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Changes in Physical and Biochemical Properties of Fenugreek

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ABSTRACT: Fenugreek (*Trigonella foenum-graecum* L.), is a highly respiring leafy vegetable enriched with many nutrients and other active ingredients such as protein, vitamin C, niacin, potassium, alkaloids, lysine and L-tryptophan as well as steroidal saponins which are beneficial for human health. Both, quantitative and qualitative losses in this vegetable can be reduced by appropriate packaging and storage techniques which have not been applied hitherto. Different physiological and biochemical characteristics which generally affect the post-harvest life of the produce were monitored during the storage period. Results of the study suggested that among all the treatments, packaging of fenugreek in two perforation packets with mustard seeds resulted in best maintenance of chlorophyll, ascorbic acid, phenols and aroma. Water accumulation was also consoled due to mustard seeds after 6 days of storage.

KEYWORDS: Fenugreek, physical, biochemical, properties, post-harvest-life, maintenance, water accumulation

I. INTRODUCTION

Fenugreek (Trigonella foenum-graceum L.) is an annual herb of leguminosae,

Fenugreek seeds

is being used as spice with its seeds and as vegetable with its leaves. It has a long history as both a culinary and medicinal herb in the ancient world. Fenugreek is known as Greek hay. Its seeds have a strong aroma and somewhat bitter in taste. Fenugreek is native to Southern Europe, the Mediterranean region and Western Asia. It is cultivated from Western Europe to China for the aromatic seeds and is still grown for fodder in parts of Europe and Northern Africa. The seeds are very hard, and difficult to grind. Seed extract is used in imitation vanilla, butterscotch and rum flavoring and is the main flavoring in imitation maple syrup.¹





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Fenugreek greens

Rich in vitamins and minerals, and because it is a seed and a legume, it is high in protein. They are also an important source of diosgenin .In Turkey, fenugreek is widely cultivated as a spice crop for a long time and is cultivated on 700 hectares with an annual production of 670 tonnes and its yield 957 kg/ha . It is an important industry and export crop. In Turkey, it is consumed for producing spice and pastirma producing (preserve of dried meat) and garlic-flavoured sausage (called çemen). Çemen is composed of crushed classical fenugreek seeds, garlic and chilli pepper mixed to a paste with some water. The çemen paste covering the slabs of pastirma is both an important factor in the flavour, and protects the meat from drying and spoiling by contact with the air² .To design equipment for aeration and storage there is a need to know various physical properties as a function of moisture content . In order to optimize the equipment design for harvesting, handling, storing and other processes of fenugreek seed, its physical properties must be known. The physical properties of fenugreek seeds are to be known; for design and improve of relevant machines and facilities for harvesting, storing, handling and processing. The size and shape are important in designing of separating, harvesting, sizing and grinding machines. Bulk density and porosity affect the structural loads, the angle of repose is important in designing of storage and transporting structures. The coefficient of friction of the seed against the various surface is also necessary in designing of conveying, transporting and storing structures.³



Some physical properties of fenugreek seeds were evaluated as a function of moisture content. The average length, width, thickness, geometric mean diameter and unit mass of the seed ranged from 4.01 to 4.19 mm, 2.35 to 2.61 mm, 1.49 to 1.74 mm, 2.40 to 2.66 mm and 0.0157 to 0.0164 g as the moisture content increased from 8.9% to 20.1% d.b. respectively. In the moisture content range, studies on rewetted fenugreek seed showed that the sphericity increased from 60.79% to 64.06%, the seed volume from 12.58 to 13.83 mm³, 1000 seed mass from 15.48 to 16.39 g and surface area from 18.09 to 22.18 mm². As the moisture content increased from 8.9% to 20.1% d.b., the bulk density, kernel density were found to decrease from 701.16 to 645.81 kg/m³ and 1240.36 to 1165.25 kg/m³, whereas angle of repose and porosity were found to increase from 14.34° to 16.88° and 43.47% to 44.58%, respectively. Fenugreek (Trigonella foenum-graecum) is an annual plant in the family Fabaceae, with leaves consisting of three small obovate to oblong leaflets.⁴ It is cultivated worldwide as a semiarid crop. Its seeds and leaves are common ingredients in dishes from the Indian subcontinent, and have been used as a culinary ingredient since ancient times.^[2] Its use as a food ingredient in small quantities is safe.^{[3][4]} Although sold as a dietary supplement,^[5] there is no clinical evidence that fenugreek has therapeutic properties.^{[4][5]} Commonly used in traditional medicine, fenugreek can increase the risk of serious adverse effects, including allergic reactions.^{[4][5]} Fenugreek is believed to have been brought into cultivation in the Near East. It is uncertain which wild strain of the genus Trigonella gave rise to domesticated fenugreek. Charred fenugreek seeds have been recovered from Tell Halal, Iraq (carbon dated to 4000 BC), and Bronze Age levels of Lachish and desiccated seeds from the tomb of Tutankhamen.^[6] Cato the Elder lists fenugreek with clover and vetch as crops grown to feed cattle.^[7]In one first-century A.D. recipe, the Romans flavoured wine with fenugreek.^[8] In the 1st century AD, in Galilee, it was grown as a staple food, as Josephus mentions it in his book, the Wars of the Jews.^[9] The plant is mentioned in the



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2nd-century compendium of Jewish Oral Law (Mishnah) under its Hebrew name tiltan.^[10]Fenugreek is used as a herb (dried or fresh leaves), spice (seeds), and vegetable (fresh leaves, sprouts, and microgreens). Sotolon is the chemical responsible for the distinctive maple syrup smell of fenugreek.^{[13][4]}Cuboid, yellow- to amber-coloured fenugreek seeds are frequently encountered in the cuisines of the Indian subcontinent, used both whole and powdered in the preparation of pickles, vegetable dishes, dal, and spice mixes such as panch phoron and sambar powder. They are often roasted to reduce inherent bitterness and to enhance flavour.^[14]Fresh fenugreek leaves are an ingredient in some curries, such as with potatoes in cuisines of the Indian subcontinent to make "aloo methi" ("potato fenugreek") curry.^[15]In Armenian cuisine, fenugreek seed powder is used to make a paste that is an important ingredient to cover dried and cured beef to make basturma.^[16]In Iranian cuisine, fenugreek leaves are called *shanbalileh*. ⁵They are one of several greens incorporated into the herb stew *ghormeh sabzi*, the herb frittata kuku sabzi and a soup known as eshkeneh. In Georgian cuisine, a related species-Trigonella *caerulea* called "blue fenugreek"—is used.^[17]In Egyptian cuisine, fenugreek is known by the Arabic name hilba or helba $a \downarrow a$. Seeds are boiled to make a drink that is consumed at home, as well as in coffee shops. Peasants in Upper Egypt add fenugreek seeds and maize to their pita bread to produce aish merahrah, a staple of their diet. Basterma, a cured dried beef, has its distinctive flavour from the fenugreek used as a coating.In Moroccan cuisine, fenugreek is used in Rfissa, a dish associated with the countryside.^[18]Fenugreek is used in Eritrean and Ethiopian cuisine.^[19] The word for fenugreek in Amharic is *abesh* (or *abish*), and the seed is used in Ethiopia as a natural herbal medicine in the treatment of diabetes.^[19]In Turkish cuisine, fenugreek seed powder is 'cemen' and used to make a paste with paprika powder and garlic that is an essential ingredient to cover dried and cured beef to make pastirma/basturma which comes from Turkish verb 'bastırmak' means to press. In a 100 gram reference amount, fenugreek seeds provide 1,350 kilojoules (323 kcal) of food energy and contain 9% water, 58% carbohydrates, 23% protein, and 6% fat, with calcium at 40% of the Daily Value (DV, table).⁶ Fenugreek seeds (per 100 grams) are a rich source of protein (46% DV), dietary fiber, B vitamins, and dietary minerals, particularly manganese (59% DV) and iron (262% DV). Fenugreek dietary supplements are manufactured from powdered seeds into capsules, loose powders, teas, and liquid extracts in many countries.^{[4][5]} Powders may also be used as a topical medication or dressing for skin wounds or eczema.^[4] There is no high-quality evidence that these products have any clinical effectiveness.^{[4][5]} Fenugreek is sometimes used as animal feed. It provides a green fodder palatable to ruminants. The seeds are also used to feed fish and domestic rabbits.^[21] Fenugreek seeds and leaves contain the molecule sotolone, which imparts the aroma of fenugreek and curry in high concentrations, and maple syrup or caramel in lower concentrations.^{[4][13]} Fenugreek is used as a flavoring agent in imitation maple and a dietary supplement.^[5] syrup or tea. as Constituents of fenugreek seeds include flavonoids, alkaloids, coumarins, vitamins, and saponins; the most prevalent alkaloid is trigonelline and coumarins include cinnamic acid and scopoletin.^[3] Research into whether fenugreek reduces biomarkers in people with diabetes and with pre-diabetic conditions is of limited quality.^[22] As of 2020, there was no high-quality fenugreek is relieve dysmenorrhea^{[4][23]} or whether safe and effective to evidence for improve lactation during breastfeeding.^[24] Studies of fenugreek are characterized as having variable,⁷ poor experimental design and quality, including small numbers of subjects, failure to describe methods, inconsistency and duration of dosing, and non-recording of adverse effects.^{[23][24]}Because research on potential biological effects of consuming fenugreek has provided no high-quality evidence for health or anti-disease effect, fenugreek is not approved or recommended for clinical use by the United States Food and Drug Administration.^{[4][5]}Although once a folk remedy for an insufficient milk supply when nursing, there is no good evidence that fenugreek is effective or safe for this use.^{[4][5][24]} There is no good evidence it is useful in traditional practices for treating dysmennorhea, inflammation, diabetes, or any human disorder.^{[4][5][23]} Use of fenugreek has potential for serious adverse effects, as it may be unsafe for women with hormone-sensitive cancers.^{[4][5]} Fenugreek is not safe for use during pregnancy, as it has possible abortifacient effects and may induce preterm uterine contractions.^{[3][4]}Some people are allergic to fenugreek, including those with peanut allergy or chickpea allergy.^{[3][4]} Fenugreek seeds can cause diarrhea, dyspepsia, abdominal distention, flatulence, perspiration, and a maple-like smell to sweat, urine or breast milk.^{[3][4][5]} There is a risk of hypoglycemia particularly



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in people with diabetes, and it may interfere with the activity of anti-diabetic drugs.^{[3][4]} Because of the high content of coumarin-like compounds in fenugreek, it may interfere with the activity and dosing of anticoagulants and antiplatelet drugs.^{[3][4]}Fenugreek sprouts, cultivated from a single specific batch of seeds imported from Egypt into Germany in 2009, were implicated as the source of the 2011 outbreak of *Escherichia coli* O104:H4 in Germany and France.^[25] Identification of a common producer and a single batch of fenugreek seeds was evidence for the origin of the outbreaks.^[26]

II. DISCUSSION

Small amount of volatile oils and fixed oil has been found in fenugreek seeds . It has been found the odor active compounds based on the fenugreek aroma detection with the help of Gas Chromatograph and these includes the olfactometry diacetyl, 1-Octene-3-one, sotolon, acetic acid; 3-Isobutyl-2-methoxypyrazine, butanoic acid, isovaleric acid, 3-isopropyl-2-methoxypyrazine, caproic acid, eugenol, 3-Amino-4,5-dimethyl-3, linalool, (Z)-1,5-Octadiene-3-one, 4-dihydro-2(5H)-Furanone with characteristic aroma of buttery like, roasty/earthy, metallic, pungent, paprika like, sweaty/rancid, flowery, musty, spicy respectively. Out of all these volatile compounds, sotolon was reported to be found most predominantly in (5s)-enantiomeric form (95%) in fenugreek.⁸

A study was conducted on sweat of human after fenugreek ingestion and it has been concluded that compounds responsible for the strong maple-syrup odor present in sweat after fenugreek ingestion are due to the following components including the following: pinene; 3-octen-2-one, 2,5-dimethylpyrazine, β -; camphor; terpinen-4-ol; 4-isopropyl-benzaldehyde; neryl acetate and β -caryophyllene but it was observed that 2,5-dimethylpyrazine to be a major component responsible for sweat odor contributing compound⁹. A list of chemical constituents is shown in Table 1 below.

	8	
S. no.	Chemical constituents of fenugreek	
Alkaloids	Trimethylamine, Neurin, Trigonelline, Choline, Gentianine, Carpaine and Betain	
Amino acids	Isoleucine, 4-Hydroxyisoleucine, Histidine, Leucine, lysine, L-tryptophan, Arginine	
Saponins	Graecunins, fenugrin B, fenugreekine, trigofoenosides A-G	
Steroidal sapinogens	Yamogenin, diosgenin, smilagenin, sarsasapogenin, tigogenin, neotigogenin, gitogenin, neogitogenin, yuccagenin, saponaretin	
Flavonoids	Quercetin, rutin, vitexin, isovitexin	
Fibers	Gum, neutral detergent fiber	
Lipids	Triacylglycerols, diacylglycerols, monoacylglycerols, phosphatidylcholine phosphatidylethanolamine, phosphatidylinositol, free fatty acids. (Chatterjee et al., 2010)	
Other	Coumarin, lipids, vitamins, minerals. 28% mucilage; 22% proteins; 5% of a stronger- swelling, bitter fixed oil.	

Table 1. Chemical constituents of fenugreek.

Fenugreek has a beneficial effect on cleansing the blood and as a diaphoretic it is able to bring on a sweat and to help detox the body. Due to pungent aroma of fenugreek, that is smelt on the skin and in under-arm perspiration. Fenugreek is also known for its lymphatic cleansing activity though its vital role is to irrigate the cells with nutrients and to remove toxic wastes, dead cells and trapped proteins from the body. Block in the lymphatic system can mean poor circulation of fluid, fluid retention, pain, energy loss and disease, anywhere in the body of a person. Fenugreek maintains mucus conditions of the body, mostly the lungs, by helping to clear congestion. It also acts as a throat



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cleanser and mucus solvent that also eases the urge to cough. Drinking water in which seeds of fenugreek have soaked helps in softening and dissolving, accumulating and hardening the masses of cellular debris. Fenugreek has been used to relieve colds, bronchial complaints, influenza, asthma, catarrh, constipation, sinusitis, pleurisy, pneumonia, sore throat, laryngitis, hay fever tuberculosis and emphysema.¹⁰

S. no.	Component used	Beneficial effects
1	Seeds	Hypoglycemic effect
2	Seeds	Hypocholesterolemic effect
3	Seed, leaves	Antioxidant
6	Seed	Lactation aid
9	Seed	Immunomodulatory effect
10	Seed	Digestive effect
11	Seeds and leaves	Decreases blood pressure
14	Seeds and leaves	Wounds and sore muscles treatment
15	Seeds, leaves	Anti-cancer agent
16	Seeds	Asthma, emphysema, pneumonia
17	Seeds leaves	Anti-ulcer agent
19	Seed	Induces growth and reproduction hormones
20	Leaves and seeds	Gastro- and hepatoprotective
21	Seed	For healthy heart
23	Seed	Prevents constipation
24	Seed, leaves	Digestive and appetizer

A list of nutraceutical properties of fenugreek is shown in Table 2. Table 2. Nutraceutical properties of fenugreek.

Hypoglycemic effect

Dietary fiber from fenugreek blunts glucose after a meal. The mechanisms for these effects have not been fully elucidated. Fenugreek seeds contain 45.4% dietary fiber (32% insoluble and 13.3% soluble), and the gum is composed of galactose and mannose. The latter compounds are associated with reduced glycemic effect. The hypoglycemic effect of fenugreek has been especially documented in humans and animals with type 1 and type 2 diabetes mellitus . Mechanism of action of an orally active hypoglycemic principle isolated from water extract of seeds of fenugreek was investigated in alloxan induced sub diabetic and overtly diabetic rabbits of different severity cases. Active component was orally administered to the subdiabetic and mild diabetic rabbits (five in each group) at a dose of 50 mg per kg body weight for period of 15 days, and result showed significant attenuation of the glucose tolerance curve and improvement in the glucose induced insulin response. The result suggested that the hypoglycemic effect may be mediated through stimulating insulin synthesis and/or secretion from the beta



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pancreatic cells. Upon prolonged administration of the same dose of the active principle for 30 days to the severely diabetic rabbits lowered fasting blood glucose significantly, but could elevate the fasting serum insulin level to a much lower extent, which suggests an extra-pancreatic mode of action for the active principle.¹¹ The effect may also be by increasing the sensitivity of tissues to available insulin. The hypoglycemic effect was observed to be slow but sustained, without any risk of developing severe hypoglycemia.

Impact of fenugreek incorporated therapeutic food on blood sugar levels of 24 non-insulin dependent diabetes mellitus patients was investigated in a study. A type of therapeutic food was developed from legumes viz., bengal gram, green gram, horse gram, dry peas and fenugreek seeds. An amount of 30 g of product was supplemented for a period of about one month and was found that both fasting and postprandial blood sugar levels were reduced significantly. So, it was concluded the usefulness of high fiber fenugreek diet in the management of diabetes .

The fenugreek extract has been investigated for its effects on blood glucose, hemorheological parameters and general properties in experimental rats having diabetics.¹² The streptozotocin-induced rats (with diabetics) were administrated by oral intragastric intubation separately with low dose, middle dose, high dose of fenugreek extract, and Metformin HCl for 6 weeks. Rats treated with fenugreek extract had an increase in body weight and a decrease in kidney/body weight ratio as compared with diabetic group. Rats treated with fenugreek extract had lower blood glucose, and glycated hemoglobin, in a dose-dependent manner as compared with diabetic group. It may be concluded that fenugreek extract can lower kidney/body weight ratio and blood glucose and also improves hemorheological properties in experimental diabetic rats following repeated treatment for 6 weeks.¹³

The galactomannan-rich soluble fiber fraction of fenugreek seeds may be responsible for the antidiabetic activity. A study on animals evaluated the hypoglycemic effects of the fenugreek seeds on dogs. The seeds (defatted) lowered blood glucose levels, plasma glucagons and somatostatin levels; carbohydrate-induced hyperglycemia also was found to be reduced. Clinical analysis showed that glycemic control was improved in a small study of patients with mild type-2 diabetes mellitus. A reduction in glycosylated hemoglobin levels and increased insulin sensitivity were observed in fenugreek recipients .

It is possible that fenugreek lowers lipids because it contains saponins that are transformed in the gastrointestinal tract into sapogenins. Fenugreek seeds contain 25% fiber that can slow the rate of postprandial glucose absorption. This may be a secondary mechanism for its hypoglycemic effect.¹⁴

Hypocholesterolemic effect

The abnormal deficiency of cholesterol level in the blood is known as hypocholesterolemic problem and oral administration of methanolic and aqueous extracts of seeds at a dose of one gram per kilogram body weight resulted in hypoglycemic effect in mice . Fenugreek seeds contain the large amount of fiber galactose and mannose are the main composition of gum. The latter compounds are associated with reduced cholesterolemia .

The fenugreek extract has been investigated for its effects on blood lipid, and in experimental rats with diabetics. The streptozotocin-induced diabetic rats were administrated by oral intragastric intubation separately with low dose, middle dose, and high dose of fenugreek extract, and Metformin HCl for about one and half month (6 weeks). As compared to diabetic group, rats treated with fenugreek extract had lower triglycerides, total cholesterol, and higher HDL cholesterol in a dose-dependent manner.¹⁵

Antioxidant activity

Scientists reported that fenugreek seed extract with methanol, ethanol, dichloromethane, acetone, hexane and ethyl acetate has a radical scavenging activity. Many researchers reported protective effect of fenugreek, on lipid peroxidation and on enzymatic antioxidants. It was reported that the proximate composition of fenugreek seeds, husk and cotyledons had the highest saponin and protein content. In contrast, husk had higher total polyphenols. At 200 µg concentration, fenugreek seed, extracts of husk and endosperm exhibited 72%, 64%, and 56% antioxidant activities respectively by free-radical scavenging activity. From the study it was indicated that separation of fenugreek seeds into husk and endosperm could have advantage of process viability with respect to prior selective fractionation of bioactive components for their effective isolation. It is studied the prophylaxis effect of fenugreek



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seeds on renal stone formation in rats. The fenugreek can be used in the treatment of patients with calcic urolithiasis. Also it is reported an anti-inflammatory potential of fenugreek¹⁶.

In a study it was observed that *Aegle marmelos* has the highest phenolic content followed by fenugreek and *Coriander sativum*; similarly the flavonoids contents are high in fenugreek followed by *C. sativum* and *A. marmelos*. Antioxidant property was checked by reducing power, NBT assay and H_2O_2 scavenging. *A. marmelos* showed the highest reducing power followed by *C. sativum* and fenugreek but fenugreek showed the highest superoxide and free radical scavenging followed by *C. sativum* and *A. marmelos* respectively.¹⁷

Anticancer effect

Cancer is one of the leading causes of mortality all around the world. Many reported studies have shown the protective effect of fenugreek seeds in experimental models of cancer using cell lines or experimental animals. It was showed that fenugreek seed extract significantly inhibited 7,12-dimethylbenz(a)anthracene-induced mammary hyperplasia and reduces its incidence in rats and advised that the anti-breast cancer protective effects of fenugreek could be due to increased apoptosis. Further, alcoholic whole plant extracts of fenugreek showed in vitro cytotoxicity against different human cancer cell lines such as IMR-32, a neuroblastoma cell line, and HT29, a cancer cell line .A selective cytotoxic effect of fenugreek extract in vitro to a panel of cancer cell lines has been observed, including T-cell lymphoma.¹⁸ It was examined the growth of MCF-7 cells, which is an estrogen receptor positive breast cancer cell line, with ethanol extracts of fenugreek, and reported that the ethanol extract of fenugreek decreased cell viability and induced early apoptotic changes such as inversion of phosphatidyl serine and decreased mitochondrial membrane potential. Further, degradation of DNA into fragments comprising multiples of approximately 180-200 base pair has also been observed. Cell cycle analysis revealed a sub-G1 apoptotic population along with cell cycle arrest at G2/M phase in fenugreek extract treated cells implicating the role of fenugreek extract-induced apoptosis in its anticancer role. According to the investigation made by treatment with fenugreek extract showed growth inhibitory effects on breast, pancreatic and prostate cancer cell lines but primary prostate or immortalized prostate cells remained unaffected.¹⁹ Inhibition of cancer cell growth by *Trigonella* is attributed to its ability to induce death of cell, despite simultaneous upregulation of growth stimulatory pathways in normal cells. It was also demonstrated anticancer activity of the ethanol extract of Trigonella in Ehrlich Ascites Carcinoma cells induced cancer in Swiss albino mice. The mice inoculated with Ehrlich Ascites Carcinoma and treated with Trigonella leaf extract showed increased life span in comparison with the tumor control, suggesting anticancer activity of fenugreek leaf extract in animal models.²⁰

A diet containing fenugreek seed powder decreased colon tumor incidence and hepatic lipid peroxidation in 1,2dimethylhydrazine treated rats and also increased activities of catalase, superoxide dismutase, glutathione Stransferase and glutathione peroxidase in liver . It is showed that diosgenin could modulate the STAT3 signaling pathway in hepatocellular carcinoma by suppressing the activation of c-Src, JAK1 and JAK2. Diosgenin also down regulated the expression of various STAT3-regulated genes, inhibited proliferation and potentiated the apoptotic effects of paclitaxel and doxorubicin, suggesting that diosgenin could be a novel and potential treatment option for hepatocellular carcinoma and other cancers. Therefore, the role of fenugreek seed and its main active constituents as new supplements in diet-based preventive/therapeutic strategies to potentially alleviate human diseases remains an important field of study for future investigations²¹.

Antibacterial and antifungal effect

The antibacterial and antifungal role of fenugreek is recently being shown. In a study by researchers, an aqueous extracts from various plant parts of fenugreek in various solvents include methanol, petroleum ether and ethyl acetate fractions of the aerial parts and determine their action against fungal strains such as *Fusarium graminearum*, *Botrytis cinerea*, *Alternaria sp.*, *Rhizoctonia solani* and *Pythium aphanidermatum*. It was found that all parts of the fenugreek plant showed antifungal potential and the magnitude of effect varies with plant parts and species of fungus. It could be suggested that fenugreek is an important source of biologically active compounds useful for developing better and novel antifungal drugs. The effectiveness of extracts obtained from



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fenugreek against Helicobacter pylori has been reported by several studies . In a study, honey samples with highest antibacterial activity against *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Escherichia coli* show maximum pollens from fenugreek than other plants. Cysteine-rich peptides, defensins are small with potent antifungal activity. The methanol soluble fraction of fenugreek extract showed nematicidal activity and caused significant mortality of *Meloidogyne javanica* larvae, indicating the potential use against nematodes.²²

It was studied the prophylaxis effect of fenugreek seeds on renal stone formation in rats. The fenugreek can be used in the treatment of patients with calcic urolithiasis. Scientists reported an anti-inflammatory potential of fenugreek.²³

III. RESULTS

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 (Tmax) was 72 h and half-life (t1/2) 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.²⁴

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 Cmax was 7.039 g/mL, zone under the curve was 0.044 g/mL hour, and t1/2 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. Studies also provided the evidence that almost 40% of the original dosage of vicenin-2 was quickly absorbed in the small intestine. 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.²⁵

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 . The study concluded that fenugreek mucilage supplementation resulted in oedema inhibition by decreasing the activities of inflammatory enzymes due to its anti-arthritic potential.²⁶

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-



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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.²⁶

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.

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.¹¹

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 $(1 \mu g/ml)$ for 15 minutes also prompted resilient phosphorylation of the receptor of insulin and protein kinase B. 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.

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



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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.¹³

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 (3hydroxy-3-methylglutaryl coenzyme A reeducates, cholesterol-7a-hydroxylase and cholesterol-27-hydroxylase) which were prompted by taking the diet high in cholesterol. 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.

Cholesterol gall-stone is controlled by some factors found in the bile known as pro and ant-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.¹⁵

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. 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. 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 microglialcells are critical factors contributing in the pathogenesis of neuropathic pain. Researchers have demonstrated the potential applications of medicinal plants for the treatment of neurological disorders using the animal models. In this regard, fenugreek has also been explored as an effective medicinal plant for the treatment of neurologenerative 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 1. 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. Similarly, Bin-Hafeez and his group induced dietary administration of 5% fenugreek seed powder for 4 weeks to analyze the neuroprotective effects against aluminium chloride-induced neurotoxicity using mice model and reported significant neuroprotective effect of fenugreek seed powder.¹⁷



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Figure 1. Fenugreek activity against neurological disorders.



In another study, 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. 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.

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. These studies support the evidence that fenugreek compounds possess momentous neuroprotective effect.¹⁹



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IV. CONCLUSIONS

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 (tri-iodothyronine) 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. 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.²¹

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.

Fenugreek is also supposed to have an estrogenic constituent. When fenugreek was given the decreased levels of serum triiodothyronine and in the triiodthyronine/thyroxine ratio, and also an escalation in the serum level of T4, have been noticed. 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. 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 drugs²³. 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.²⁶

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