



International Journal of PharmaO₂

Journal Home Page: <http://www.ijpo.in/>

(IJPO: A Peer-reviewed Bi-monthly online journal)

Review Article

An Overview: *Trigonelle foenum graecum* on Human Health

Ms. Supriya T. Garud*¹, Mr. Kundan Tiwari¹ and Mr. Amol Deshmukh²

¹Lecturer, SMBT Institute of D. Pharmacy, Dhamangaon, Nashik-422401, Maharashtra, India.

²Asst. Prof. SMBT College of Pharmacy, Dhamangaon, Nashik-422401, Maharashtra, India.

ARTICLE INFO

Article history:

Received: 26/08/2021;

Revised: 01/09/2021

Accepted: 04/09/2021;

Available online:
06/09/2021.

Key Words:

Fenugreek,

*Trigonella foenum -
graecum*,

Traditional medicine

Please cite this article as:

Garud, S. *et al.* An Overview: *Trigonelle foenum graecum* on Human Health. 3(5), 0210- 0221.

ABSTRACT

Current lifestyle, stress, and pollution have dramatically enhanced the progression of several diseases in human. Fenugreek (*Trigonella foenum-graecum*) commonly known as Methi is an annual herb belonging to family Fabaceae. It is cultivated worldwide as a semiarid crop, and its seeds are a common ingredient in dishes from the Indian subcontinent. This plant has medicinal alkaloids, steroid compounds, and saponin and many uses have been mentioned for this plant in traditional medicine. Fenugreek seeds contain a substantial amount of fiber, phospholipids, glycolipids, oleic acid, linolenic acid, linoleic acid, choline, vitamins A, B1, B2, C, nicotinic acid, niacin, and many other functional elements. Therefore, in addition to the pharmacological effects of fenugreek in different approaches for diseases have also been discussed.

©2021 Published by International Journal of PharmaO₂. This is an open access article.

*Corresponding author: Mrs. Supriya Garud-Ohol, Assistant Professor, SMBT Institute of D. Pharmacy, Dhamangaon, Nashik-422401, Maharashtra, India. Contact+91-8149507273; e- mail: garudsupriya12@gmail.com.

INTRODUCTION

Many chemicals are measure encountered by human either accidentally as a result of their within the atmosphere or by contact throughout activity and recreational activities or by bodily process of food additives. The importance of together with meditative herbs within the dietary decisions is well-known for maintaining the health life style and preventing many varieties of diet-related ailments together with polygenic disease, cancer, cardiovascular disease, inflammation and vas diseases.

Plant seeds and leaves square measure used not solely as food however conjointly as an ingredient in ancient medicines. Concerning seventy to ninety seven totally different species of fenugreek square measure being cultivated round the world. Because it has origin from Balkan state, the species name *foenum-graecum* suggests that 'Greek hay'. Though it's a well-recognized spice that has been added within the human foods, literature conjointly give U.S.A. the utilization of this natural tonic to cure many varieties of lifestyle-related disorders like vas

diseases, hypercholesteremia, hyperglycaemia, cancer, liver ailments and sexual disorders like testosterone-deficiency syndrome. Fenugreek is additionally thought of as an expensive supply of dietary fiber and different necessary nutrients required for correct growth and development. Studies have conjointly affirmed the Nutraceuticals and physiological properties of fenugreek that support the potential applications of fenugreek in developing varied useful food product and pharmaceutical product (Mallik A., *et. al.* 2019).

As fenugreek is wealthy in many phytochemicals, alkaloids, carbohydrates, hormone saponins, amino acids and minerals square measure gift in fenugreek, it may be used for nutritionary, nutraceutical, meditative and therapeutic functions. Fenugreek has been extensively used as a flavor attention in many ancient cuisines. To boot, the meditative properties of fenugreek like anticarcinogenic, medicine, inhibitor, hypocholesterolemic, anti-lithogenic antimicrobial and medical specialty properties create it a very important compound to be employed in food and pharmaceutical industries. Additionally to the meditative properties of fenugreek, it's conjointly been used as a wetter and stabilizer in numerous varieties of food product. Moreover, use of fenugreek extracts or powders has conjointly been rumored for developing shop and extruded product.

NUTRITIONAL WORTH OF FENUGREEK

Fenugreek (Fig.1) features a huge diversity of nutrients and bioactive compounds that area unit needed for up the health and practicality of biological systems. The fenugreek seeds have 58% carbohydrates, 23- 26 % proteins, 0.9% fats and 25 % fiber. Similarly, fenugreek leaves have 6 June 1944, 4.4%, 1.1% carbohydrates, proteins and fiber severally. Moreover, fenugreek additionally contains differing types of minerals like metallic element (603 mg/100 g), metallic element (42 mg/100 g), atomic number 20 (75 mg/100 g), zinc (2.4 mg/ one hundred g), atomic number 25 and copper (0.9 mg/100 g) and iron (25.8 mg/100 g). Ascorbic acid (220 mg/100 g) and β carotene (19 mg/100 g) also are thought of because the vital elements of fenugreek.



Fig. 1: Fenugreek Plant

Fenugreek is additionally a chic supply of many vital amino acids like amino acid, glutaminic acid, leucine, aminoalkanoic acid and essential amino acid. To boot, it contains minute quantities of sulfur-containing amino acids (cysteine and methionine) having vital physiological roles in body. The foremost copiously gift free amino-alkanoic acid in fenugreek is (2S, 3 R, 4S)-4-hydroxyisoleusine. Concerning eightieth of amino-alkanoic acid content of dry fenugreek seeds consists of the non-protein amino-alkanoic acid 4-hydroxyisoleusine and through the section of growth, this amino-alkanoic acid proliferates apace. Studies have disclosed that the proteins gift within the fenugreek area unit of higher quality as compared to the opposite plant proteins. In Associate in nursing investigation, Feyzi and his coworkers compared the standard of fenugreek macromolecules with soya macromolecule isolate and affirmed that fenugreek seeds contain higher macromolecule contents with higher amino-alkanoic acid profile as compared to soya s protein isolate. To boot, fenugreek proteins were wealthy in amino acid and glutaminic acid. Results additionally declared that fenugreek proteins have higher denaturation temperature, foaming properties, solubility and stability as compared to soy macromolecules and so are often utilized as a good protein supply in varied useful foods. Moreover, sotolone, a very important useful phytochemical used as seasoning flavor, could be a prompting ingredient of fenugreek (Syed A.Q. *et. al* 2020).

Fenugreek contains vital quantities of alkaloids (trigonella, trigocoumarin, niacin, trimethyl coumarin). It additionally contains alternative vital, valuable compounds like flavonoid and polyphenols. Within the alcoholic extracts of the

fenugreek plant, in type of flavonoid, like quercetin, luteolin, vitexin, and 7, 4-dimethoxy flavanones, is present. Other teams have according alike results of the existence of aglycones, kaempferol, quercetin, tricetin, and naringenin. The compounds were sequestered from the precise components of fenugreek plant and additionally from the excerpts and hydrolysates of stems, leaves and flowers. The phytochemical examination of fenugreek exposed that the most of flavonoids area unit existent as glycosides that area unit complicated thanks 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) area unit rare samples of flavonol glycosides existing in fenugreek. Apigenin-6-C-glucoside (isovitexin) and apigenin-8-C-glucoside (vitexin) were sequestered by fenugreek seeds. The incidence of isoflavonoid phytoalexins aglycones, like medicarpin and maackiain, during this herb has additionally been according. These area unit called 'induced isoflavonoids' which might be made thanks to some external factors like microbial activities. (Goyal S. *et.al* (2016))

MECHANISM OF ACTION OF FENUGREEK

Fenugreek seed square measure mixtures of diverse compounds like alkaloids, proteins, super molecule, fiber and this compound play a significant role within the inhibition of assorted styles of pathologic process. flavorer may be a made supply of inhibitor and such potentiality inhibit the pathologic process through radical scavenging activity. Fenugreek therapeutic role evidences as pre-treatment of seasoning extract fixed activities of all the enzymes and so displayed a complete protecting result on additive result of cyclophosphamide and l-buthionine-SR-sulfoximine. Restoration of glutathione by extract treatment would possibly show a big role in backing cyclophosphamide - induced necrobiosis and free radical-mediated macromolecule peroxidation in bladder (Ahmad A.*et. al* 2016).

Chronic inflammation might increase the danger of assorted diseases, like cancers, rheumatism

and different diseases. However, its regulation may be a key step towards inhibition of pathologic process. During this context, fenugreek play important role within the inhibition of pathologic process through its anti-inflammatory drug activity. Flavorer proved role within the inflammation as inhibition of lump by the plant extract at doses of one hundred and two hundred mg/ kilogram and activity of the plant at doses of one hundred and two hundred wasn't considerably completely different from those of non-steroidal anti-inflammatory drug and Dexamethasone intensol. Among the ready formulations of the plant, three and five-hitter creams of the fenugreek showed the foremost inhibition of lump that weren't important from corticosteroid ointment. Flavorer conjointly shows a vital role within the management of polygenic disorder and it had been explained as mechanism of action of seeds of fenugreek was investigated in alloxan elicited sub diabetic. The treatment showed substantial reduction of the aldohexose tolerance curve in addition as improvement within the aldohexose elicited internal secretion response, proposing that the hypoglycemic result can be mediate via stimulating internal secretion synthesis and/or secretion from the beta exocrine gland cells of Langerhans. Moreover, fenugreek seeds play role within the inhibition of growth through modulating numerous activities together with cell signaling pathways. Fenugreek extract showed role within the decrease of the cell viability and cause the induction of early apoptotic changes together with flipping of phosphatidylserine in addition as decrease of mitochondrial membrane potential. flavorer conjointly play role in management of assorted diseases through hepatoprotective, anti-microbial, cardioprotective and neuroprotective effects (Mooventhan A. *et al*. 2017).

PHARMACOLOGICAL & THERAPEUTIC USE OF FENUGREEK:

Anti-oxidant activity

Several fractions of the germinated seeds were included to explore their antioxidant potential at various levels. An aqueous fraction of fenugreek displayed the maximum antioxidant activity compared with other fractions. This study discloses substantial antioxidant activity in

germinated fenugreek seeds which might be due partly to the being there of flavonoids and polyphenols. The role of fenugreek seeds on blood lipid peroxidation as well as antioxidant status in diabetic rats was investigated. In this study, it was observed increased lipid peroxidation and changes in circulating antioxidants were noticed in the diabetic state. Supplementation of fenugreek seeds in the diet caused lowered lipid peroxidation and amount of glutathione and beta-carotene were increased and the alphanatocopherol content was decreased. The study reveals that disturbed free radical metabolism in diabetic animals might be normalized by fenugreek seed supplementation in the diet. Fenugreek seed oil was extracted and evaluated for its chemical compositions and antioxidant activity against (DPPH) and (ABTS+•) radicals, total phenolic content and total flavonoid content of the oil were also investigated. Result showed a total number of 23 chemical compounds were detected. Furthermore, the oil of fenugreek seed indicated a strong antioxidant radical scavenging activity against both DPPH and ABTS assays. The total phenolic content as well as total flavonoid content of the oil were 38.97} 0.34 mg GAE/gram oil and 14.417} 0.23 mg QE/ gram oil.²⁰ Crude extracts of fenugreek were prepared with different solvents such as methanol, ethanol, dichloromethane, acetone, hexane and ethyl acetate. The finding confirmed that all extracts of the fenugreek display antioxidant activity and findings propose that the fenugreek extracts might act as strong source of antioxidants. Another study result revealed that *A. marmelos* showed the highest phenolic content followed by *T. foenum* and *C. sativum* whereas flavonoids contents are high in *T.foenum greacum* followed by *C. sativum* and *A. marmelos*. Antioxidant property was checked by reducing power, NBT assay and H₂O₂ scavenging. *A. marmelos* displayed the highest reducing power followed by *C. sativum* and fenugreek but fenugreek exhibited the highest superoxide and free radical scavenging followed by *C. sativum* and *A. marmelos* respectively.(Almatroodi A. S. et al.(2021)

Anti-inflammatory activity

The anti-inflammatory as well as anti-arthritis activities of fenugreek seeds were examined. Result revealed that with 0.5 mL/kg fenugreek seed petroleum ether extract treatment, there was 37% and 85% reduction in inflammation of the paw in carrageenan and formaldehyde-induced paw edema. In complete Freund's adjuvant - induced arthritis, a biphasic increase in paw volume followed by decrease was seen. There was 42.5% reduction in the weight of cotton pellets and significant reductions in the elevated SGPT and ALP activities in serum and liver of fenugreek seed petroleum ether extract treated rats.²³ The inhibition of edema by the plant extract at doses of 100 and 200 mg/kg were meaningfully different from the control group. This activity of the plant at doses of 100 and 200 was not meaningfully different from those of ibuprofen and dexamethasone. Amongst the prepared formulations of the plant, 3 and 5% creams of the fenugreek showed the most inhibition of edema. The functional food quality of fenugreek seeds by determining the lipid peroxidation (LPO) and cyclooxygenase enzyme (COX) inhibitory activities of their ethyl acetate, hexane, methanolic and water extracts was investigated. The extracts inhibited lipid peroxidation, cyclooxygenase enzyme -1 and cyclooxygenase enzyme -2. Moreover, isolates, without the saccharides, inhibited lipid peroxidation and cyclooxygenase enzyme -1 and -2 enzymes between the ranges of 8–89%, 4–51% and 15–70%, respectively, at 25 µg/ml. (Shishodia S, et. al 2006).

Hepatoprotective effect

The hepatoprotective effect of the ethanolic extract of Fenugreek seeds against carbon tetrachloride induced liver damage in rats was examined. Result revealed that extract of Fenugreek seeds showed highly hepatoprotective effect against carbon tetrachloride induced-necrosis with less effect against fatty changes, this could be due to the antioxidant action of the active constituents in the extract that counteract and scavenge the intermediates free radicals of carbon tetrachloride.³ The hepatoprotective effect of fenugreek seed polyphenolic extract against ethanol-induced hepatic injury and apoptosis in rats was evaluated. Chronic ethanol administration produced liver damage that was

established by the elevation of markers of liver dysfunction—liver function enzymes, lactate dehydrogenase, bilirubin and gamma-glutamyl transferase in plasma and reduction in liver glycogen. Ethanol administration resulted in adaptive induction of the activities of cytochrome p450 and cytochrome-b5 and reduction in cytochrome-c-reductase and Glutathione-S-transferase, a phase II enzyme. Treatment with extract restored the levels of markers of liver injury as well as alleviated the alterations in alcohol metabolizing and detoxification enzymes and the electron transport component cytochrome-c reductase. The protective effects of aqueous extract of against carbon tetrachloride, induced hepatotoxicity in rats was examined. Result confirmed that carbon tetrachloride increased serum transaminases, hepatic lipid peroxidation and hepatic enzymatic antioxidants activities. Moreover, fenugreek aqueous extract improved the harmful effects of carbon tetrachloride and normalised all tested biomarkers toward the control values. Overall, study concluded that aqueous extract of fenugreek plays a protective role against carbon tetrachloride -induced liver damages in rats. Fenugreek was evaluated for hepatoprotective and antioxidant influence in mice. Result revealed that activities of serum aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase and alkaline phosphatase elevated with prolonged feeding of HCD. Activities of these enzymes were decreased in animals fed basal control/ fenugreek containing diets after initial exposure to HCD, and were prominent in fenugreek groups (Kandhare, A. et.al.2015).

Gastroprotective effect

The role of fenugreek seeds compared to omeprazole was examined on ethanol-induced gastric ulcer. Result demonstrated that aqueous extract and a gel fraction isolated from the seeds exhibited noteworthy ulcer protective effects. The cytoprotective effect of the seeds appeared to be not only due to the anti-secretory action but also to the effects on mucosal glycoproteins. The fenugreek seeds also prevented the rise in lipid peroxidation induced by ethanol seemingly by increasing antioxidant potential of the gastric mucosa thereby lowering mucosal injury. The

effect of fenugreek seeds compared with ranitidine was investigated on aspirin-induced gastric ulcer. Result revealed that gel fraction isolated from the seeds displayed important ulcer protective effect. The fenugreek seed gel also prevented the rise in lipid peroxidation induced through aspirin presumably via enhancing antioxidant potential of the gastric mucosa thus decreasing mucosal injury. The effect of Fenugreek seed extract in Indomethacin induced gastric ulcer models was investigated. Finding revealed that fenugreek treated group showed a significant decrease in ulcer index as well as volume of gastric juice and acidity when compared to control positive group. Oxidative enzyme study designated a substantial increase in Catalase, *Superoxide dismutase* and *Glutathione* value in treated group when compared with control positive group. (Buqui, G. A., et. al. 2015).

Neuro-protective effect

The neuro-protective effect of fenugreek seed powder against aluminum chloride induced experimental AD model was examined. Administration of germinated fenugreek seed powder mixed with ground standard rat feed showed role in the protection of aluminum chloride induced memory and learning impairments, Al overload, acetyl-cholinesterase hyperactivity, amyloid β burden. Finding based on result confirm the neuro-protective effect of fenugreek seeds 30. The effect of treatment with fenugreek seed extract on the function of sciatic nerves of neuropathic mice was assessed. Result confirms that neuropathy was induced in mice through pyridoxine intoxication. Then, animals were treated with 0.2, 2 and 20 mg/kg of hydro-alcoholic extract of fenugreek seeds and fenugreek showed anti neuropathic effect and restores the function of nerve fibers. Moreover, electrophysiological recordings stated that the highest rate of healing was occurred in 20mg/kg fenugreek extract treated animals. Another study was formed to identify and evaluated SFSE-T, a standardized hydroalcoholic extract of *Trigonella foenum-graecum* L. seeds in animal models of Parkinson's disease. The concentration of trigonelline in a test sample of SFSE-T was found to be 82%. SFSE-T showed a significant increase in the number of ipsilateral rotations as

compared with vehicle control group when tested in 6-OHDA-induced unilateral lesioned rats (Joglekar M. et al. 2012).

Cardio-protective effect

Cardio protective effect of fenugreek on isoproterenol- induced myocardial infarction based on *in vivo* and *in vitro* was examined. The results designated the cardioprotective effect that detected in rats received fenugreek and additionally isoproterenol showed significantly decreased levels of TBARS and enhanced the activities of both enzymatic and non-enzymatic antioxidants in myocardial infarcted rats when compared to groups received isoproterenol and group received fenugreek. Over all, based on finding study demonstrated that cardioprotective effect of fenugreek on lipid peroxidation and antioxidant defense system during isoproterenol-induced myocardial infarction in rats.³³ The cardioprotective effect of a combination of fenugreek seeds and garlic was assessed in hypercholesterolemic rats administered isoproterenol. Myocardial infarction was induced with isoproterenol injection. Moreover, increased circulatory troponin, changed activities of cardiac ATPases, increased serum iron and decreased ceruloplasmin established myocardial infarction. Elevated lipid peroxides accompanied with reduced antioxidant molecules caused by isoproterenol and change activities of antioxidant enzymes in serum and heart in induced myocardial necrosis were countered by dietary fenugreek, garlic, and fenugreek plus garlic. The cardioprotective effect of dietary fibre-rich fenugreek seeds and garlic was evaluated both individually and in combination in isoproterenol induced myocardial infarcted rats. Result showed that dietary fenugreek, garlic or fenugreek plus garlic was found to improve the pathological changes in heart tissue and lipid abnormalities in serum and the heart, the beneficial effect being higher with the combination of fenugreek and garlic, invariably amounting to an additive effect (Kaviarasan Vet. al.2007).

Hypocholesterolemic/hypolipidemic activity

The effect of consumption of germinated fenugreek seed powder on the blood lipid profiles of hypocholesterolemic adults was investigated. The outcomes of the study designated that consumption of the seed at both

the levels resulted in a hypocholesterolemic effect. Between the two levels, higher levels of consumption, i.e., 18.0 gram of the germinated seed resulted in a significant reduction in total cholesterol and LDL levels. The hypocholesterolemic and antioxidant activities of various extracts of fenugreek seeds were examined in cholesterol-fed rats. These results displayed that the ethyl acetate extract of the fenugreek seeds had a significant hypocholesterolemic effect and antioxidant activity in cholesterol-fed rats, whether this is somewhat due to the presence of flavonoids in the extract. Effects of fenugreek on serum lipid profile in hypercholesteremic type 2 diabetic patients were studied. Administration of fenugreek seed powder caused significant reduction of serum total cholesterol, triacylglyceride and LDL-cholesterol in hypercholesteremic group. Whereas lipid profile in hypercholesteremic type 2 diabetic patients without fenugreek were not significant and fenugreek seed powder would be measured as effective agent for lipid lowering purposes. The relationship between the lipid effects, the phenolic content, and the antioxidative effects of an ethyl acetate extract of fenugreek was investigated. Administration of fenugreek ethyl acetate extract meaningfully decreased the plasma levels of total cholesterol, triglycerides, and low-density lipoprotein cholesterol, while increasing the plasma level of high-density lipoprotein cholesterol. Also, the content of TBARS and catalase and superoxide dismutase activities in liver, heart and kidney decreased suggestively after oral administration of the extract compared with those of rats fed a cholesterol-rich diet. Hypolipidemic effect of fenugreek seeds and its comparison with atorvastatin on experimentally induced hyperlipidemia in rabbits was examined. Result of the study confirms that atorvastatin displayed a more potent hypolipidemic activity. It reduced serum total cholesterol, TG and VLDL cholesterol, and the atherogenic index highly significantly as compared to fenugreek. Hypolipidemic effect of fenugreek in hypercholesterolaemic patients was investigated. Result of the study demonstrated that there were no significant changes in lipid profile of group I

received placebo 50 gm (rice powder and Bengal gram powder in equal measures) patients. In groups II -placebo 25 gm + FG 25 gm and Group III -FG 50 gm serum cholesterol, triglycerides and VLDL levels were significantly decreased when compared to group I. Hypolipidemic effect of thermostable extract of fenugreek seeds was evaluated *in vitro* by engaging differentiating and differentiated 3T3L1 cells, and HepG2 cells cultured in normal or sterol enriched conditions. Results indicate that hypolipidemic effect of thermostable extract of fenugreek seeds is due to inhibition of fat accumulation as well as upregulation of LDLR. Taken together, the study suggests that thermostable extract of fenugreek seeds might have possible application in the managing of dyslipidemia and its related metabolic disorders. Inhibitory effect of aqueous extract of *Trigonella foenum-graecum* seeds on fat accumulation and dyslipidemia in high fat diet- induced obese rats was investigated. Result showed that AqE-TFG treatment reduced the hepatic and cardiac thiobarbituric acid reactive substances and elevated the antioxidant enzyme levels. Moreover, liver and uterine WAT lipogenic enzyme and glucose-6-phosphate dehydrogenase activities were restored towards normal levels. (Sultan S.I. Al 2015)

Anti-microbial activity

The silver nanoparticles of fenugreek seed showed antibacterial activities against both gram-negative and gram-positive bacteria. The ultrasound assisted nanoparticles showed higher stability and antibacterial and antioxidant activity compared with the nanoparticles fabricated by magnetic stirring. The antimicrobial mechanisms and anticancer properties of the AgNPs synthesized using the seed extract of *Trigonella foenum-graecum* L was investigated. Result revealed that MIC of the AgNPs against *Aspergillus flavus*, *Trichophyton rubrum* and *Trichoderma viridiae* were each 250 µg mL⁻¹, respectively. The extracellular protein concentration, levels of lactate dehydrogenase and alkaline phosphatase enzyme in the AgNPs treated bacterial pathogens demonstrated greater antimicrobial mechanism. The antimicrobial activities of biosynthesized nanoparticles were examined through Kirby-Bauer method. The TF-TiO₂ nanoparticles exhibited substantial

antimicrobial activity against all the tested microorganisms (Reddy RR, et.al 2011).

Anti-diabetic effect

A recent study result reported that administration of *Trigonella foenum-graecum* seed powder solution showed noticeable effects in improving lipid metabolism in type II diabetic patients. So, *Trigonella foenum-graecum* seed may deliver new alternatives for the clinical management of type II diabetes. The effects of ethanol extract of Fenugreek seeds on the blood glucose levels in alloxan-induced diabetic rats were investigated. The hypoglycemic effect of extract was compared with that of the antidiabetic drug glimepiride, 4mg/kg single dose. The extract showed significant activity against the diabetic state induced by alloxan. The most effective dose recognized was 1g/kg but that is still lower than the standard antidiabetic drug. A study was performed to evaluate the effects of supplementation with fenugreek seeds on plasma glucose and serum levels of cholesterol and insulin in alloxan-induced diabetic and in non-diabetic rabbits. Supplementation with fenugreek resulted in a significant decrease in glucose level of diabetic group of rabbits and a slight effect in non-diabetic rabbits. Moreover, supplementation with fenugreek lowered the cholesterol level slightly in diabetic groups. The result established that antidiabetic and insulin mimetic effects of fenugreek seeds in rabbits. The effect of oral feeding of *Trigonella foenum-graecum* seed powder (TSP) has been studied on blood glucose, monoamine oxidase, membrane fluidity, and glucose transporter-4 accumulation in the alloxan-induced diabetic rat brain was investigated. Result demonstrated that diabetic rats showed hyperglycemia with almost four-fold high blood glucose levels. Increased MAO activity with correlated increase in genomic DNA degradation in the diabetic brain supports the hypothesis that catecholamine oxidation is an important source of oxidative stress decreased of GLUT4 expression with diabetes in the brain. Overall study concluded that TSP exerts its anti-diabetic and neuroprotective effects, probably mediated through a decrease in hyperglycemia and oxidative stress thereby ameliorating the control and management of diabetic complications. (Prema A et. al. 2016)

Nephroprotective effect

A study was performed on rats to evaluate the role of fenugreek on nephrotoxicity induced by aluminum chloride (AlCl₃). Result revealed that treatment with the whole fenugreek seed powder (5% in the diet) showed its effectiveness in restoring normal plasma values of urea, creatinine, ALP and glucose, as well as re-increasing the TAS, inhibiting LPO and improving histopathological changes in the injured kidneys. The renoprotective efficacy of IND01 in animal model of diabetes with and without ischemia reperfusion injury was examined. Alloxan administration with or without ischemia reperfusion showed symptoms of severe nephropathy (decreased creatinine clearance, increased BUN, presence of glomerular matrix formation, tubular necrosis, interstitial inflammation as well as fibrosis. The daily oral administration of IND01 exhibited powerful and mild renoprotective effects on biochemical parameters against diabetic rats without ischemia (early nephropathy) and with ischemia model respectively. IND01 exhibited moderate protection from histological abnormalities in kidney of alloxan-induced rats without ischemia reperfusion injury (Farshad H. et.al.2013).

Role in Respiration

A study was performed to determine the efficiency of *Trigonella foenum graecum* (fenugreek) seeds in mild asthma. The participants were divided to three groups randomly. One group received fenugreek syrup one received honey syrup and the third got placebo. Duration of treatment was four weeks. Quality of life, Lung function tests and IL-4 levels were evaluated before and after treatment. After study there was substantial increase in quality of the life as well as lung function tests and IL-4 levels in fenugreek and honey groups. Moreover, FEV1 level was better more than 10% in fenugreek group. Treatment was well tolerated. No serious side effects were reported during the study. (Farshad H. et.al.2013)

Immunomodulatory effects

Immunomodulatory activity of aqueous extract of *Trigonella foenum graecum* L., was assessed in mice. Mice were treated with three doses of extract (50, 100 and 250 mg/kg body weight per

os) for 10 days. At doses of 50 and 100 mg/kg, a significant increase in relative organ weight of thymus was noticed. As regards lymphoid organ cellularity, cellularities of thymus and bone marrow were significantly increased. *T. foenum graecum* extract elicited a significant ($p < 0.001$) increase in the DTH response at doses of 50 and 100 mg/kg, Humoral immunity as measured by PFC showed an elevated response at a dose of 100 mg/kg, and in HT test, plant extract also showed modulatory effect at all the doses. The immunomodulatory activity of ethanolic extract of Fenugreek was studied for phagocytic activity, cell mediated and humoral immune system based on mice model. Fenugreek showed considerably high phagocytic index against control group, demonstrating stimulation of the reticulo-endothelial system. Substantial decrease in mean difference, in the foot paw thickness in DTH indicates its anti-inflammatory activity. In Fenugreek treated groups at 200 and 400 mg/kg doses showed significant increase in antibody titer whereas in T-cell population test, exhibited substantial increase in T-cell rosette formation against control (Farshad H. et.al. 2013).

Role in bone/osteoporosis

The effects of fenugreek seed on bone mechanical properties in rats with normal and decreased estrogen level (developing osteoporosis) was investigated. Result revealed that fenugreek seed added to food did not meaningfully affect bone mineralization and serum turnover markers, independently of the estrogen status. It inclined to increase the strength of the tibial metaphysis (cancellous bone) in non ovariectomized rats, and increased the strength of the femoral diaphysis (compact bone) in ovariectomized rats. Finally, study concluded that low dietary intake of fenugreek seed may cause slight favourable skeletal effects, while at high doses it might damage the skeletal system. The role of dietary *Trigonella foenum graecum* seed extract on bone structure and mechanical properties in ovariectomized rats was examined. Result revealed that maximum flexor load to break femur bone was meaningfully low in ovariectomized rats in comparison with control rats. Supplementation with *Trigonella foenum graecum* pointedly improved the maximum flexor load and tibia dry weight

compared to ovariectomized untreated rats. *Trigonella foenum graecum* administration also meaningfully conserved the trabecular and cortical bone thickness compared to ovariectomized rats. Overall, this finding advocates that dietary intake of *Trigonella foenum graecum* seeds can improve the bone structure and biomechanical properties in ovariectomized rats demonstrating that *Trigonella foenum graecum* may be an alternative treatment approach to prevent the menopause induced osteopenia. (Gaur V. et.al, 2013)

Role in reproductive system

The effects of fenugreek seeds on the severity of primary dysmenorrhea among students was examined. Unmarried Students were arbitrarily allocated to two groups who got fenugreek or placebo. Result demonstrated that pain severity at baseline did not differ suggestively between the two groups. Pain severity was meaningfully reduced in both groups after the intervention; however, the fenugreek group experienced significantly larger pain reduction. Moreover, systemic symptoms of dysmenorrhea decreased in the fenugreek seed group. Overall, study concluded that prescription of fenugreek seed powder during menstruation can reduce the severity of dysmenorrhea. (Gaur V. et.al, 2013),

Anti-cancer effect

Medicinal plants or their active compound has proven role in cancer inhibition and prevention. Moreover, Medicinal plants or their chief ingredients confirm its role in cancer management through modulating various biological activities. The extract from the seeds of fenugreek, are cytotoxic *in vitro* to a panel of cancer but not normal cells was examined. Treatment with 10-15 ug/mL of extract showed growth inhibitory to breast, pancreatic and prostate cancer cell lines. When tested at higher doses (15-20 ug/mL), extract continued to be growth inhibitory to PCa cell lines. Moreover, at least part of the growth inhibition is due to induction of cell death, as noticed by incorporation of Ethidium Bromide III into cancer cells exposed to extract. The effect of diosgenin on breast cancer cell lines was examined. Cytotoxic assays revealed that diosgenin decreased the viability of both the ER

positive MCF-7 cells and ER negative MDA 231 cells. A substantial induction of apoptosis by diosgenin was noticed in both the breast cancer cell lines. In MCF-7 cells diosgenin induced p53 protein expression and also down regulated ER activation. Though, in MDA 231 cells diosgenin increased caspase activation and also down regulated Bcl-2 protein expression. Another study based on osteosarcoma reported that diosgenin inhibits receptor-activated nuclear factor-kappa B ligand-induced osteoclastogenesis, suppresses tumor necrosis factor-induced invasion, and blocks the proliferation of tumor cells. Moreover, diosgenin suppressed TNF-induced NFkappaB activation, activation of IkappaBalpha kinase, IkappaBalpha phosphorylation, IkappaBalpha degradation, p65 phosphorylation, and p65 nuclear translocation via inhibition of Akt activation. Finally, study propose that diosgenin suppresses proliferation, inhibits invasion, and suppresses osteoclastogenesis *via* inhibition of NF-kappaB-regulated gene expression and enhances apoptosis. Another study based on a mouse xenograft model reported that a combination of Thymoquinone (TQ) and diosgenin (DG) meaningfully reduced tumor volume, mass as well as increased apoptosis. Thymoquinone (TQ) and diosgenin (DG), alone and in combination, inhibit cell proliferation as well as induce apoptosis in squamous cell carcinoma. The combination of Thymoquinone (TQ) and diosgenin (DG) is a potential antineoplastic therapy in this common skin cancer.⁵ The effect of diosgenin on TRAIL-induced apoptosis in colorectal cancer cell lines was examined. It was reported that diosgenin sensitizes colorectal cancer cell lines HT-29 cells to TRAIL-induced apoptosis. Mechanisms primary this sensitization mostly involved diosgenin-induced p38 MAPK pathway activation and subsequent DR5 overexpression. Additionally, it was confirmed that diosgenin alone, TRAIL alone or combination treatment increased cyclooxygenase-2 expression and that the use of a cyclooxygenase-2 inhibitor further increased apoptosis induction.⁷⁵ Anti-cancer activity of diosgenin and its mechanisms in chronic myeloid leukemia (CML) cells. Diosgenin-induced autophagy and cytotoxicity were conveyed by

reactive oxygen species generation and mammalian target of rapamycin signaling pathway inhibition. Result confirmed that diosgenin clearly generates reactive oxygen species and this oxidative pressure not only produces cytotoxic effect on chronic myeloid leukemia cells and induces autophagy. The preventive effectiveness of fenugreek seed and its major constituent, diosgenin, on azoxymethane-induced rat colon carcinogenesis during initiation and promotion stages was investigated. Dietary FSP at 1% and diosgenin at 0.1% fed only during the promotional stage also inhibited total ACF up to 33%. Additionally, diosgenin induced apoptosis in HT-29 cells at least in part by inhibition of bcl-2 and via induction of caspase-3 protein expression. The impact of diosgenin on the human mammary carcinoma cell line and to examine its therapeutic potential against *N*-nitroso-*N*-methylurea - induced experimental breast cancer. *In vitro* studies, diosgenin significantly inhibited the proliferation of MCF-7 cells in a dose dependent manner and. Elevated lipid peroxidation in *N*-nitroso-*N*-methylurea-induced breast cancer-bearing animals were drim down due to management with steroidal diosgenin. From the finding, it was reported that diosgenin may be used as a chemoprotective agent against human mammary carcinoma. The anticancer properties and proteomic profiles of fenugreek seeds, and is encouraged by the clinical profile of a case of primary CNS T cell lymphoma that countered to fenugreek treatment and resulted in tumor regression. It was noticed that selective cytotoxic effects of fenugreek extract *in vitro* to a panel of cancer cell lines, including T-cell lymphoma. Overall, *in vitro* effect of fenugreek as a substance with significant cytotoxicity to cancer cells points to the potential usefulness of fenugreek in the prevention and treatment of cancer. Crude methanol extract of Fenugreek seeds was prepared and its anticancer mechanism was assessed, through HepG2 cell line. Result confirmed that extract treatment showed a cytotoxic effect and apoptosis induction in a dose-dependent manner that was arbitrated by upregulation of p53, Bax, PCNA, and caspase-3 activation in HepG2 cells. Overall, extract act as a promising nontoxic herbal with therapeutic

potential to induce apoptosis in HepG2 cells via p53, Bax, and PCNA upregulation in caspase-3 dependent manner.

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.

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. 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 (Madhesh M. 2011).

CONCLUSION

Fenugreek is historically assumed and supposedly consumed as a medicative plant since prehistoric time and is without doubt thought of safe to human health. Its biological process worth and biologically active compound profile square measure unquestionably appreciated by life science. Moreover, drought, saline and

serious metal tolerability, wide ability to varied climatic regions and marginal lands square measure the potentialities of this crop to carry a righteous place in agricultural systems. However, sadly simply many advances are created for crop improvement nevertheless. Hence, a large gap continues to be existing notably in varietal development and additional specifically in biotechnologically expedited breeding.

ACKNOWLEDGEMENTS

Authors are thankful to the Principal and management of SMBT Institute of D. Pharmacy, Nashik-422401, India.

FUNDING SUPPORT

None.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. Ahmad A., Alghamdi S., Mahmood K. (2016). Fenugreek a multipurpose crop: Potentialities and Improvements, Saudi Journal of Biological Sciences, 2(3), 300–310.
2. Almatroodi A. Alsahli S. (2021). Fenugreek (*Trigonella Foenum-Graecum*) and its Active Compounds: A Review of its Effects on Human Health through Modulating Biological Activities, Pharmacognosy Journal, 13(3), 813-821.
3. Buqui, G. A., Sherwin K. (2015). Characterization of Intestinal Absorption of C-glycoside Flavonoid Vicenin-2 from *Lychnophora ericoides* Leafs in Rats by Nonlinear Mixed Effects Modeling, Brazilian journal of pharmacognosy, 2(5), 212–218.
4. Farshad H. Behzad V., Shafiee M. (2013). Fenugreek seed extract treats peripheral neuropathy in pyridoxine induced neuropathic mice, Excli Journal, 1(2), 282–290.
5. Gaur S., Bodhankar L., Mohan V., Thakurdesai P. (2013). Neurobehavioral assessment of hydroalcoholic extract of *Trigonella foenum-graecum* seeds in rodent models of Parkinson's disease, *Pharmaceutical Biology*, 51(5), 550–557.
6. Goyal S., Gupta N, Chatterjee S. (2016). Investigating Therapeutic Potential of *Trigonella*

foenum-graecum L. as Our Defense Mechanism against Several Human Diseases, Journal of Toxicology, 21(1), 53-62

7. Joglekar M. (2012), Comparative analysis of antioxidant and antibacterial properties of *Aegle marmelos*, *Coriandrum sativum* and *Trigonella foenum graecum*. Actan Biol. Indica, 1 (1),105-108.

8. Kandhare, A. Bodhankar S., Mohan V. (2015). Pharmacokinetics, Tissue Distribution and Excretion Study of a Furostanol Glycoside-based Standardized Fenugreek Seed Extract in Rats. *Renal Failure*, Informa healthcare, 3(7), 1208–1218.

9. Kandhare, A., Bodhankar S., Mohan V. (2016). Development and Validation of HPLC Method for Vicenin-1 Isolated from Fenugreek Seeds in Rat Plasma: Application to Pharmacokinetic, Tissue Distribution and Excretion Studies, *Pharmaceutical Biology*,5(4), 2575–2583.

10. Kaviarasan V. (2007). Fenugreek (*Trigonella foenum graecum*) seed polyphenols protect liver from alcohol toxicity: a role on hepatic detoxification system and apoptosis in Chang liver cells, *Epub*, 62(4), 299- 304.

11. Liu, Y. (2012). Compounds in functional food fenugreek spice exhibit anti-inflammatory and antioxidant activities. *Food Chem.*, 13(1), 1187–1192.

12. Madhesh M., Revathi R., Vaiyapuri M. (2011). Cardio protective effect of fenugreek on isoproterenol-induced myocardial infarction in rats, *Indian Journal of Pharmacology*, 43(5), 516–519.

13. Mallik A., Bhattacharjee C. (2019). *Trigonella foenum-graecum*: A review on its traditional uses, phytochemistry and pharmacology, *International Journal of Advances in Scientific Research*, 5(5), 1-12.

14. Mooventhan A. (2017). A Narrative Review on Evidence-based Antidiabetic Effect of Fenugreek (*Trigonella foenum-graecum*), *International Journal of Nutrition, Journal of Pharmacology*,7(4), 84-87.

15. Pandian R., Viswanathan P. (2002). Gastroprotective effect of fenugreek seeds (*Trigonella foenum-graecum*) on experimental

gastric ulcer in rats, Journal of Ethnopharmacology, 8(1), 393– 397.

16. Prema A., Manivasagam T. (2016). Fenugreek Seed Powder Nullified Aluminium Chloride Induced Memory Loss, Biochemical Changes, A β Burden and Apoptosis via Regulating Akt/GSK3 β Signaling Pathway. Plos one, 11(11), 01-19.

17. Pundarikakshudu K, Shah D. (2016). Anti-inflammatory activity of fenugreek (*Trigonella foenum-graecum* Linn) seed petroleum ether extract. Indian Journal of Pharmacology, 48(4), 441-444.

18. Reddy RR, (2011), Hepatoprotective and antioxidant effect of fenugreek (*Trigonella foenum-graecum*) seeds in mice under lithogenic condition. Journal of Food Biochemistry, 3(5), 1619–26.

19. Said A.M., Al-Khashali D. (2011). The hepatoprotective activity of Fenugreek seeds' extract against carbon tetrachloride induced liver toxicity in rats, Al-Mustansiriyah Journal of Pharmaceutical Sciences, 9(1) 94-103.

20. Shishodia S, Aggarwal B. (2006). Diosgenin inhibits osteoclastogenesis, invasion, and proliferation through the downregulation of Akt, I kappa B kinase activation and NF-kappa B-regulated gene expression. Oncogene, 25(10),1463-1473.

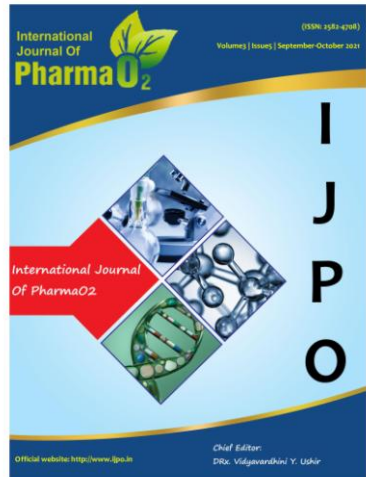
21. Singaravelu S. Sankarapillai J., Chandrakumari A. (2018). Effect of *Trigonella foenum-graecum* (Fenugreek) Seed Extract in Experimentally Induced Gastric Ulcer in Wistar Rats. A Multifaceted Journal in the field of Natural Products and Pharmacognosy, 10(6), 1169-73.

22. Sultan S.I. Al and S.M. El-Bahr, (2015). Effect of Aqueous Extract of Fenugreek (*Trigonella foenum-graecum* L.) On Selected Biochemical and Oxidative Stress Biomarkers in Rats Intoxicated with Carbon Tetrachloride. International Journal of Pharmacology, 11: 43-49.

23. Syed A.Q. Rashid Z. (2020). Nutritional and therapeutic properties of fenugreek (*Trigonella foenum-graecum*): a review, International journal of food properties, 23(1), 1777–1791.

24. Thirunavukkarasu V, Anuradha C.V. (2007). Gastroprotective effect of fenugreek seeds

(*Trigonella foenum-graecum*) on experimental gastric ulcer in rats. Journal of Herbs, Spices, & Medicinal Plants, 12(3), 13–25.



IJPO is

- Peer reviewed
- Bi-monthly
- Rapid publication
- Submit your next manuscript at journalpharma02@gmail.com