides an overview of the history, cultivation, nutritional components, nutraceutical role, safety, and toxicological properties of fenugreek. Its main aim is to summarize the benefits of this "golden seed" and its associated aspects.

Keywords: Antidiabetic, Dietary Fiber, Fenugreek, Nutraceutical, Traditional, Therapeutic.

INTRODUCTION

Fenugreek (*Trigonella foenum-graecum*) is an annual dicotyledonous aromatic leguminous plant which is self-pollinating and belongs to the sub-family Papilionaceae, family Fabaceae [1-4] and is packed with nutraceutical properties. It is used for multiple purpose, and holds an important place amongst seed spices, condiments, leafy vegetables and medicine [5]. It is known by different names across the globe, in India it is commonly known as 'Methi', in France 'fenugrec/Trigonelle', in Spain 'Alholva/Fenogreco', in Japan 'koroha', in Italy 'fieno greco' [6]. The different identities and other related information of fenugreek is provided in Table 1. The literal meaning of latin word "foenum-graecum" is 'Greek hay' which indicates its role as a forage crop in past and the Greek word 'Trigonella' means 'little triangle' depicting the triangular shape of flower [7, 8]. Fenugreek plant produces green trifoliate leaves, white to yellow color flower and can attain a height of 1-2 feet, the pods are generally 15 cm in length and can carry 10-20 seeds. Seeds are golden yellow in colour with an average height, width and thickness of 4.01-4.19 mm, 2.35-2.60 mm and 2.40-2.66 mm, respectively [9]. Among the various part of fenugreek plant, seeds are the most well studied part and are a good source of proteins, fats, minerals and dietary fats. It is annually grown in India, Turkey, Canada, Egypt, Ethopia, Northern Iran, Northern Africa and in Western Asia. Fenugreek is a versatile plant that can adapt to different growing environments, climatic conditions, and geographical locations, making it widely distributed. India is the largest producer of fenugreek globally, with a total production of 241,183 tons under an area of 156,156 hectares in 2020-21 and 248,203 tons covering an area of 167,468 hectares in 2021-22 [11]. Based on its morphological characteristics, the growing period of fenugreek is classified into five groups: very early (80-85 days), early (80-90 days), mid-early late (90-100/115 days), and very late (120-140 days) [12].

Fenugreek seeds are highly nutritious and contain numerous active components, making them an important nutraceutical plant. The leaves are a rich source of protein, minerals, and vitamin C, while the seeds are high in iron, phosphorus, lysine, and lipids. The whole seeds and dried plants are also used as insect and pest repellents for grain storage. Fenugreek seeds contain saponins, which are converted to sapogenins when they enter the gastrointestinal tract. Other phytochemicals found in fenugreek seeds include alkaloids, oils, galactomannan, mucilages, amino acids (such as methionine, valine, tryptophan, arginine, lysine, and threonine), minerals, and vitamins A, C, D, and B1 [13]. Fenugreek is a good source of dietary fiber, with 40-45% being insoluble and 20-25% being soluble mucilaginous fiber [14-16]. Additionally, fenugreek seeds contain 20-25% proteins [17,18], 6-5% fatty acids [19-23], and 2-5% steroidal saponins [24-28].

Table 1: Fenugreek worldwide identification

Preferred scientific name	***Trigonella foenum-graecum L***
Preferred common name	Fenugreek
International common names	
English	Common fenugreek, goat's horn, greek hay-seed
French	Fenugrec, sénegré
Spanish	Fenugreco
Hindi	Methi
Portuguese	Fenacho, fenogregq
Local common names	
Germany	Bockshornklee, griechischer schabzigerklee
Indonesia	Kelabet, klabet
Italy	Fieno Greco
Malaysia	Halba, kelabat, venthiam
Myanmar	Penantazi, venthiam
Maldives	Venthiam
Netherlands	Fenegriek
Sweden	Bockhornskloever
EPPO code	TRKFG (Trigonella foenum-graecum)

Source: [10]

Nutraceutical properties of fenugreek seed and its role in managing different diseases

Fenugreek is amongst one of the oldest recognized and documented medicinal plants and is believed to be originated in parts of Asia or in Mediterranean region [29,30]. Medicinal properties of fenugreek have been found in many religious scripture, ancient literature and travel records. It is extensively used worldwide as a spice, herb, food and medicine. Fenugreek seeds are traditionally used in Unani, Ayurvedic and Chinese medicines. The nutraceutical value of fenugreek is mainly due to three major chemical constituents, steroidal sapogenins, isoleucine and galactomannans [7,9], these three works synergistically to provide additional health benefits. Fenugreek seeds are rich in fiber, saponins, gum, alkaloids, flavonoids, iron, vitamin A, B and C [31]. Fenugreek is used in treating several disease beacause of its diverse chemical constituents that render it antimicrobial, antioxidant, antidiabetic, antihyperlipidemic, antiobesity, anticancer, anti-inflammatory, carminative, aphrodisiac, emollient properties [32]. It is also used as a lactation stimulant in India [33]. Table 2 depicts the pharmacological benefits and the underlying mechanism behind various nutraceutical properties of fenugreek seed.

Anti-diabetic effect

At present, there are many commercial synthetic drugs available in the market for managing carbohydrate metabolism disorders like diabetes, but these drugs often have undesirable side effects and can be expensive. As a result, it is important to explore natural alternatives for managing metabolic diseases like diabetes. Research has been conducted on the potential benefits of fenugreek seeds in managing diabetes. The high soluble fiber content in fenugreek seeds slows down the digestion and absorption of carbohydrates [56], which can help reduce blood glucose levels. In one study, diabetic patients were given fenugreek seed powder as a supplement for three months [57], and their fasting and post prandial blood sugar levels decreased, indicating that fenugreek can be an effective natural supplement for managing blood glucose levels. Another study investigated [58] the effects of fenugreek seed powder solution in diabetic patients and found that it improved dyslipidemia by reducing total cholesterol, triglycerides, and low-density lipoproteins, while increasing high density lipoproteins levels. Fenugreek juice was consumed by 20 borderline diabetic patients for a period of one month and their PPBS level were taken before and after one month and a considerable decrease in PPBS was observed. Similarly, investigation [59] showed that powdered, germinated, and defatted fenugreek seed consumption reduced PPBS and fructosamine levels.

Cardioprotective & hypolipidemic effect

Cardiovascular disease is linked to oxidative stress and the accumulation of reactive oxygen species (ROS), which can cause inflammation in the body. This can ultimately result in cellular damage, cardiac fibroblast proliferation, cellular apoptosis, and cell death [60]. However, fenugreek seed extract has been found to decrease TBARS levels and increase total thiol concentration and catalase activity, ultimately reducing inflammation and oxidative stress in the heart [61]. Furthermore, research has shown that fenugreek can improve the antioxidant status of the heart in hypercholesterolemic rats, leading to decreased inflammation and oxidative stress [61]. Fenugreek seed powder has also been found to decrease total cholesterol, triglycerides, and low-density lipoprotein levels, while increasing high-density lipoprotein levels in newly diagnosed type II diabetic patients [58]. In diabetic rats, the diosgenin component of fenugreek seeds has been found to reduce intracellular calcium concentration, leading to a decrease in tissue fatty acids and an anti-hyperlipidemic effect [62]. Finally, feeding fenugreek seeds to rats exposed to gasoline fumes has been found to alleviate biochemical and histological changes in alveolar tissue, ultimately reducing lung inflammation [63].

Anti-cancer and Anti-inflammatory effect

Numerous medicinal herbs and plants contain active components that can play a protective role in cancer treatment. In particular, fenugreek seed extract has been found to inhibit the proliferation of more than half of the human breast cancer MCF-7 cell line at a concentration of 400 µg/ml without necrosis or apoptosis, according to research by Al-Timimi [44]. Diosgenin, a steroidal saponin found in fenugreek seeds with a structure similar to estrogen, has been shown to have pro-apoptotic and anticancer activity both in vitro and in vivo by multiple researchers [64]. Fenugreek ethanolic extract has been found to inhibit cell viability and tube formation while inducing cell cytotoxicity in chick chorioallantoic membrane, and fenugreek seed oil has been found to decrease cancerous cell viability [56,65]. Additionally, methanolic fenugreek seed extract has been found to decrease metastasis and proliferation in MCF-7 cancer cells [66]. However, the exact anticancer mechanism of fenugreek is still unclear and requires further research to determine its specific working action.

Fenugreek seed contains saponins, flavonoids, and alkaloids that exhibit anti-inflammatory and antioxidant activity by reducing cytokines, which are pro-inflammatory compounds that can lead to inflammation and diseases. Research has shown that an aqueous ethanolic extract of fenugreek seed administered at a level of 200 mg/kg bw to carrageenan-induced oedemetic mice resulted in a significant reduction in inflammation [67]. In a study on albino rats with complete Freund's adjuvant (CFA)-induced arthritis, an ethanolic extract of fenugreek given at a dose of 200 and 400 mg/kg for 22 days

resulted in decreased paw odema, interleukin (IL)-1α, IL-1β, IL-2, IL-6, tumor necrosis factor-α (TNF-α) levels, while increasing red blood cells, haemoglobin, superoxide dismutase and glutathione synthetase levels [68]. Fenugreek can also be used as a natural alternative for minor pain and inflammation instead of synthetic drugs [69]. Gas liquid chromatography analysis of petroleum ether extract of fenugreek seed showed that it contained 12.51% linolenic acid, 33.61% oleic acid, and 40.37% linolenic acid [70]. When given at a dose of 0.5 ml/kg to rats, this extract resulted in a 37% and 85% reduction in inflammation of the paw in carrageenan and formaldehyde-induced paw edema, respectively.

Antioxidant, Gastroprotective and Antibacterial effect

Metabolic reactions in body produces ROS such as hydroxyl radical, superoxide, peroxides, singlet oxygen and alpha oxygen [71]. Study [72] on effect of ethanolic fenugreek seed extract on rats with complete freund's adjuvant (CFA) induced rheumatoid arthritis showed that it has a protective effect against inflammation. Accumulation of these ROS is the underlying cause of initiation of various metabolic diseases [73]. Antioxidants reduces the oxidative stress by scavenging the free radicals thus, preventing the body from their adverse effects [74]. Fenugreek seeds ae packed with polyphenolic compounds that imparts beneficial effects like antioxidant activity, anti-inflammatory property, hyperlipidemic effect, etc. Twenty-three chemical compounds were detected in fenugreek seed oil [75], amongst which the major components were linoleic acid, palmitic acid, linoleic acid methyl ester, pine and 4-pentyl-1-(4-propylcyclohexyl)-1-cyclohexene. The presence of these compounds imparted it a strong free radical scavenging effect.

Rats with ethanol induced gastric ulcer were given aqueous fenugreek seed extract for 21 days and an increase in activity of antioxidant enzyme like superoxide dismutase, catalase and glutathione peroxidase was observed. Histopathological examination showed that antioxidant and anti-inflammatory property of fenugreek extract protected against gastric damage by ethanol [76]. Similar observations showed [77] that fenugreek seed extract protects gastric mucosa, decreases ulcer lesions and reduces the oxidative stress. Study on Indomethacin induced gastric ulcer models revealed that treatment of fenugreek seed extract significantly decreases the ulcer index, volume of gastric juice and acidity [78].

Misuse and over exploitation of conventional antibiotics has led to the need of development of novel antibacterial medication. Plants sources with active components has proven to be an effective source for extracting compounds with antibacterial property. Ethanolic and aqueous extract of fenugreek seed showed prominent effect as antibacterial agent on many pathogenic bacterial strains [44]. Similarly, [79] it was found that aqueous and methanolic extract of fenugreek seeds shows inhibitory effect against fungal (*Aspergillus flavus, Aspergillus niger* and *Trichoderma viride*) and bacterial (*Escherichia coli, Serratia marcescens* and *Bacillus cereus*) species.

Table 2: Health and pharmacological benefits of fenugreek

Medicinal properties reported	Component Involved	Mechanism	References
Antidiabetic	Dietary fiber (Galactomannan) Flavone c-glycosides Trigonelline	Delays the absorption of carbohydrates in stomach , inhibits digestive enzymes, increases bowel motion thus results in lowering blood sugar levels Stimulates insulin signalling system.	[34-38]
Anticancer	Alkaloids, Saponins	Blocks cancer progression by acting on p53 expression and indirectly controls telomere length Stops cancer cells from multiplying	[36,39,40]
Antioxidant	Phenols, Flavonoids	Inhibits lipid peroxidation in red blood cells (RBC)	[36,41]
Antiobesity	Soluble dietary fiber (4-hydroxyisoleucine)	Lowers plasma triglycerides flushes away carbs from body before they reach the bloodstream	[36, 42, 43]
Antifungal & antibacterial	Hydroalcholic compounds (polyphenols & flavonoids)	Inhibit growth of bacteria	[36,44,45]
Anti-Inflammatory	Flavone c-glycoside Saponins	Inhibit lipid peroxidation and cyclooxygenase (COX-1&-2) activity Inhibitory effect on prostaglandins and bradykinins	[46, 47]
Anti-sterility and anti-androgenic effects	Diosgenin	Improves sperm count, motility and viability	[48,49]
Gastro-protective effect	Sulfhydryl	Protects mucosa against lesions and maintains mucosal integrity Acts as an antioxidant	[50,51]
Antinociceptive	Alkaloids	Inhibition of cyclooxygenase and lipoxygenase	[47, 52, 53]
Cardioprotective effect	Dietary fiber Flavonoids Saponins (Diosgenin)	Prevent irregular blood clotting by reducing platelet aggregation. Decreases inflammation	[49, 54, 55]

Toxicity and safety of fenugreek

Fenugreek is approved by FDA [80] as a GRAS (generally recognized as safe) ingredient. Traditional medicine uses herbs and plant-based products for different conditions and are widely accepted due to their fewer side effects and toxicity but there can be some adverse side effects when these are consumed excessively. Wide-ranging dosages and differing preparations have been used in studies, so there is no single recommended dose. Some of the side effects include dizziness, flatulence and transient diarrhoea [81]. Diosgenin and yamogenin are two major steroidal sapogenins present in fenugreek that are known to exhibit teratogenicity and antifertility activity. During pregnancy, consumption of fenugreek seeds is not safe as it led to abortion and neurological problems in offspring [82]. Flavonoids can easily cross placenta, at higher doses, it leads to production of free radical that damages DNA and this poses risk to foetus [83]. Excess consumption of fenugreek by a normal person can lead to hypoglycaemia. Lactone orthodihydroxy cinnamic acid and scopoletin are coumarin compounds found in fenugreek seeds that hinders platelet aggregation and increases risk of bleeding [84]. Thus, it is advised that before taking any herbal remedy, one should learn about all the harmful effects of overconsumption and should always consume as per the recommended values. Table 3 depicts various studies on toxicological effects of fenugreek.

Table 3: Studies on toxicological effects of fenugreek

Dose of test compound	Duration of test	Route	Results	Ref
600 mg/kg bw/day fenugreek seed extract to male mouse	28 days	Oral	Degenerative changes in testis histoarchitecture Adverse effect on germ cell dynamics and oxidative status in testis	[85]
Lyophilized aqueous extract of germinated fenugreek at a dosses of 500, 800 and 1000 mg/kg /day to swiss albino rats	Gestation day 0 to postnatal day 0	Oral gavage	Decreased fertility Spontaneous abortion Neurobehavioral disorder in offsprings	[82]
5000 mg/kg of standardized fenugreek seed extract to swiss albino mice	28 days	Oral	Intake of 4350 mg/kg showed median lethal dose (LD_{50}) and 250 mg/kg showed NOAEL	[86]
305 and 610 mg/ kg bw/day fenugreek capsule (commercially available)	90 days	Oral gavage	Teratogenic, foetotoxic, reproductive changes and the abnormal shapes of the sperms	[87]
Hydroalcoholic extract of fenugreek seed at a level of 50, 100 and 200 mg/kg/2days to female mouse	20 days	Intra peritoneal Injection	Decreased LH and FSH levels Decreased folliculogenesis	[88]
Lyophilized aqueous extract from fenugreek seeds at doses of 500 and 1000 mg/kg/day to mated female mice	Gestation day 0 to postnatal day 0	Oral gavage	Altered brain development, intrauterine growth retardation and retarded postnatal growth of pups	[89]
Fenugreek decoction in three dose of 0.8g/kg, 1.6 g/kg and 3.2 g/kg to female rats	Gestation period of 20 days	Intra peritoneal injection	Increased fetal mortality rate	[90]
30% of fenugreek as diet to male and female rabbits	3 months	Oral	Reduced male testis weight (~25%) Reduced sperm concertation (~43%) Reduced testosterone level (65.8%) Smaller fetal and placenta size Decrease in estrogen and progesterone levels	[91]
100mg/day/rat steroidal extract of fenugreek to female rats	15 days	Oral	Reduction in weight of ovary and uterus Reduced acid and alkaline phosphatase activity in ovary and uterus	[92]

CONCLUSION

For centuries, natural plant-based remedies have been used in traditional medicines like Unani, Ayurvedic and Chinese medicine to treat various diseases. Fenugreek is a highly beneficial herb with diverse chemical constituents such as alkaloids, flavonoids, saponins, steroids, and dietary fibers, linoleic and linolenic acids, and proteins. These compounds give fenugreek its antimicrobial, antioxidant, antidiabetic, antihyperlipidemic, anti-obesity, anticancer, anti-inflammatory, carminative, aphrodisiac, and emollient properties. Many studies have shown the effectiveness of fenugreek in treating various diseases, as highlighted in this review. However, more research is needed to identify the specific components responsible for different side effects of fenugreek when consumed in excess. Overall, fenugreek has the potential to be utilized in various industries for health benefits.

Conflict of interest

The authors declare that they have no conflict of interest.

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