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Nutritional and therapeutic properties of fenugreek (*Trigonella foenum-graecum*): a review

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ABSTRACT

Current lifestyle, eating habits, stress, environmental factors and intensive use of synthetic chemicals in food processing and agriculture have radically increased the progression of several human diseases. Globally, researchers have been looking for natural therapeutic substances that can be used to treat or delay the onset of these lifestyle-related disorders. Numerous types of medicinal plants have shown the potential to be frequently used in the therapeutics due to the presence of several bioactive compounds. Among these, fenugreek is an important herb which has been recognized as an imperative medicinal plant by various scientists around the world. This herb has been widely reported as beneficial against numerous diseases such as cancer, hypercholesterolemia, diabetes and inflammation. Due to its medicinal value, the extracts/powders from different parts of fenugreek have been effectively utilized in food and pharmaceutical industries. Accordingly, the present review is an attempt to highlight the important nutritional benefits and curative applications of fenugreek as an effectual therapeutic agent against different diseases.

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Introduction

The importance of including medicinal herbs in the dietary choices is well-known for maintaining the health lifestyle and preventing several types of diet-related ailments including diabetes, cancer, hypertension, inflammation and cardiovascular diseases.^[1] Despite the astonishing advancements in the medicine and combinatorial drug development, use of herbal plants for treating or preventing various diseases is being enormously practiced due to their vast nutraceutical properties and safety aspects. Numerous crop plants are nutritious, functional, medicinal and nutraceutical in nature. Fenugreek is known as one of the plants having all these traits and an eminent spice crop used in human diets.^[2]

Fenugreek (*Trigonella foenum-graecum* L.) belongs to the *Fabaceae* family and has been used as an important spice since ancient times.^[3] About 70 to 97 different species of fenugreek are being cultivated around the world. As it has origin from Greece, the species name *foenum-graecum* means ‘Greek hay’.^[4] Although it is a familiar spice that has been added in the human foods, literature also provide us the use of this natural tonic to cure several types of lifestyle-related disorders such as cardiovascular diseases, hypercholesterolemia, hyperglycemia, cancer, liver ailments and sexual disorders such as testosterone-deficiency syndrome.^[1,5] Fenugreek is also considered as a rich source of dietary fibre and other

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Table 1. Nutritional/health impacts of fenugreek components.

Nutritional components	Health impacts
4- hydroxyisoleucine (amino acid)	Insulin stimulating activity
Fiber (soluble dietary fiber, galactomannans, non-starch polysaccharides)	Binding of food toxins, protection of colon mucus membrane, promoting insulin secretion, water retention in the intestine, controlling glucose absorption
Phenolic acids	Antioxidant properties
Micronutrients (Vitamins and minerals)	Regulatory functions
Flavonoids	Antioxidant properties
Protodioscin	Inhibition of leukemic cells
Diosgenin	Hepatoprotective, anti-carcinogenic

important nutrients needed for proper growth and development. Studies have also affirmed the nutraceutical and physiological properties of fenugreek which support the potential applications of fenugreek in developing numerous functional food products and pharmaceutical products.^[6]

As fenugreek is rich in several phytochemicals, alkaloids, carbohydrates, steroidal saponins, amino acids and minerals are present in fenugreek, it can be used for nutritional, nutraceutical, medicinal and therapeutic purposes.^[3] Fenugreek has been extensively used as a flavour enhancer in several traditional cuisines. Additionally, the medicinal properties of fenugreek such as anticarcinogenic, antidiabetic, antioxidant, hypocholesterolemic, anti-lithogenic antimicrobial and immunological properties, make it an important compound to be used in food and pharmaceutical industries.^[7] In addition to the medicinal properties of fenugreek, it has also been used as an emulsifier and stabilizer in different types of food products. Moreover, use of fenugreek extracts or powders has also been reported for developing bakery and extruded products.^[8]

Nutritional value of fenugreek

Fenugreek has a vast diversity of nutrients and bioactive compounds which are required for improving the health and functionality of biological systems. The fenugreek seeds have 58% carbohydrates, 23-26% proteins, 0.9% fats and 25% fibre. Similarly, fenugreek leaves have 6%, 4.4%, 1.1% carbohydrates, proteins and fibre respectively.^[8] Furthermore, fenugreek also contains different types of minerals such as potassium (603 mg/100 g), magnesium (42 mg/100 g), calcium (75 mg/100 g), zinc (2.4 mg/100 g), manganese and copper (0.9 mg/100 g) and iron (25.8 mg/100 g). Vitamin C (220 mg/100 g) and β carotene (19 mg/100 g) are also considered as the important components of fenugreek.^[8,9]

Fenugreek is also a rich source of several important amino acids such as aspartic acid, glutamic acid, leucine, tyrosine and phenylalanine. Additionally, it contains minute quantities of sulfur-containing amino acids (cysteine and methionine) having significant physiological roles in body. The most abundantly present free amino acid in fenugreek is (2S, 3 R, 4S)-4-hydroxyisoleusine. About 80% of amino acid content of dry fenugreek seeds consists of the non-protein amino acid 4-hydroxyisoleusine and during the phase of growth, this amino acid proliferates rapidly. Studies have revealed that the proteins present in the fenugreek are of better quality as compared to the other plant proteins. In an investigation, Feyzi and his coworkers compared the quality of fenugreek proteins with soy protein isolate and affirmed that fenugreek seeds contain higher protein contents with better amino acid profile as compared to soy protein isolate.^[10] Additionally, fenugreek proteins were rich in aspartic acid and glutamic acid. Results also stated that fenugreek proteins have higher denaturation temperature, foaming properties, solubility and stability as compared to soy proteins and therefore can be employed as an effective protein source in various functional foods. Moreover, sotolone, an important functional phytochemical used as seasoning flavor, is a prompting ingredient of fenugreek.^[11]

Fenugreek contains significant quantities of alkaloids (trigonella, trigocoumarin, nicotinic acid, trimethyl coumarin). It also comprises other important, valuable compounds like flavonoids and polyphenols. In the alcoholic extracts of the fenugreek plant, extensive variety of flavonoids, such as quercetin, luteolin, vitexin, and 7, 4-dimethoxy flavanones, is present. Some other groups have

reported alike results of the existence of aglycones, kaempferol, quercetin, tricetin, and naringenin.^[12] The compounds were sequestered from the specific parts of fenugreek plant and also from the excerpts and hydro lysates of stems, leaves and flowers. The phytochemical examination of fenugreek exposed that the maximum of flavonoids are existent as glycosides which are complex due to the conjugation with carbohydrates by C-glycosidic and O-glycosidic bond. Quercetin-3-O-rhamnoside (quercitrin), vitexin-7-O-glucoside (afroside), and apigenin-6-C-glucoside (isovitexin) are rare examples of flavonol glycosides existing in fenugreek.^[13] Apigenin-6-C-glucoside (isovitexin) and apigenin-8-C-glucoside (vitexin) were sequestered by fenugreek seeds. The occurrence of isoflavonoid phytoalexins aglycones, such as medicarpin and maackiain, in this herb has also been reported. These are known as 'induced isoflavonoids' which can be produced due to some external factors such as microbial activities.^[11] A generalized discussion about the nutritional impacts of fenugreek has been provided in Table 1.

Bio-availability of active compounds of fenugreek

As fenugreek is rich various functional ingredients, therefore, the bio-availability of these components is very important. In rats, the bio-availability of furastanol glycoside secluded by the extract of fenugreek seed was tested. Researchers considered the pharmacokinetics, tissue delivery, and elimination after oral dose of 200 mg/kg of furastanol glycoside extract. Researchers distinguished that after only one administration, the zone under the curve was 0.177 g/mL h; supreme concentration time period (T_{max}) was 72 h and half-life (t_{1/2}) was 40.10 h. The extract was engrossed gradually down the intestine and took moderately gentle distribution. This glycoside was also noticed in tissues of lungs and brain, representing its channel via blood-brain barricade.^[14]

In another study, it was stated that pharmacokinetics and tissue delivery of flavonol glycoside, vicenin-1. Researchers testified, later one oral administration of 60 mg/kg of vicenin-1, the C_{max} was 7.039 g/mL, zone under the curve was 0.044 g/mL hour, and t_{1/2} was 11.60 h. The supply of vicenin-1 in various rat tissues, the flavonol glycoside was perceived in greater amount in the lungs and liver and much little concentrations in the adrenal glands, brain, and kidneys.^[15] Studies also provided the evidence that almost 40% of the original dosage of vicenin-2 was quickly absorbed in the small intestine.^[16] The glycoside has many beneficial effects in living organisms. The bioavailability of this compound is very important to play the role as antioxidant as well as anti-inflammatory in living organisms.

Therapeutic effects of fenugreek

Role in controlling rheumatoid arthritis

Rheumatoid arthritis is a joint disease in which chronic inflammation occurs, which is characterized by the injury of tissue and synovial proliferation. Elevated energy expenditures and pro-inflammatory cytokines such as interleukin (IL-6) and tumour necrosis factor-alpha (TNF- α) perform a major role to increase joint soreness and painfulness. In a study, to check the fenugreek mucilage role to prevent the arthritis in adjuvant tempted rats with arthritis. On the seventh, fourteenth and 21st day, the paw volume was measured. Rats were given anaesthesia, samples of blood and tissues were taken to examine the enzymes which cause inflammation such as cyclo-oxygenase, lipo-oxygenase; assessed the readings of cytokines such as inter leucine-6, TNF- α , arthritic ratio and rheumatoid aspect. At the 21st day of adjuvant arthritis, fenugreek mucilage at the dose level of 75 mg/kg showed the maximum results to stop the oedema in rats. These results were compared with the results of standard drug used against oedema 'indomethacin', and fenugreek showed the better effect against oedema. The actions of enzymes which induce inflammation and the amount of mediators were becoming less after the treatment with mucilage of fenugreek. The study of synovial fluid's function and structure, exhibits slight inflammation with usual synoviocytes (mesothelial cells), supplements of fenugreek were given to normalize the characters of these cells.^[17] The study concluded that fenugreek mucilage

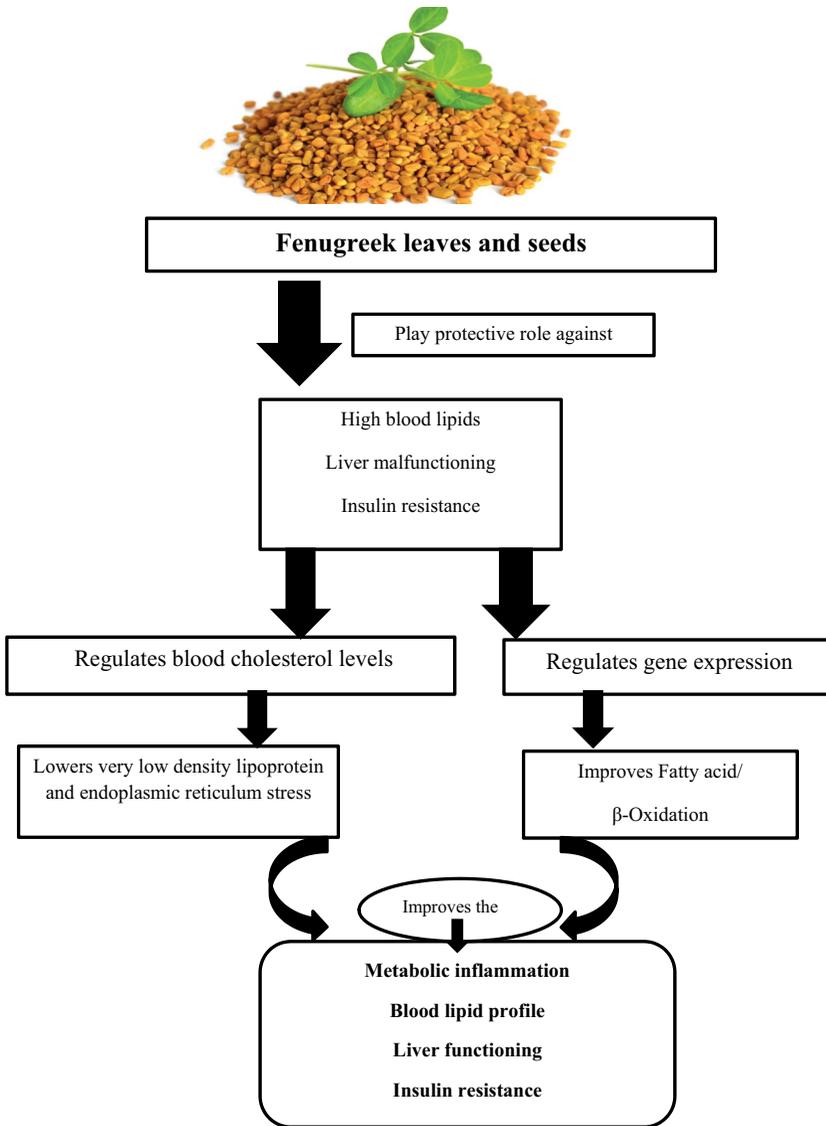


Figure 1. Role of fenugreek leaves and seeds against hyperlipidemia, liver malfunctioning and insulin resistance.^[18]

supplementation resulted in oedema inhibition by decreasing the activities of inflammatory enzymes due to its anti-arthritic potential.

Role to ameliorate VLDL overproduction and insulin resistance

Figure 1 shows the different part of fenugreek to improve the conditions of hyperlipidemia, liver malfunctioning and insulin resistance.^[18]

Hepatic SREBP-1 c inactivation by improved manifestation of Insig-1 and Insig-2

Hepatic steatosis and high level of lipids in blood induced through the lower levels of CREBH (cyclic adenosine monophosphate responsive element-binding protein H) caused via decreased hepatic

insulin-induced gene-2a manifestation, that results into hepatic lipogenesis and hyper activation of SREBP-1 c (sterol regulatory element-binding protein). Mouse models were used to check the effect of the seeds of fenugreek in lowering the amount of lipids in the blood. For 7 weeks, 2 different groups of mice were nurtured as a control food with vehicle or a food that consists of 2% powder of fenugreek seed in vehicle. Between these two groups, weight of body and intake of food were observed.

Appearance of insulin-induced gene-1 and insulin-induced gene-2b messenger RNAs, were induced after the consumption of fenugreek seed shown in the examination of the protein appearance of insulin-induced gene-1 and insulin-induced gene-2 and mRNA in the tissues of the liver of mouse. Protein levels of insulin-induced gene-1 and insulin-induced gene-2 were expressively up-regulated in fenugreek-fed mice. Analysis of the changes after the transcription step exposed that seed of fenugreek consumption reduced the stimulation of SREBP-1 c by the breakdown through proteolysis, shown by the fewer vigorous form of SREBP-1 c (N terminus of SREBP-1 c) in the hepatocyte which were treated.

The results were constant when insulin-induced gene-1 and insulin-induced gene-2 appearance increased which helps to keep SREBP-1 c on the endoplasmic reticulum also avoiding its movement from its place as well as triggering in Golgi apparatus. Final outcomes shows that by increasing the expression of insulin-induced gene-1 and insulin-induced gene-2 by intake of fenugreek in very low amount just 2%, it hold back the triggering of SREBP-1 c as well as hinder the lipid synthesis in the liver.⁽¹⁸⁾

Increased insulin sensitivity by upregulation of glucose transporters

For 7 weeks, CREBH-null mice were given a diet high in fat-containing seed of fenugreek 2% or vehicle as control, to consider the insulin sensitivity. Diet, which was high in fat lowers the glucose tolerance in CREBH-null rats were shown in a glucose tolerance test. By taking the fenugreek enhanced glucose tolerance, showed by the noteworthy reduction of plasma glucose levels at 30, 60, 90 and 120 minutes later the glucose injection of 2 g per kg through intraperitoneal injection. After 15 to 30 min of injection, levels of the glucose in the blood, touch the peak and then a drop happens after 30 min, in both vehicle-treated as well as fenugreek treated rats. The peripheral tissues and organs such as muscles, liver, adipose tissue of the fenugreek treated rats, uptake the blood glucose quickly, that's why the concentration of plasma glucose lowers much faster than the vehicle-treated rats. From the blood, the transportation of glucose into hepatocytes and adipocytes are carried out by the glucose transporters 2 (Glut-2) and glucose transporters 4 (Glut-4), respectively. After the intake of fenugreek, increased level of Glucose transporter-2 and Glucose transporter-4 in the liver and adipose tissue was shown by the analysis of messenger RNA appearance of Glucose transporter-2 and Glucose transporter-4. That's why the swift acceptance of glucose takes place in the rats fed with the fenugreek. Additional by inspecting the molecules which give signals to insulin in the liver, fenugreek action improved stimulation of receptors of insulin directed by the sturdier tyrosine phosphorylation signal upon insulin management.⁽¹⁸⁾

In the hepatocytes, increased insulin sensitivity is shown by the mice which were fed with fenugreek as phosphorylation at Akt Ser-473 was much resilient instead of control group. Trigonelline increased the insulin sensitivity in cells of McA, it was shown when *in vitro*, compared to the mock-treated cells, the pre-treating McA cells by trigonelline (50 M) for monitored by insulin usage (1 µg/ml) for 15 minutes also prompted resilient phosphorylation of the receptor of insulin and protein kinase B.^[18] So the seeds of fenugreek increase sensitivity of insulin through controlling the transporters of glucose and signalling transduction in the adipose tissue and liver. The fenugreek has great potential to control both type of diabetes, type 1 and type 2 as it improves the condition of insulin resistance. It also helps the liver to perform its function better.

Anticancer perspectives

One of the primary causes of death nowadays is cancer in the world. Serious side effects occur with generally used therapeutic medicines which only increase the life span of patient from few months or some years. Plant-based active components have shown their potential to be used as suitable and safe alternatives having significantly explored anticancer effects.^[19] In this regard, active ingredients of vegetables and fruits are being utilized to prevent the chances of cancer.^[20] Efforts are ongoing to use the other approaches and ideas which can be effective in the prevention of cancer. In these attempts, studies are available in which animals and cell lines were used as the investigational models of cancer proved the effect of seeds of fenugreek against cancer.^[21]

It was revealed that a compound protodioscin derived from fenugreek exhibits an effect to inhibit the growth against HL60 cells by prompting apoptotic modifications.^[22] In another study, extract from the seeds of fenugreek expressively stop the mammary hyperplasia induced by 7,12-dimethylbenz-anthracene and diminished the occurrence of it in rats. It is recommended that increased apoptosis after this edible herb consumption shows effect against breast cancer. The extract of the whole plant of fenugreek (*Trigonella foenum-graecum*) exhibit the cytotoxicity effect *in vitro* against the most of the different types of cancer cell lines in human like a neuroblastoma, IMR-32 and HT29 cancer cell line.^[23]

Researchers inspected the outcome of extracts of fenugreek (aqueous as well as ethanol) on the development of breast cancer cell line (an estrogen receptor), MCF-7 cells and stated as decreased mitochondrial membrane potential and inversion of phosphatidylserine by the early apoptotic changes and decreased cell viability after the consumption of ethanol extract. Further, when DNA splits into more pieces comprising many of approximately 180–200 base pair has also been witnessed.^[24]

In another study, the anti-cancer properties of fenugreek extract were investigated against breast, pancreatic and prostate cancers. The findings exposed that the applied extract was effective in inhibiting the growth of cancer cell lines of pancreatic and breast cancers however, no effect was shown on primary or immortalized prostate cells. The possible mechanism for anti-cancer properties of *Trigonella foenum graecum* extract was the induction of programmed cell death.^[25]

In Balb-C mice model of Ehrlich ascites carcinoma (EAC), extract of the seed of fenugreek shows the effect against the neoplastic. In mice when the alcohol extract of the fenugreek was administered before and after injection of EAC cell, there was the 70% reduction in tumour cell growth.^[26] The extract of fenugreek exhibits a noteworthy effect against the inflammation and improved macrophage cells count as well as peritoneal ooze cells count.^[23]

Fenugreek seed's ability to lessen hepatic oxidative stress and its antioxidant properties were applied in wistar rats with colon cancer which is induced by 1,2-dimethylhydrazine (DMH). 100% colon tumor was induced by treating them with DMH also showed the increased lipid peroxidation and in the liver-reduced glutathione amount, catalytic activity, glutathione peroxidase, glutathione transferase and sphincter of oddi dysfunction. The food consist of the seed powder of fenugreek abridged tumor in colon occurrence and lipid peroxidation in DMH-treated rats and in liver it also amplified activities of catalase, glutathione peroxidase, sphincter of oddi dysfunction and glutathione transferase.^[27]

Trigonella against gall-stone and gastric ulcer

In a study of Pandian and his colleagues, use of *Trigonella foenum* seed showed antiulcer effect. The consequence of the seeds of fenugreek is analogous to the medicine omeprazole that is used as the blocker of proton pump in the treatment of gastro-intestinal issues such as gastritis, gastroesophageal reflux disease, gastric ulceration and duodenum ulceration. In a rat model in which gastric ulcer was induced by ethanol, the gel portion and aqueous extract from the seeds of fenugreek have effects on mucosal glycoproteins and ant secretory action plays a protecting role against ulcer. Ethanol-induced mucosal injury and lipid peroxidation can be avoided by improving the prospective of the mucosa of

gastric against oxidation by the fenugreek seed consumption. Gastric lesion formation can be prevented by the soluble gel fraction of fenugreek and its results are better than omeprazole. Gastro protective and anti-secretory activities of fenugreek seeds are due to the presence of polysaccharides and flavonoids presence in the gel portion of fenugreek.^[28]

Many researchers have shown the anti lithogenic influence of the seeds of dietary fenugreek. By giving the high cholesterol diet (0.5%) (HCD) to mice for 10 weeks with or without the supplementation of (12%) fenugreek or (2%) onion, lithogenic disorders were induced. 75% reduction in cholesterol gallstones by fenugreek supplementation, 27% reduction by the onion supplementation and 76% reduction in cholesterol gallstone was investigated when the combination of both fenugreek and onion were given. Showing highest anti lithogenic effect of *Trigonella foenum* only, and the onion does not have any influence to increase the anti lithogenic effect. Thus, in serum, bile and liver the cholesterol/phospholipid ratio was decreased dramatically. Fenugreek reversed the changes in the activities of the enzymes of the liver (3-hydroxy-3-methylglutaryl coenzyme A reductase, cholesterol-7 α -hydroxylase and cholesterol-27-hydroxylase) which were prompted by taking the diet high in cholesterol.^[29] HCD caused the inflammation in the gall bladder and increase the addition of fat of liver, this inflammation and fat is considerably decreased by the fenugreek and by its mixture with onion.^[30]

Cholesterol gall-stone is controlled by some factors found in the bile known as pro and anti-crystallizing factors. Rats were fed with diet high in cholesterol for 10 weeks, and the effect on the composition of bile with the fenugreek in diet was examined. Due to the supplementation of the fenugreek with HCD, increases the flow rate of bile, and cholesterol nucleation time, and decreases the cholesterol saturation index in bile, cholesterol, total as well as glycoprotein and lipid peroxides. It also has the increasing effect on total bile acid and biliary phospholipid, representing that useful anti lithogenic consequence of fenugreek in diet is because of control cholesterol crystallization which lowered the cholesterol amount of bile and inflection of the nucleating and anti-nucleating proteins.^[31]

As the seed of fenugreek is famous for its effect against the high cholesterol, its supplementation has a very positive role in the prevention and cure of cholesterol gallstone (CGS). In mice when for the 10 weeks the lithogenic diet having 0.5% cholesterol was given along with the seed powder of fenugreek, it decreases the occurrence of cholesterol gallstone.^[29] The anti lithogenic effect of *Trigonella foenum* is accredited to its lowering effect against the high cholesterol outcome as it considerably reduced the cholesterol in liver and serum when the animals were given the diet having high cholesterol.^[21] By the work of many researchers on the antiulcer and anti-cholesterol gallstone influence of fenugreek in the recent years, it is proved that active compounds like flavonoids in aqueous extract, gel and seed of fenugreek have positive effect in these diseases.

Fenugreek against neurological disorders

Neurological disorders such as neuropathic pain are one of the most prevalent conditions and empirical evidence suggests that inflammatory cytokines and microglial cells are critical factors contributing in the pathogenesis of neuropathic pain.^[32] Researchers have demonstrated the potential applications of medicinal plants for the treatment of neurological disorders using the animal models.^[32,33] In this regard, fenugreek has also been explored as an effective medicinal plant for the treatment of neurodegenerative diseases.

The bioactive compounds present in the fenugreek extracts have also shown the potential to reduce the risk of several neurological disorders. Several studies support the effectiveness of fenugreek compounds against various neurological diseases such as depression, Alzheimer disease and Parkinson disease etc. as illustrated in [Figure 2](#).^[34] For example, Khalil and his coworkers applied fenugreek saponins (0.05–2.0%) through diet on rats for 45 days and found that dietary administration of fenugreek saponins resulted in the inhibition of apoptosis and acetylcholinesterase (AChE) activity thus induced neuroprotective effects.^[35] Similarly, Bin-Hafeez and his group induced dietary administration of 5% fenugreek seed powder for 4 weeks to analyze the neuroprotective effects against

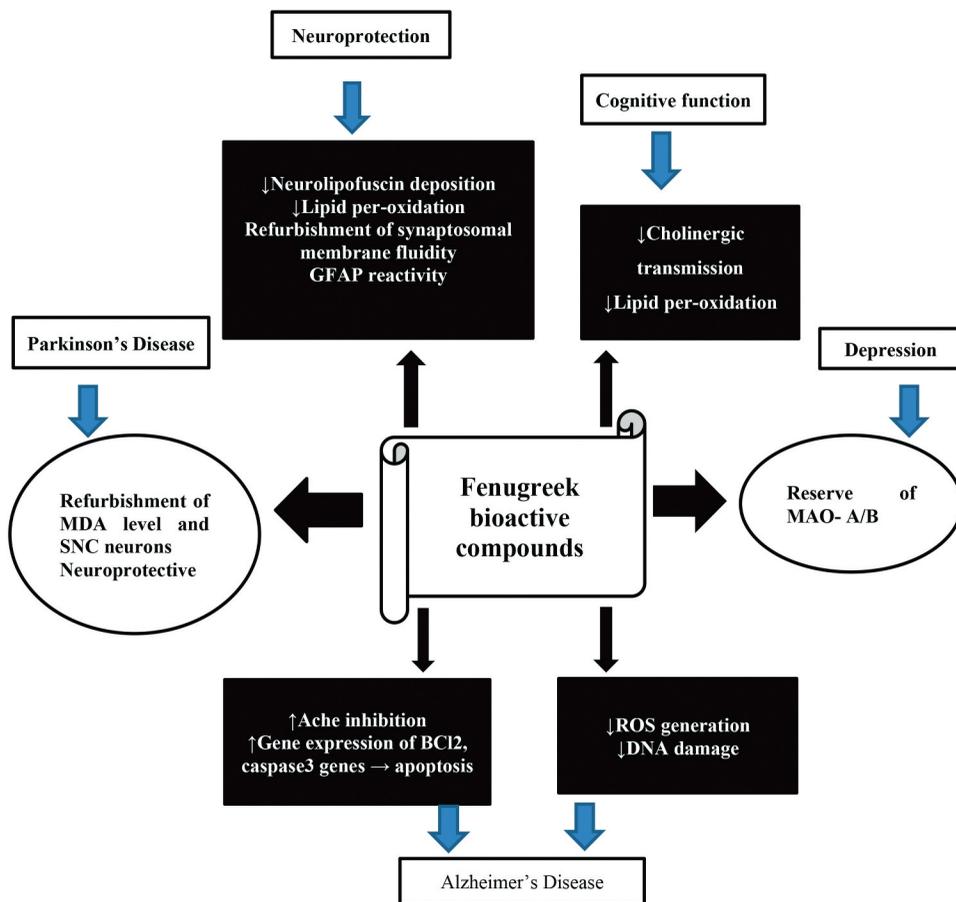


Figure 2. Fenugreek activity against neurological disorders.

aluminium chloride-induced neurotoxicity using mice model and reported significant neuroprotective effect of fenugreek seed powder.^[36]

In another study, Garcia-Miralles and coworkers reported that ethanolic extract of fenugreek at various doses (100–500 mg/kg) were useful in attenuating the depression through inhibiting the activity of MAO (monoamine oxidase) A and B inhibitor clorgyline resulting in improved neurotransmission.^[37] Likewise, it has also been reported that *Trigonella* (100 mg/kg) plays an important role in reducing the incidence of Parkinson disease by preventing the rotational behaviour and by restoring SNC (substantia nigra compact) neuron and MDA (malondialdehyde) levels.^[38]

Wang and his colleagues explored the mechanisms of fenugreek flavonoids as antidepressant agents through animal modelling. The findings concluded that fenugreek flavonoids significantly reduced the behavioural abnormalities by altering the pathways and expressions of proteins and enzymes in a positive way. Additionally, the activities of different neurotransmitters have also been influenced in a positive way such as decreased MAO activity.^[39] These studies support the evidence that fenugreek compounds possess momentous neuroprotective effect.

Antibacterial and antifungal properties of *Trigonella*

The role of fenugreek against the bacteria and fungi is newly exposed. Haouala and his group described the activity of different parts of plant fenugreek as the antifungal, such as the seeds (ground and non-

ground), leaves, stems and roots by making their aqueous extracts in methanol, petroleum ether, ethyl acetate then by using these extracts against the strains of fungus as *Botrytis cinerea*, *Fusarium graminearum*, *Alternaria sp.*, *Pythium aphanidermatum* and *Rhizoctonia solani*. Antifungal potential was shown by all the extracts made by different parts of plant and the specific fungal species and specific part of plant decided the degree to which it is effective. Moreover, the researchers recognized the main antifungal activity was due to the methanol fraction, that is completely repressed the *R. solani* and *Alternaria* species growth. From this study, this conclusion can be drawn that *Trigonella foenum* can be proved as useful source of dynamic biological compound for improved and new drugs against fungus as antifungal.^[40] Recently, Sudan and his colleagues explored the antifungal activity of fenugreek seed extracts against *Microsporium gypseum*. The reported results depicted that the ethanolic extract of fenugreek seeds at 100 µmL concentration developed highest inhibitory zone (16.5 mm) exhibiting 38.4% inhibition.^[41]

Many researchers worked on the efficiency of the extract of fenugreek in contradiction of *Helicobacter pylori*.^[42,43] In a research, *Trigonella* shows the maximum pollens in honey samples which have the highest action against these bacteria *Pseudomonas aeruginosa*, *E. coli* and *Staphylococcus*.^[44] Peptides rich in cysteine shows the maximum activity against the fungus majorly *Defensins*. Olli et al. (2006) have efficaciously copied complementary DNA derived from fenugreek of 225bp defending rich in cysteine known as Tfgd1. *E. coli* shows antifungal activity due to the recombinant protein present in it.^[45] The fraction of fenugreek extract soluble in methanol exposed as nematocide and shows the possibility to use it against nematodes because it causes the death of 92% larvae of *Meloidogyne javanica*.^[46] It is one of the most important characteristics of fenugreek. It can use in many food products against microbes and fungus as well as it has positive effect in body against harmful bacteria.

Effect of *Trigonella* against pulmonary fibrosis

Pulmonary fibrosis is one of the primary lungs disease in which stiffening and damaging of lungs tissues take place Asththat ultimately results in improper breathing. The study was designed to clarify the oxidation reduction balance and mechanism of inflammation relationship in pulmonic fibrosis. The pulmonic structure is predominantly susceptible to reactive oxygen species prompted damage due to its constant contact to poisonous contaminants. Rats were treated with BLM firstly to make a tentative experimental unit of pulmonic fibrosis, then the aqueous acetonetic extract and powder supplementation of the seeds of fenugreek to check its potential as anti-inflammatory and antioxidant. The main outcome that was observed is fenugreek has useful properties by constraining inflammatory reaction and peroxidation of lipid in fibrosis pulmonic. Nonetheless additional studies on the seeds of fenugreek are needed to be prepared to clarify its molecular mechanism. Therefore, the different treatments that contain antioxidants could add to forthcoming real remedies of pulmonic fibrosis.^[47] It is the need of time to add the fenugreek in our daily diet, for its high nutritional profile as well as it can help in avoidance of pulmonic fibrosis, even if it is of unidentified aetiology.

Fenugreek against obesity

Several investigations report that hydroxyl isoleucine ameliorates insulin resistance caused by obesity. Researchers proposed that hydroxyl isoleucine down-regulated a tumour necrotic factor-transforming catalyst which causes the change of mTNF to sTNF. The studies also provide the information about the pathway of signal transduction and upgraded the insulin confrontation, which is induced by obesity in adipocytes (3T3-L1).^[48] Alike findings have been described in Zucker rats, which were obese given the seeds of fenugreek. Researcher experiments the livers of the rats which were obese, the decrease in tumour necrosis factor intensities, important rise in receptors of membrane and TNF receptor 2. In additional research, it was demonstrated that fibre present in fenugreek ominously suppresses the hunger and amplified in obese experimental units. Dietary supplementation of fenugreek is proved to have significant effect on loss of weight for short period of time.^[49] When the

fenugreek powder was given to obese rats for 14 weeks, they noticed the change in nutritional values, body measurements and decrease in the body weight was detected. Galacto-mannan that is present in the seeds of fenugreek capture and excrete the sugars from body before it moves in the blood, this causes the loss of weight.^[50]

When aqueous fenugreek extracts were given to high-fat-fed rats, they reported noteworthy decrease in the weight of body, as well as in body mass index and drop in serum lipid profile and cardiac hazard elements. Leptin levels in the adipose tissue are reduced by the fenugreek to control the appetite.^[51] Similar interpretations were prepared in rats that were obese due to monosodium glutamate.^[52] In mice, the activity of furanostolic saponins (Fenfuro™) obtained from fenugreek on the insulin resistance was assessed. The results concluded that administration of Fenfuro™ reduced the phosphorylation of protein kinase B stimulated by insulin. Fenfuro™ also dropped the assembly of fat and better insulin sensitivity and glucose acceptance.^[53] It can be proved very useful in weight loss without any major side effect.

Fenugreek in asthma treatment

Asthma is one of the most prevailing lungs disorder in which the bronchial tubes or airways become inflamed and tightened the pathway for inhalation and exhalation of air. To treat the mild asthma, the study was conducted to check the safety and efficiency of the extract of the seeds of when used as supplement. TPM formula was used by adding the syrup of fenugreek in honey solution. In comparison with the placebo and honey syrup, the aqueous extract of the seeds of fenugreek amended the Quality of Life and the tests of lung functioning in patients having mild asthma. Extract of the seed of fenugreek when used, it headed to a ten percent (10%) rise in FEV1 (forced expiratory volume in one second) and FEV1/FVC heights, in calculation of an imperative decline in serum cytokine IL-4 heights. By the findings of study, it can be suggested that in the treatment of mild asthma, use of the aqueous extract of fenugreek can prove beneficial just with the few side effects. Fenugreek was nominated amongst TPM treatments. During the study, once picking simple grouping to perceive fenugreek special effects or side effects more closely, agreeing to TPM, fenugreek works to better functioning of lung as helps the lung secretions and as a lung tonic.^[54]

In the fenugreek, the polyphenols having low molecular weight known as flavonoids are the major part, which are active during the treatment of asthma and play the role against asthma to some extent. In different studies, due to the presence of flavonoids in fenugreek, it shows the antioxidant effects by constraining the lipid peroxidation and guard the airways from the stress of oxidation.^[55] Stimulation of mast cells and basophils are also interrupted by the flavonoids.^[56] Fenugreek has antioxidant influence along with the presence of a flavonoid named as quercetin, which can stop the formation of crystals of Charcot-Leyden, and eosinophil cationic proteins that cause the pathogenesis in asthma. Fenugreek likewise has the capacity to decrease the injury triggered by oxidative mediators.^[57] Different stages such as the formation of micro capillary tubule and cell migration in the angiogenesis can be prevented by the flavonoids.^[58] As exposed in prior researches, in asthma pathogenesis the changes in vascular plays a significant role.^[59] It has been confirmed that the seeds of fenugreek have the distinct effect as an anti-inflammatory.^[60] Recovered asthmatic cough and comfort in the secretions of lungs are achieved because of the presence of 28% mucilage component of fenugreek seeds, this is the additional conceivable mechanism of act of fenugreek.^[54] In atrophy and asthma problem, the both IL4 was chosen as Th2 profile to check the position of the association between the imbalance of cytokine (Th1/Th2).^[61] The efficacy of the fenugreek was much better than honey, when both fenugreek and honey was used in the process of treatment to reduce the IL4 levels. Swelling of airway and synthesis of Ig-E could be happened when IL4 separated after T lymphocytes and mast cells.^[62] Other studies resolute the consequence of interleukin4 antibodies, interleukin5 antibodies, interleukin13 antibodies in asthma pathogenesis therefore production balances among TH1 and TH2 cytokines could be supportive in management of asthma.^[63] *Trigonella foenum graecum* has an extensive range of dosage. 25 g of powdered seed of fenugreek was finely endured and no side effect was seen, in a human study.^[62]

Acute injuriousness values (LD50) recognized for fenugreek are 5 gram/kg in rats when given orally and 2 gram/kg in rabbit use as dermal from extract of alcoholic seed. The following important subject of the study was the part of honey. Decrease level of IL4, improved lung function, increase the Quality of Life, in the outcomes showed when honey syrup was used for the patients of asthma. When the fenugreek and honey syrups are used in combination, it accelerated the efficacy of formula but when used separately, the result of fenugreek syrup was better than that of honey syrup. Honey is used in many treatments of TPM as a protective agent, but in lung diseases, it also plays more beneficial role.^[54]

At the end, in the primary study when the honey-based syrup of aqueous extract of *Trigonella foenum-graceum* (Fenugreek) was used as supplement in the treatment of mild asthma, it exhibited the satisfactory results. In the treatment of mild asthma, fenugreek syrup therapy can be recommended as adjuvant therapy, due to upright consequences and sound forbearance of the syrup of fenugreek.^[61] From the different studies, it can be concluded that the daily use of fenugreek can help to avoid the symptoms of asthma. It also helps in improving the function of lungs and respiratory tract as it acts as tonic. In spite of the efficiency of the seeds of fenugreek established through the study, the main mechanism involved behind its effectiveness is still mysterious, and more researches and studies based on the multiple samples are required.

Safe use and adverse effects of fenugreek

Clinically noteworthy harmful adverse effects of fenugreek are not reported in the review of the literature on fenugreek. Even though fenugreek is conventionally considered harmless and fine stomached, but certain side effects are linked with its usage. Those patients who are allergic to fenugreek or allergic to chickpeas must be cautioned in using fenugreek as the possible cross-reactivity can occur. Curry powder containing fenugreek act as allergen in the patient diagnosed with severe bronchospasm, wheezing and diarrhea. Transient diarrhea, dizziness and flatulence are other side effects caused by fenugreek. After supplementation, blood glucose level must be monitored as hypoglycemia is the effect of fenugreek. T3 (triiodothyronine) production decreases after consumption of fenugreek and it causes the weight reduction. Fenugreek preparations can have coumarin derivatives, causes the increased risk of bleeding due to increased prothrombin time and the international normalized ratio (INR). Fenugreek use must be avoid during pregnancy as it has the potential to stimulate the uterine contractions, observed in animal studies.^[64] The use of fenugreek must be in moderation or in specific dose when used as therapeutic agent. Overdose can have adverse effects on health. Individuals must be conscious about any sign of allergy or any sudden decrease in blood glucose and must visit the physician timely.

Interaction of fenugreek with drugs

The structural properties of fenugreek fibre can cause hindrance in the intestinal absorption of oral medication. Therefore, fenugreek and its products should be taken with the time gap from prescribed medication. Blood glucose levels must be monitored when fenugreek is taken with hypoglycemic agents, because fenugreek can lower the serum glucose levels more than expected. It was observed 14% reduction in potassium levels of small group of healthy subjects when an aqueous extract of fenugreek were given. Thus, fenugreek may precipitous low levels of potassium in blood when used in mishmash with some water pills, purgatives, mineralocorticoids, or other K-lowering agents in blood.^[65]

Fenugreek is also supposed to have an estrogenic constituent. When fenugreek was given the decreased levels of serum triiodothyronine and in the triiodothyronine/thyroxine ratio, and also an escalation in the serum level of T4, have been noticed.^[64] The hypokalemic, hypoglycemic and estrogenic increased effect has been seen, when taken with their respective drugs. It can also have interaction with other drugs. One must be careful with timing and frequency, when taken with some specific medication.

Conclusion

In the present review, attempt has been made to elaborate on the reported nutritional and pharmacological uses of fenugreek. Due to its chemical constituents and active compounds like alkaloids, amino acids, flavonoids, it acts as good antioxidant as well as anti-inflammatory agent. Additionally, the clinical applications of fenugreek are also attributed to its diverse chemical composition, which make this plant a strong to alleviate the dependence on various synthetic drugs for curing the diseases. However, further research is needed to explore the modern isolation techniques for bioactive components for the development of novel functional foods and drugs. Moreover, economically feasible molecular farming approaches based on microbial bioreactors should also be studied to synthesize the recombinant pharmaceutical proteins by using the *in vitro* cultured plant cells. Likewise, proper investigations consisting of well-planned clinical studies are direly needed to produce prosperous results for the mankind.

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