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Review Article

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A Brief Study on Fenugreek (*Trigonella Foenum-Graecum*): A Review

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ABSTRACT

Fenugreek (*Trigonella foenum-graecum*) is one of the oldest medicinal plants with exceptional medicinal and nutritional profile. Fenugreek is native to southern Europe and Asia, is an annual herb with white flowers and hard, yellowish brown and angular seeds, known from ancient times, for nutritional value beside of it medicinal effects. 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, calcium, iron and many other functional elements. *Trigonella foenum-graecum* was used as a traditional remedy for the treatment of various diseases. In this study after a general discussion of chemical constituents, the biological and pharmacological actions of fenugreek such as Anti-diabetic activity, Hypocholesterolaemic properties, Immunomodulatory activity, Anti-oxidant activity, Anti-cataract activity and Anti- carcinogenic activity were briefly reviewed. Current lifestyle, eating habits, stress, environmental factors and intensive use of synthetic chemicals in food processing and agriculture have radically increased the progression of several human diseases. Globally, researchers have been looking for natural therapeutic substances that can be used to treat or delay the onset of these lifestyle-related disorders. Overall, this review highlights the morphology, adaptability, nutritional constituents, and associated functionality and medicinal significance of Fenugreek.

Key Words: *Fenugreek (Trigonella foenum-graecum), Immunomodulatory activity, Anti-oxidant activity, Anti-cataract activity and Anti- carcinogenic activity.*

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INTRODUCTION

Fenugreek belongs to Fabaceae family; it was named, Trigonella, from Latin language that means "little triangle" due to its yellowish-white triangular flowers [1]. It is named as Methi (Hindi, Urdu, Punjabi and Marathi), Hulba (Arabic), Moshoseitaro (Greek), Uluva (Malayalam), Shoot (Hebrew), Dari (Persian), and heyseed in English. Fenugreek (*Trigonella foenum-graecum* L.) is one of the oldest medicinal plants from Fabaceae family originated in central Asia ~4000 BC [2]. Its description and benefits had been reported in the Ebers Papyrus (one of the oldest maintained medicinal document) earlier in 1500 BC in Egypt [3]. It is being commercially grown in India, Pakistan, Afghanistan, Iran, Nepal, Egypt, France, Spain, Turkey, Morocco, North Africa, Middle East and Argentina [4]. The most accurate number of species of fenugreek has not been identified till now. Taxonomists such as Linnaeus noted that 18 species of *Trigonella* are currently in a total of 260 species. Taxonomic classification of fenugreek was presented (Table 1). Most species, including *Trigonella foenum graecum* L., are diploids with 2n = 16 chromosomes. However, some species of *Trigonella* may include 18, 28, 30, 32 or 44 chromosomes [5]. Fenugreek has different pharmacological attributes such as a hypoglycemic[6] , hypercholesterolemia[7-12] , gastroprotective[13] , chemo-preventive[14] , an anti-oxidant[15] , and laxative[16] and appetite stimulation[17]. The plant contains alkaloids[18] flavonoids[19], salicylate[20], and nicotinic acid[21]. Fenugreeks are harmless for human consumption.

Table 1: Taxonomy of *Trigonella foenum-graecum*

Kingdom	Plantae
Super division	Angiosperms
Division	Eudicots
Class	Rosids

Order	Fabales
Family	Fabaceae
Subfamily	Faboideae
Tribe	Trifolieae
Genus	Trigonella
Species	Foenum

Figure.1 *Trigonella foenum-graecum*

Morphology
Appearance: Solid-rhomboidal seeds, 3 to 5 mm long, 2 mm thick. Hard, pebble-like.
Colour: Yellowish brown-light brown
Odour: characteristic spicy
Taste: Bitter and mucilaginous

The Fenugreek Plant

The fenugreek seeds sown in well prepared soil sprouts in three days. Seedling grows erect, semi-erect or branched and attains a height of 30 to 60 cm. It contains pinnate compound, trifoliate leaves, auxiliary white to yellow flowers, and 3-15 cm long thin pointed beaked pods and every pod contains 10-20 oblong greenish-brown seeds with unique hooplike groves[22]. Fenugreek is the only single plant of Fabaceae family which is pollinating annual leguminous bean[23].

Stem

Fenugreek having a number of steroidal sapogenins. Only the oily embryo contains diosgenin, the trimethylcoumarin, alkaloid trigonelline, trigocoumarin and nicotinic acid are been found in stem. Mucilage is a dominant ingredient of the seeds [24]. Further researches proved that approximately 28% mucilage, 5% of a stronger smelling, bitter fixed oil, 22% proteins, a volatile oil, two alkaloids and a yellow colouring substance are present in stem [25].

Figure.2 Stem of *T. foenum graecum*

Leaves

Fenugreek leaves are trifoliate, triangular stipules, 10- 30mm long, 5-15 mm wide, truncate at apex, narrowed towards the base, margins shallowly serrate to dentate glabrous. The leaves contain 7 saponin compounds, known as graecunins and these are glycosides of diosgenin. Leaves having rich sources of mineral and vitamin contents like phosphorus, iron, carotene, calcium, riboflavin, thiamine and vitamin-c [26] .

Figure.3 Leaves of *T. foenum graecum*

Seeds

Seeds are rhomboidal, pebble like shape, 3-5 cm. long, 2mm thick, plain surface, yellow in colour. Bulk of the fenugreek seed is dietary fiber and protein both of which have no taste or flavor[27] . Plant tissue cultures from seeds grown under optimal conditions have been found to produce as much as 2% diosgenin with fewer quantities of gitongenin and trigogenin. The major components of fenugreek seeds are highly carbohydrates, proteins, flavonoids, alkaloids, saponin, free amino acids, glycosides, mucilage, minerals and much more[28]. Further investigations have shown its effectiveness in diminishing blood glucose levels, treating gastric abnormalities on lowering cholesterol[29].

Figure.4 Seeds of *T. foenum graecum*

Cultivation

Fenugreek requires 5–10 days for germination while the first trifoliate leaf appears 5–8 days after germination. It is a fast growing plant, which may grow on dry grasslands, cultivated or uncultivated lands, hillsides, planes as well as field edges but it requires a fair amount of sunlight. Fenugreek needs four to seven months to reach maturity[30]. Flowering period is midsummer (June to August) and seeds ripen during late summer (August to September). It is a drought tolerant plant and grows well in tropical climate with mild winter and cool summer; however, its leaf and flower development is temperature dependent[31].

Figure.5 Germination of *T. foenum graecum*

Nutritional value of Fenugreek

Fenugreek has a vast diversity of nutrients and bioactive compounds which are required for improving the health and functionality of biological systems. The fenugreek seeds have 58% carbohydrates, 23- 26% proteins, 0.9% fats and 25% fibre. Similarly, fenugreek leaves have 6%, 4.4%, 1.1% carbohydrates, proteins and fibre respectively[32]. Furthermore, fenugreek also contains different types of minerals such as potassium (603 mg/100 g), magnesium (42 mg/100 g), calcium (75 mg/100 g), zinc (2.4 mg/ 100 g), manganese and copper (0.9 mg/100 g) and iron (25.8 mg/100 g). Vitamin C (220 mg/100 g) and β carotene (19 mg/100 g) are also considered as the important components of fenugreek[32,33].

Fenugreek is also a rich source of several important amino acids such as aspartic acid, glutamic acid, leucine, tyrosine and phenylalanine. Additionally, it contains minute quantities of sulfur-containing amino acids (cysteine and methionine) having significant physiological roles in body. The most abundantly present free amino acid in fenugreek is (2S, 3 R, 4S)-4-hydroxyisoleusine. About 80% of amino acid content of dry fenugreek seeds consists of the non-protein amino acid 4-hydroxyisoleusine and during the phase of growth, this amino acid proliferates rapidly. Studies have revealed that the proteins present in the fenugreek are of better quality as compared to the other plant proteins. In an investigation, Feyzi and his coworkers compared the quality of fenugreek proteins with soy protein isolate and affirmed that fenugreek seeds contain higher protein contents with better amino acid profile as compared to soy protein isolate.[34] Additionally, fenugreek proteins were rich in aspartic acid and glutamic acid. Results also stated that fenugreek proteins have higher denaturation temperature, foaming properties, solubility and stability as compared to soy proteins and therefore can be employed as an effective protein source in various functional foods. Moreover, sotolone, an important functional phytochemical used as seasoning flavor, is a prompting ingredient of fenugreek.[35]

Fenugreek contains significant quantities of alkaloids (trigonella, trigocoumarin, nicotinic acid, trimethyl coumarin). It also comprises other important, valuable compounds like flavonoids and polyphenols. In the alcoholic extracts of the fenugreek plant, extensive variety of flavonoids, such as quercetin, luteolin, vitexin, and 7, 4-dimethoxy flavanones, is present. Some other groups have reported alike results of the existence of aglycones, kaempferol, quercetin, tricin, and naringenin[36]. The compounds were sequestered from the specific parts of fenugreek plant and also from the excerpts and hydro lysates of stems, leaves and flowers. The phytochemical examination of fenugreek exposed that the maximum of flavonoids are existent as glycosides which are complex due to the conjugation with carbohydrates by C-glycosidic and O-glycosidic bond. Quercetin-3-O-rhamnoside (quercitrin), vitexin-7-Oglucoside (afroside), and apigenin-6-C-glucoside (isovitexin) are rare examples of flavonol glycosides existing in fenugreek[37]. Apigenin-6-C-glucoside (isovitexin) and apigenin-8-C-glucoside (vitexin) were sequestered by fenugreek seeds. The occurrence of isoflavonoid phytoalexins aglycones, such as medicarpan and maackiaian, in this herb has also been reported. These are known as 'induced isoflavoniods' which can be produced due to some external factors such as microbial activities[35].

Table 2: Crude or proximate composition of fenugreek seeds and leaves[38]

Particulars	Contents (g/100 g)	References
Carbohydrates	42.3	[38]
Gum (seeds)	20.9	[39]
Ash (seeds)	3.38	[40]
Fibre (seeds)	50.0	[41]
Soluble		
Raw	21.7	[42]
Germinated	10.3	[42]
Insoluble		
Raw	26.8	[42]
Germinated	23.9	[42]
Fibre (leaves)		
Soluble	0.7	[43]
Insoluble	4.2	[43]
Dietary fibres	48.0	[44]
Fats (Seed)	7.9	[38,41]
Fats (Leaves)	1.0	[41]
Protein (Seed)	25.4	[38]
Protein (Leaves)	4.4	[41]
Moisture (Seed)	7.49	[40]
Moisture (Leaves)	86.0	[40]

Table 3: Lipid profile of Fenugreek seeds[45]

Lipid Species Identified	Amount (g/100 g)
Triacylglycerols	4.330 ± 0.011
Triacylglycerols	0.280 ± 0.008
Monoacylglycerols	0.180 ± 0.005
Phosphotidylcholine	0.110 ± 0.002
Phosphotidylethanolamine	0.036 ± 0.003
Phosphotidylinositol	0.009 ± 0.001
Free fatty acids	0.160 ± 0.001

Table 4: Vitamin profile and their respective concentrations in fenugreek

Particulars	Plant part	Units	Value/100 g	References
Vitamin C	Seed	Mg	12-43	[46,47]
Vitamin C	Leaves	Mg	52.0	[47]
Vitamin B_1	Seed	mg	0.41	[46]
Vitamin B_2	Seed	mg	0.36	[46]
Vitamin B_6	Seed	mg	0.600	[48]
Vitamin A, RAE	Seed	µg-RAE	3.0	[48]
Vitamin A	Seed	IU	60-100	[46]
Niacin	Seed	mg	6.0	[46]
Nicotinic Acid	Seed	Mg	1.1	[46,47]
Nicotinic Acid	Leaves	µg	800	[47]
β-carotene	Leaves	mg	2.3	[47]
β-carotene	Seeds	µg	96	[47]
Thiamine	Leaves	µg	40	[47]
Thiamine	Seeds	µg	340	[47]
Riboflavin	Leaves	µg	310	[47]
Riboflavin	Seeds	µg	290	[47]
Folic acid	Seeds	µg	84	[47]

Table5: Mineral contents (mg/100 g) of fenugreek seeds[49]

Minerals	mg/100 g of fenugreek seed extract
Potassium (K)	603.0 ± 15.0
Magnesium (Mg)	42.0 ± 5.0

Calcium (Ca)	75.0 ± 9.0
Zinc (Zn)	2.4 ± 0.2
Manganese (Mn)	0.9 ± 0.1
Copper (Cu)	0.9 ± 0.1
Iron (Fe)	25.8 ± 1.2

Table 6: Biologically active constituents of Fenugreek and their classifications

Chemical Group	Compounds	References
Alkaloids	Trigonelline, choline, carpaine	[50,51,52]
Amino Acids	Lysine, histidine, 4-hydroxyisoleucine, tryptophan, tyrosine, cystine, arginine	[53,54,55]
Coumarins	Methyl coumarin, trigocumarin, trimethyl coumarin	[56]
Flavonoids	Naringenin, lilyn, kaempferol, vecenin-1, tricin 7-O-D glucopyranoside, saponaretin, isovitexin, isoorientin. Orientin, vitexin, luteolin, quercetin	[57,58,59]
Saponins	Fenugrin, foenugracin, glycoside, yamogenin, trigonoesides, smilagenin, gitogenin, sarsasapogenin, yuccagenin, hederagin, diosgenin, tigonenin, neotigogenin	[53]
Others	Vitamin A, folic acid, ascorbic acid, thiamin, riboflavin, biotin, nicotinic acid, gum	[60,61]

Nutritional/health impacts of fenugreek components

Table 7. A generalized discussion about the nutritional impacts of fenugreek

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

PHARMACOLOGICAL ACTIONS OF FENUGREEK

Anti-diabetic activity

The harmful side effects of synthetic drugs, the enormous cost and the in ability of existing modern therapies to control all pathological aspects and the poor advance therapies for many rural populations in developing countries are the major drawback of synthetic drugs, to overcome these issues the plant compounds are used now a days, fenugreek plays a vital role in treating several diseases. The anti-diabetic activity of fenugreek was briefly discussed. Postprandial blood glucose response has reduced by soluble fiber, Galactomannan, it is isolated from Canadian grown fenugreek seeds. In vitro studies were conducted to identify the effect of galactomannan on intestinal glucose uptake in genetically determined lean and obese rats. The viscosity of different combinations of galactomannan solutions was prepared. The galactomannan as of the viscous property it has potential to reduce intestinal absorption of low or high concentration of glucose and; therefore for the benefit of blood glucose control[62].

It was reported that adding 100 g fenugreek powder containing 50 percent dietary fiber for a period of 10 days decreased 25 percent blood glucose level among the type II diabetes patients[63]. It has been shown that soluble fiber fraction reduced postprandial elevation in blood glucose level of Type 2 model diabetic rats by hindering the digestion of sucrose. Administering fenugreek soluble fiber orally twice daily at a dose of 0.5 g/ kg for 28 days resulted in reducing the serum fructosamine level with no significant change in the insulin level when compared with the control. It is concluded that soluble fiber had a beneficial effect on dyslipidemia and it could inhibit platelet aggregation in Type 2 model diabetic rats[64].

The anti-diabetic properties of a Soluble Dietary Fibre [SDF] fraction of Trigonella foenum-graecum were evaluated. Administration of SDF fraction [0.5 g/kg body weight] to normal, type 1 or type 2 diabetic rats significantly improved oral

glucose tolerance. Effects of soluble dietary fibre of Trigonella foenum-graecum on sucrose absorption from the gut, on intestinal glucose absorption, on intestinal disaccharidase activity and gastrointestinal motility, on insulin secretion, on glucose uptake and insulin action were determined.They demonstrated that SDF fraction of Trigonella foenumgraecum significantly improved glucose homeostasis in type I and type II diabetes by delaying carbohydrate digestion and absorption, and enhancing or mimicking insulin action. After oral sucrose ingestion in non-diabetic and type 2 diabetic rats, SDF fraction suppressed the elevation of blood glucose. Glucose transport in 3T3-L1 adipocytes and insulin action was increased by Trigonella foenum-graecum. They indicated that the SDF fraction of Trigonella foenum-graecum seeds applies anti diabetic effects mediated during inhibition of absorption and carbohydrate digestion, and enhancement of peripheral insulin action[65].

It is reported that addition of fenugreek (5.5 g) to 50 g carbohydrate portions of white bread and jam and fried rice meaningfully diminish incremental area under the plasma glucose response curve (IAUC) in comparison with food without fenugreek. It is noted that postprandial plasma glucose and satiety (PPG) remarkably decreased and increased respectively between obese persons[66].

Diabetes	4-hydroxyisoleucine (amino acid) stimulates insulin production thereby control blood sugar level	53,67,68
	Polyphenolic compounds exhibit anti-diabetic effects	51,69
	Curative effects of fenugreek seed powder is a potential neuropathic medicine in diabetes	70

Hypocholesterolaemic Properties

There are different important scientific information and clinical data done on the efficacy of dietary fiber, especially the soluble counterpart such as beta-glucans or galactomannans in the management of hypercholesterolemia. Fenugreek derived galactomannans, due to its unique structure of galactose to mannose 1:1 ratio, have shown to have the maximum efficacy in lowering the plasma cholesterol level[71]. Furthermore, soluble fiber fractions reduce only the dangerous low-density lipoproteins and triglycerides intake, whereas keeping the good high-density cholesterols intact[72].

In a study which was done on 60 individuals with diabetes and high cholesterol and triglycerides level, who regularly received 25 g of fenugreek fiber powder containing nearly 50 percent fiber content, a significant decrease in blood glucose, LDL cholesterol and triglycerides level up was shown whereas HDL level had no decrease (43). The biochemical mechanism of soluble fiber as a hypolipidemic agent can be explained primarily by its capacity to bind bile acids, which are therefore excreted rather than recycled to the blood reduced blood cholesterol. Fermentation of soluble fiber may be done by bacteria in the clone which produce short chain fatty acids can reduce cholesterol synthesis[73].

Eidi et al. (2007) reported that an ethanolic extract of FEN decreased total cholesterol and triacylglycerol in streptozotocin induced diabetic rats. The mechanism was not determined, but the hypolipidemic effect could be due to the inhibition of carbohydrate and fat absorption due to the fibre contained in the extract[74]. Raju and Bird (2006) reported that a reduction in liver weight and less marbling of liver fat was observed during supplementing the diet of Zucker obese rats with 5 % FEN seed when compared to obese controls[75]. The effects of two concentrations of FEN seed powder (12.5 g and 18.0 g/ day) on the blood lipid profile of human subjects over a month was studied by Sowmya and Rajyalakshmi (1999)[76]. They understood that both concentrations led to a reduction in total cholesterol and low-density lipoprotein (LDL). It should be noted that there are several published studies on the hypolipidemic potential of fenugreek in animals, while only a few ones in humans. Some of the mechanisms which proposed for the effects are stimulation of bile formation in the liver and the transformation of cholesterol into bile acids, the viscosity of the digest reducing cholesterol and bile acid absorption and the production of volatile fatty acids by fiber fermentation, which seems to prevent hepatic cholesterol synthesis[77].

Hypercholesterolemia	Anti-oxidants from seeds control high blood cholesterol	40,47
	Flavonoids from ethyl acetate extracts of seeds exhibit hypocholesterolemic abilities	78

Immunomodulatory activity

An agent that increases or reduces the immune responses is known as immunomodulator and such effect is immunomodulatory effect. Fenugreek in the diet showed a mark reduction in signs & symptoms of diabetes like polyuria, urine sugar, renal hypertrophy, excessive thirst and glomerular filtration rate[79]. Aqueous extract of fenugreek was investigated to ameliorate additive urotoxicity of buthionine, sulfoximine and cyclophosphamide by restoring the anti-oxidant status and reversing the cyclophosphamide-induced cell death in free radical-mediated lipid peroxidation in the

urinary bladder[80]. To assess the immunomodulatory activity male albino mice were treated with three doses of aqueous extract of fenugreek 50, 100, 250 mg/kg of body weight respectively for 10 days. The increase in thymus weight was due to by an increase in cell counts. This may be due to the stimulatory effect of plant extract on the lymphocytes and bone marrow hematopoietic cells[81].

Immunodeficiency	Natural antioxidants help to strengthen immune system Immunomodulatory and Immune stimulatory effects	82 83

Anti-oxidant activity

Since the antioxidant activity of a plant is due to its active phytochemicals, it has been announced that fenugreek possesses a great antioxidant property that has a beneficial effect on the liver and pancreas because of its phenolic and flavonoid compound. It has been stated that fenugreek seed extract reduces lipid peroxidation and hemolysis in RBC[84]. Dixit et al. 2005 have shown that the aqueous fraction of fenugreek exhibit higher antioxidant activity compared with other fractions[85]. Fenugreek extract scavenges hydroxyl radicals and inhibits H2O2- induced lipid peroxidation in rat liver mitochondria[86].

Germinated fenugreek seeds showed more beneficial than dried seeds due to the fact that the bioavailability of different constituents of fenugreek seed were increasesed by germination[87]. In fact, significant antioxidant activity in germinated fenugreek seeds may be related to the presence of flavonoids and polyphenols. It was reported that mustard and fenugreek seeds showed hypoglycemic and antihyperglycemic activities in diabetic mice, which could be due to the presence of antioxidant carotenoids in those spices[88].

The functional food quality of fenugreek seeds were assessed by determining the lipid peroxidation [LPO] and cyclooxygenase enzyme [COX] inhibitory activities in hexane, ethyl acetate, methanolic and water extracts using MTT, LPO, COX-1 and COX-2 enzyme inhibitory assays. The extracts inhibited LPO by 55–95%, COX-1 by 6–87% and COX-2 by 36–70%, respectively, at 250 g/ml. Bioassay-guided purification of these extracts yielded triglycerides, fatty acids, saccharides and flavonoid-Cglycosides. The antioxidant and anti-inflammatory activities exhibited by the isolated compounds from fenugreek seeds support its anecdotal health applications[89].

Anti-cataract activity

Cataract is the opacification in the eye lens and leads to 50% of blindness worldwide. Cataract remains the leading cause of visual disability, and it contributes 50% blindness worldwide.57Several risk factors have been known in the pathogenesis of senile cataract. Despite aging, diabetes, smoking, gender, steroids, and nitric oxide are liable for the growth of cataract[90].

The anti-catatact potential of *Trigonella foenum graecum* was evaluated in selenite induced in vitro medium. The medium was supplemented with selenite and aqueous extract of *T. foenum graecum* to the test group. An increasing level of malondialdehyde and diminishing level of GSH were seen in control as compared to standard lenses. *T. foenum graecum* amazingly restored glutathione & decreased malondialdehyde levels. It also plays an important part in restoration in the anti-oxidant enzymes such as superoxide dismutase, glutathione, peroxidase, catalase and glutathione-s-transferase. Fenugreek protects against the experimental cataract due to its anti-oxidant properties and also significantly restored the GSH levelin a dose-dependent manner[91].

Anti-Carcinogenic Activity

One of the primary causes of death nowadays is cancer in the world. Serious side effects occur with generally used therapeutic medicines which only increase the life span of patient from few months or some years. Plant-based active components have shown their potential to be used as suitable and safe alternatives having significantly explored anticancer effects[92]. In this regard, active ingredients of vegetables and fruits are being utilized to prevent the chances of cancer[93]. Efforts are ongoing to use the other approaches and ideas which can be effective in the prevention of cancer. In these attempts, studies are available in which animals and cell lines were used as the investigational models of cancer proved the effect of seeds of fenugreek against cancer[94].

It was revealed that a compound protodioscin derived from fenugreek exhibits an effect to inhibit the growth against HL60 cells by prompting apoptotic modifications[95]. In another study, extract from the seeds of fenugreek expressively stop the mammary hyperplasia induced by 7,12- dimethylbenz-anthracene and diminished the occurrence of it in rats. It is recommended that increased apoptosis after this edible herb consumption shows effect against breast cancer. The extract of the whole plant of fenugreek (Trigonella foenum-graecum) exhibit the cytotoxicity effect in vitro against the most of the different types of cancer cell lines in human like a neuroblastoma, IMR-32 and HT29 cancer cell line[96].

In another study, the anti-cancer properties of fenugreek extract were investigated against breast, pancreatic and prostate cancers. The findings exposed that the applied extract was effective in inhibiting the growth of cancer cell lines of pancreatic and breast cancers however, no effect was shown on primary or immortalized prostate cells. The possible mechanism for anti-cancer properties of Trigonella foenum graecum extract was the induction of programmed cell death[97].

In Balb-C mice model of Ehrlich ascites carcinoma (EAC), extract of the seed of fenugreek shows the effect against the neoplastic. In mice when the alcohol extract of the fenugreek was administered before and after injection of EAC cell, there was the 70% reduction in tumour cell growth[98]. The extract of fenugreek exhibits a noteworthy effect against the inflammation and improved macrophage cells count as well as peritoneal ooze cells count[96].

Fenugreek contains a crystalline steroid sapogenin, Diosgenin as a starting material for the synthesis of steroid hormones such as cortisone and progesterone. It has the potential to prevent invasion, suppress proliferation and osteoclastogenesis through inhibition of necrosis factor and enhances apoptosis induced by cytokines and chemotherapeutic agents[99].

Cancer	Polyphenolic compounds from seed possess anti-carcinogenic activities	56,100,101

Effect on body weight and obesity

It was observed that the food rich in dietary fiber and protein could increase secretion of the anorexigenic and insulinotropic hormone, glucagon-like peptide-1 (GLP-1) to improve glucose tolerance and reduce weight gain[102]. It has been indicated in some studies, that fenugreek seed extract supplementation is effective in reducing the body and adipose tissue weight. The probable mechanism may be due to flushing out the carbohydrates from the body before entering the blood stream resulting in weight loss and high content of soluble fiber in fenugreek that forms a gelatinous structure which may have effects on slowing the digestion and absorption of food from the intestine and create a sense of satiety[103].

Table 8. Pharmacological and therapeutic benefits of fenugreek as recurrently reported

Disease/ Disorders	Description	References
Myocardial infarction	Trigonelline (anti-oxidant) detoxification of free radicals, high lipid peroxidation and enzymes prevents Myocardial injuries	104
Skin irritation	Seeds extracts reduces the skin irritation and pain Seed powder paste produces skin healing, moisturizing, smoothening, whitening	58 59
Indigestion & flatulence	Fenugreek has been used as laxative It stimulates appetite and act as laxative	58 105
Inflammation	Reduces swelling and pain Mucilage from seed detoxify the oxidants and free radicals to reduce inflammation	58,106 107
Anemia	Prevents red blood cell oxidation Being rich in iron (Fe) seeds are valuable to reduce anemia Restoration and Fe nutrition in iron deficiency patients	51,84 108 109
Aging	Antioxidants improves reduces cell death and aging	84
Kidney disorders	Protects functional and histopathologic abnormalities of kidney in diabetic patients Reduces catalase (CAT) contents and superoxide dismutase (SOD) activity in hypercholesterolemia patients Inhibit accumulation of oxidized DNA to prevent kidney injuries	60,110 111 112
Others	Respiratory disorders, bacterial infection, epilepsy, gout, chronic cough, paralysis, dropsy, piles, heavy metal toxicity, liver disorders and arthritis	84,111,113,114,115

CONCLUSION

Over the last few years, several studies have been carried out on the medicinal and functional properties of fenugreek seeds. Fenugreek is rich in fiber, protein, and due to its valuable bioactive components has promising therapeutic and application. Antidiabetic, antioxidant, anticarcinogenic, hypoglycemic activity, hypocholesterolemic activity are the major

medicinal properties of the fenugreek demonstrated in various studies. Based on these several healthful benefits, fenugreek can be recommended and be a part of our daily diet and incorporated into foods in order to produce functional foods. High fiber, protein content and other bioactive compounds make it a naturally several health promoting herb. Anti-cataract effect of this plant is a significant pharmacological activity, which should be focused more in the future.

REFERENCE

1. Flammang A., Cifone M., Erexson G., Stankowski L(2004). Genotoxicity testing of a fenugreek extract. *Food Chem. Toxicol.*;11:1769–1775.
2. Altuntas E., Ozgoz E., Taser O.F(2005). Some physical properties of fenugreek (*Trigonella foenum-graceum* L.) seeds. *J. Food Eng*;71:37–43.
3. Betty R. Spice India; 2008. The Many Healing Virtues of Fenugreek; pp. 17–19.
4. Flammang A., Cifone M., Erexson G., Stankowski L(2004). Genotoxicity testing of a fenugreek extract. *Food Chem. Toxicol.*;11:1769–1775.
5. Acharya SN, Thomas JE, Bas SK(2006), Fenugreek: an "old world" crop for the "New world", Biodiversity,7, 3-4.
6. Sharma RD, Raghuram TC, Rao NS(1990). Effect of fenugreek seeds on blood glucose and serum lipids in type I diabetes, Eur. J. Clin. Nutr, 44, 301–306.
7. Srinivasan K, (2006). Fenugreek [Trigonella foenum-graecum]: A review of health beneficial physiological effects, Food-Reviews- International, 22, 203–224.
8. Vikas S(2003), Indian Agriculture, Economic Data Research Center, New Delhi, India, 585–587.
9. Acharya SN, Thomas JE, Bas SK(2006), Fenugreek: an "old world" crop for the "New world", Biodiversity,7, 3-4.
10. Sharma RD, Raghuram TC, Rao NS(1990), Effect of fenugreek seeds on blood glucose and serum lipids in type I diabetes, Eur. J. Clin. Nutr, 44, 301–306.
11. Zia T, Nazrul Hasnain S,Hasan SK(2001), Evaluation of the oral hypoglycaemic effect of Trigonella foenum-graecum L. in normal mice, Journal of Ethnopharmacology, 75,191–195.
12. Stark A, Madar Z(1993), The effect of an ethanol extract derived from fenugreek (Trigonella foenum-graecum) on bile acid absorption and cholesterol levels in rats, British Journal of Nutrition, 69, 277– 287.
13. Suja Pandian R, Anuradha CV, Viswanathan P(2002), Gastroprotective Effect of fenugreek seeds (Trigonella foenum graecum) on experimental gastric ulcer in rats, J Ethnopharmacol, 81, 393– 397.
14. Amin A, Alkaabi A, Al-Falasi S, Daoud SA(2005), Chemopreventive activities of Trigonella foenum-graecum (Fenugreek) against breast cancer, Cell Biology International, 687–694.
15. Hettiarachchy NS, Glenn KC, Gnanasambandam R, Johnson MG(1996), Natural antioxidant extract from fenugreek (Trigonella foenumgraecum) for ground beef patties, Journal of Food Science, 516–519.
16. Riad S, El-Baradie AA(1959), Fenugreek mucilage and its relation to the reputed laxative action of this seed. Egyptian Journal of Chemistry, 163–168.
17. Petit P, Sauvaire Y, Ponsin G, Manteghetti M, Fave A, Ribes G(1993), Effect offenugreek seed extraction on feeding behavior in the rat: metabolic-endocrine correlates, Pharmacology, Biochemistry and Behavior, 45, 369–374.
18. Jain SC, Madhu A(1988), Regulation oftrigonellin in Trigonella species by chemical mutagenic treatments, Indian Drugs, 26, 14–16.
19. Kamal R,Yadav R(1991), Flavonoids from Trigonella polycertain-vivo and invitro. Journal of Phytological Research, 4, 161–165.
20. Swain AR, Dutton SP, Truswell AS(1985), Salicylates in foods. Journal of American Dietary Association, 85, 950–960.
21. Rajalaksmi R, Nanavaty K, Gumashta A(1964), Effect of cooking procedures on the free and total niacin content of certain food. Journal of Nutrition and Dietetics, 1, 276–280.
22. Srinivasan K(2006), Fenugreek (Trigonella foenum-graecum): A Review of Health Beneficial Physiological Effects, Food Reviews International, 203-224.
23. Balch PA(2003). Prescription for dietary wellness (2nd edn). Penguin group, New York.
24. Blank I(1996). The flavor principle of fenugreek. Nestlé research center. 211th ACS Symposium. New, 24-28.
25. Sowmya P, Rajyalakshmi P(1996). Hypocholesterolemic effect of germinated fenugreek seeds inhuman subjects, Plant Foods Hum Nutr. 53, 359-365.
26. Brar JK, Rai DR, Singh A, Kaur N(2013). Biochemical and physiological changes in fenugreek (Trigonellafoenumgraceum L.) leaves during storage under modified atmosphere packaging, Journal of food science and technology. 50(4), 696–704.
27. Senthil A, Mamatha BS, Vishwanath P, Bhat KK, Ravishankar GA(2010). Studies on development and storage stability of instant spice adjunct mix from seaweed, Journal of food science and technology, 6.
28. Srinivasan K(2006). Fenugreek (Trigonellafoenum-graecum): A Review of Health Beneficial Physiological Effects, Food Reviews International, 203-224.
29. Balch PA(2003). Prescription for dietary wellness (2ndedn). Penguin group, New York.
30. Petropoulos G.A(2002). Taylor and Francis; London and New York: Fenugreek – The Genus Trigonella.

31. McCormick, K., Norton, R., Eagles, H.A., (2006). Fenugreek has a role in south-eastern Australian farming systems. In: Proceedings of "Groundbreaking stuff", 13th Annual Agronomy Conference, Perth, Australia, 2006, 639.
32. Wani, S. A.; Kumar, P(2018). Fenugreek: A Review on Its Nutraceutical Properties and Utilization in Various Food Products. J. Saudi Society Agri. Sci, 17, 97–106.
33. Al-Jasass, F. M.; Al-Jasser, M. S(2012). Chemical Composition and Fatty Acid Content of Some Spices and Herbs under Saudi Arabia Conditions. Sci. World J, 2012, 1–5.
34. Feyzi, S.; Varidi, M.; Zare, F.; Varidi, M. J(2015). Fenugreek (Trigonella Foenum Graecum) Seed Protein Isolate: Extraction Optimization, Amino Acid Composition, Thermo and Functional Properties. J. Sci. Food Agric, 95, 3165–3176.
35. Nagulapalli, V. K. C.; Swaroop, A.; Bagchi, D.; Bishayee, A(2017). A Small Plant with Big Benefits: Fenugreek (Trigonella Foenum-graecum Linn.) For Disease Prevention and Health Promotion. Mol. Nutri. Food Res, 61, 1600950.
36. Petropoulos, G. A.(2002). Fenugreek: The Genus Trigonella; Boca Raton, Florida, USA: CRC Press.
37. Rayyan, S., Fossen, T., & Andersen, Ø. M. (2010). Flavone C-glycosides from seeds of fenugreek, Trigonella foenum-graecum L. Journal of agricultural and food chemistry, 58(12), 7211-7217.
38. El Nasri N.A., El Tinay A(2007). Functional properties of fenugreek (*Trigonella foenum graecum*) protein concentrate. *Food Chem*;2:582–589.
39. Kakani R.K., Anwer M.M., Meena S.S., Saxena S.N(2009). Advance production technology of fenugreek. *NRCSS Tech. Release*:1–24.
40. Sowmya P., Rajyalakshmi P(1999). Hypocholesterolemic effect of germinated fenugreek seeds in human subjects. *Plant Foods Hum. Nutr*;4:359–365.
41. Montgomery J. University of Alberta; USA: 2009. The potential of fenugreek (*Trigonella foenum-graecum*) as a forage for dairy herds in central Alberta; pp. 4–15.
42. Muralidhara, Narasimhamurthy K., Viswanatha S., Ramesh B.S(1999). Acute and subchronic toxicity assessment of debitterized fenugreek powder in the mouse and rat. *Food Chem. Toxicol*;37:831–838.
43. Altuntas E., Ozgoz E., Taser O.F(2005). Some physical properties of fenugreek (*Trigonella foenum-graceum* L.) seeds. *J. Food Eng*;71:37–43.
44. Brummer Y., Cui W., Wang Q(2003). Extraction, purification and physicochemical characterization of fenugreek gum. *Food Hydrocol*;3:229–236.
45. Chatterjee S., Variyar P.S., Sharma A(2010). Bioactive lipid constituents of fenugreek. *Food Chem*;1:349–353.
46. Leela N., Shafeekh K(2008). CAB International; Pondicherry, India: Fenugreek, Chemistry of Spices.
47. Srinivasan K(2006). Fenugreek (*Trigonella foenum-graecum*): a review of health beneficial physiological effects. *Food Rev. Int*;2:203–224.
48. USDA, 2011. National Nutrient Database for Standard Reference, Release 24.
49. Al Jasass F.M., Al Jasser M.S(2012). Chemical composition and fatty acid content of some spices and herbs under Saudi Arabia conditions. *Sci. World J.*
50. Lee S.J., Umano K., Shibamoto T., Lee K.G(2005). Identification of volatile components in basil (*Ocimum basilicum* L.) and thyme leaves (*Thymus vulgaris* L.) and their antioxidant properties. *Food Chem*;1:131–137.
51. Kaviarasan S., Naik G., Gangabhagirathi R., Anuradha C., Priyadarsini K(2007). In vitro studies on antiradical and antioxidant activities of fenugreek (*Trigonella foenum graecum*) seeds. *Food Chem*;1:31–37.
52. Rababah T.M, Ereifej K.I, Esoh R.B, Al-u'datt M.H, Alrababah M.A, Yang W(2011). Antioxidant activities, total phenolics and HPLC analyses of the phenolic compounds of extracts from common Mediterranean plants. *Nat. Prod. Res*;6:596–605.
53. Gupta A, Gupta R, Lal B(2011). Effect of *Trigonella foenum-graecum* (fenugreek) seeds on glycaemic control and insulin resistance in type 2 diabetes mellitus: a double blind placebo controlled study. *J. Assoc. Phys. India*. p.1057–1061.
54. Ruby B., Gaskill S., Slivka D., Harger S(2005). The addition of fenugreek extract (*Trigonella foenum-graecum*) to glucose feeding increases muscle glycogen resynthesis after exercise. *Amino Acids*;1:71–76.
55. Ruby B., Gaskill S., Slivka D., Harger S(2005). The addition of fenugreek extract (*Trigonella foenum-graecum*) to glucose feeding increases muscle glycogen resynthesis after exercise. *Amino Acids*;1:71–76.
56. Raju J., Gupta D., Rao A.R., Yadava P.K., Baquer N.Z(2001). *Trigonella foenum graecum* (fenugreek) seed powder improves glucose homeostasis in alloxan diabetic rat tissues by reversing the altered glycolytic, gluconeogenic and lipogenic enzymes. *Mol. Cell. Biochem*;1–2:45–51.
57. Blumenthal M., Goldberg A., Brinckmann J(2000). American Botanical Council, Integrative Medicine Communications; Newton, MA, USA: Herbal Medicine: Expanded Commission E Monographs; pp. 130–133.
58. Sauvare Y., Pett P., Baissao Y., Ribes G(2000). Chemistry and pharmacology of fenugreek. In: Mazza G., Oomah B.D., editors. *Herbs, Botanicals and Teas.* Technomic Publishing Company Inc.; PA, USA: pp. 107–129.
59. Meghwal M., Goswami T.K(2012). A review on the functional properties, nutritional content, medicinal utilization and potential application of fenugreek. *J. Food Process Technol*;3
60. Hamden K., Masmoudi H., Carreau S., Elfeki A(2010). Immunomodulatory, beta-cell, and neuroprotective actions of fenugreek oil from alloxan-induced diabetes. *Immunopharmacol. Immunotoxicol*;32:437–445.

61. Chatterjee S., Variyar P.S., Sharma A(2010). Bioactive lipid constituents of fenugreek. *Food Chem*;1:349–353.
62. Srichamroen A, Thomson ABR, Field CJ, Basu TK(2008), In vitro intestinal glucose uptake is inhibited by galactomannan from Canadian fenugreek seed (Trigonella foenum graecum L) in genetically lean and obese rats, Nutrition Research, 29, 49-54.
63. Hammerness P, Basch E, Ulbricht C, Barrette E-P, Foppa I, Basch S, et al(2003). St. John's wort: a systematic review of adverse effects and drug interactions for the consultation psychiatrist. Psychosomatics;44(4):271-82.
64. Hannan J, Rokeya B, Faruque O, Nahar N, Mosihuzzaman M, Azad Khan A, et al(2003). Effect of soluble dietary fibre fraction of Trigonella foenum graecum on glycemic, insulinemic, lipidemic and platelet aggregation status of Type 2 diabetic model rats. J Ethnopharmacol;88(1):73-7.
65. Hannan JMA, Ali L, Rodeya B, Khaleque J, Alchter M, Flatt PR, Abdel Wahab YHA(2006), Soluble dietry fibre fractions of Trigonella foenumgraecum (fenugreek) seed improves glucose homeostatis in animal models of type 1 and type 2 diabetes by delaying carbohydrate digestion and absorption and enhancing insulin action, British Journal of Nutrition, 97, 514-521.
66. Robert SD, Ismail AA-S, Wan Rosli WI(2014). Trigonella Foenum-Graecum Seeds Lowers Postprandial Blood Glucose in Overweight and Obese Individuals. Journal of nutrition and metabolism; 2014: 1-5.
67. Zia T., Hasnain S.N., Hasan S(2001). Evaluation of the oral hypoglycaemic effect of *Trigonella foenum-graecum* L. (methi) in normal mice. *J. Ethnopharmacol*;2:191–195.
68. Vats V., Grover J., Rathi S(2002). Evaluation of anti-hyperglycemic and hypoglycemic effect of *Trigonella foenum-graecum* Linn, *Ocimum sanctum* Linn and *Pterocarpus marsupium* Linn in normal and alloxanized diabetic rats. *J. Ethnopharmacol*;1:95–100.
69. Broca C., Manteghetti M., Gross R., Baissac Y., Jacob M., Petit P., Ribes G(2000). 4-Hydroxyisoleucine: effects of synthetic and natural analogues on insulin secretion. *Eur. J. Pharmacol*;3:339–345.
70. Nanjundan P., Arunachalam A., Thakur R(2009). Antinociceptive property of *Trigonella foenum graecum* (fenugreek seeds) in high fat diet-fed/low dose streptozotocin-induced diabetic neuropathy in rats. *Pharmacology*:24–36.
71. Brummer Y, Cui W, Wang Q(2003). Extraction, purification and physicochemical characterization of fenugreek gum. Food Hydrocolloid;17(3):229-36.
72. Boban PT, Nambisan B, Sudhakaran PR(2006). Hypolipidaemic effect of chemically different mucilages in rats: a comparative study. Brit J Nutr;96(06):1021-9.
73. Favier, M. L., Moundras, C., Demigné, C., & Rémésy, C. (1995). Fermentable carbohydrates exert a more potent cholesterol-lowering effect than cholestyramine. Biochimica et Biophysica Acta (BBA)-Lipids and Lipid Metabolism, 1258(2), 115-121.
74. Peran L, Sierra S, Comalada M, Lara-Villoslada F, Bailón E, Nieto A, et al(2007). A comparative study of the preventative effects exerted by two probiotics, Lactobacillus reuteri and Lactobacillus fermentum, in the trinitrobenzenesulfonic acid model of rat colitis. Brit J Nutr;97(01):96-103.
75. Eidi A, Eidi M, Esmaeili E(2006). Antidiabetic effect of garlic (Allium sativumL.) in normal and streptozotocin-induced diabetic rats. Phytomedicine;13(9):624-9.
76. Sowmya P, Rajyalakshmi P(1999). Hypocholesterolemic effect of germinated fenugreek seeds in human subjects. Plant Food Hum Nutr;53(4):359-65.
77. Parthasarathy VA, Chempakam B, Zachariah TJ(2008). Chemistry of spices: CABI;
78. Belguith-Hadriche O., Bouaziz M., Jamoussi K., Simmonds M.S., El Feki A., Makni-Ayedi F(2013). Comparative study on hypocholesterolemic and antioxidant activities of various extracts of fenugreek seeds. *Food Chem*; 2:1448–1453.
79. Shetty AK, Salimath PV(2009). Reno-protective effects of fenugreek (Trigonella foenum greacum) during experimental diabetes, e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism, e137–e14.
80. Bhatia, K., Kaur, M., Atif, F., Ali, M., Rehman, H., Rahman, S., & Raisuddin, S. (2006). Aqueous extract of Trigonella foenum-graecum L. ameliorates additive urotoxicity of buthionine sulfoximine and cyclophosphamide in mice. Food and Chemical Toxicology, 44(10), 1744-1750.
81. VanFurt R(1982). Current view on the mononuclear phagocytsystem, Immunobiology, 161, 178-85.
82. Kaviarasan S., Vijayalakshmi K., Anuradha C(2004). Polyphenol-rich extract of fenugreek seeds protect erythrocytes from oxidative damage. *Plant Foods Human Nutr*;4:143–147.
83. Bin-Hafeez B., Haque R., Parvez S., Pandey S., Sayeed I., Raisuddin S(2003). Immunomodulatory effects of fenugreek (*Trigonella foenum graecum* L.) extract in mice. *Int. Immunopharmacol*; 2:257–265.
84. Kaviarasan S, Vijayalakshmi K, Anuradha C(2004). Polyphenol-rich extract of fenugreek seeds protect erythrocytes from oxidative damage. Plant Food Hum Nutr; 59(4):143-7.
85. Dixit P, Ghaskadbi S, Mohan H, Devasagayam T(2005). Antioxidant properties of germinated fenugreek seeds. Phytother Res;19(11):977-83.
86. Kaviarasan S, Anuradha C(2007). Fenugreek (Trigonella foenum graecum) seed polyphenols protect liver from alcohol toxicity: a role on hepatic detoxification system and apoptosis. Pharmazie;62(4):299-304.
87. Altuntaş E, Özgöz E, Taşer ÖF(2005). Some physical properties of fenugreek (Trigonella foenum-graceum L.) seeds. J Food Eng;71(1):37-43.

88. Grover J, Yadav S, Vats V(2002). Medicinal plants of India with anti-diabetic potential. J Ethnopharmacol;81(1):81-100.
89. Yunbao Liu, Rajesh Kakani, Muraleedharan Nair G(2011), Compounds in functional food fenugreek spice exhibit anti-inflammatory and antioxidant activities, Food Chemistry, 1187-1192.
90. Varma SD, Kavita RH(2007), Susceptibility of the ocular lens to nitric oxide: implications in cataractogenesis, J Ocular Pharmacol Therap, 23, 188–195.
91. Gupta SK, Kalaiselvam V, Srivasta S, Saxena R, Agarwal SS(2009). Trigonella foenum graecum (fenugreek) protects against selenite-Induced oxidative stress in experimental cataractogenesis, Biol Trace Elem Res, 258-268.
92. Mohammadinejad, R.; Shavandi, A.; Raie, D. S.; Sangeetha, J.; Soleimani, M.; Hajibehzad, S. S.; Thangadurai, D.; Hospet, R.; Popoola, J. O.; Arzani, A.; et al(2019). Plant Molecular Farming: Production of Metallic Nanoparticles and Therapeutic Proteins Using Green Factories. Green Chem. DOI: 10.1039/C9GC00335E.
93. Tohidi, B.; Rahimmalek, M.; Arzani, A(2017). Essential Oil Composition, Total Phenolic, Flavonoid Contents, and Antioxidant Activity of Thymus Species Collected from Different Regions of Iran. Food Chem, 220, 153–161.
94. Yadav, U. C.; Baquer, N. Z(2014). Pharmacological Effects of Trigonella Foenum-graecum L. In Health and Disease. Pharm. Biol, 52, 243–254.
95. Hibasami, H.; Moteki, H.; Ishikawa, K.; Katsuzaki, H.; Imai, K.; Yoshioka, K.; Ishii, Y.; Komiya, T(2003). Protodioscin Isolated from Fenugreek (Trigonella Foenumgraecum L.) Induces Cell Death and Morphological Change Indicative of Apoptosis in Leukemic Cell Line H-60, but Not in Gastric Cancer Cell Line KATO III. Int. J. Mol. Med, 11, 23–26.
96. Verma, S. K.; Singh, S. K.; Mathur, A(2010). In Vitro Cytotoxicity of Calotropis Procera and Trigonella Foenum-graecum against Human Cancer Cell Lines. J. Chem. Pharm. Res, 2, 165–861.
97. Shabbeer, S.; Sobolewski, M.; Anchoori, R. K.; Kachhap, S.; Hidalgo, M.; Jimeno, A.; Davidson, N. E.; Carducci, M.; Khan, S. R(2009). Fenugreek: A Naturally Occurring Edible Spice as an Anticancer Agent. Cancer Boil. Ther, 272–278.
98. Sur, P.; Das, M.; Gomes, A.; Vedasiromoni, J. R.; Sahu, N. P.; Banerjee, S.; Sharma, R. M.; Ganguly, D. K(2001). Trigonella Foenum Graecum (Fenugreek) Seed Extract as an Antineoplastic Agent. Phytother. Res., 15, 257–259.
99. Montgomery J(2009). The potential of fenugreek (Trigonellafoenum-graecum) as a forage for dairy herds in central Alberta. University of Alberta, USA, 4-15.
100. Yoshinari O., Igarashi K(2010). Anti-diabetic effect of trigonelline and nicotinic acid, on KK-Ay mice. *Curr. Med. Chem.*;20:2196–2202.
101. Mohamed W.S., Mostafa A.M., Mohamed K.M., Serwah A.H(2015). Effects of fenugreek, Nigella, and termis seeds in nonalcoholic fatty liver in obese diabetic albino rats. *Arabian J. Gastroenterol.*;16:1–9.
102. Reimer RA, Russell JC(2008). Glucose tolerance, lipids, and GLP- 1 secretion in JCR: LA- cp rats fed a high protein fiber diet. Obesity;16(1):40-6.
103. Geetha M, Suneel K, Krupanidhi A, Muralikrishna K, Avin A, Prashanth P(2011). Effect of fenugreek on total body and organ weights: A study on mice. Pharmacologyonline;3:747-52.
104. Panda S., Biswas S., Kar A(2013). Trigonelline isolated from fenugreek seed protects against isoproterenol-induced myocardial injury through down-regulation of Hsp27 and a B-crystallin. *Nutrition.*;29:1395–1403.
105. Petit P., Sauvaire Y., Ponsin G., Manteghetti M., Fave A., Ribes G(1993). Effects of a fenugreek seed extract on feeding behaviour in the rat: metabolic-endocrine correlates. *Pharmacol. Biochem. Behavior.*;2:369–374.
106. Thakur, A., Sarvaiya, J., Bhavsar, S., Malik, J., 1994. Studies on anti-inflammatory activities of Trigonella in rats. Update Ayurveda. Bombay, India.
107. Ahmadiani A., Javan M., Semnanian S., Barat E., Kamalinejad M(2001). Anti-inflammatory and antipyretic effects of *Trigonella foenum-graecum* leaves extract in the rat. *J. Ethnopharmacol*;2:283–286.
108. James A.D., Bogenschutz-Godwin M.J.(2002), duCellier J., Duke K.P. second ed. CRC Press; Boca Raton, London, New York, Washington, D.C.: Medicinal Herbs. Handbook; p. 296.
109. Mahmoud N.Y., Salem R.H., Mater A.A(2012). Nutritional and biological assessment of wheat biscuits supplemented by fenugreek plant to improve diet of anemic rats. *Acad. J. Nutr.*;1:1–9.
110. Thakran S., Siddiqui M., Baquer N.Z(2004). *Trigonella foenum graecum* seed powder protects against histopathological abnormalities in tissues of diabetic rats. *Mol. Cell. Biochem.*;1–2:151–159.
111. Belguith-Hadriche O., Bouaziz M., Jamoussi K., Simmonds M.S., El Feki A., Makni-Ayedi F(2013). Comparative study on hypocholesterolemic and antioxidant activities of various extracts of fenugreek seeds. *Food Chem.*;2:1448–1453.
112. Xue W., Lei J., Li X., Zhang R(2011). *Trigonella foenum graecum* seed extract protects kidney function and morphology in diabetic rats via its antioxidant activity. *Nutr. Res*;7:555–562.
113. Ahmadiani A., Javan M., Semnanian S., Barat E., Kamalinejad M(2011). Anti-inflammatory and antipyretic effects of *Trigonella foenum-graecum* leaves extract in the rat. *J. Ethnopharmacol* ;2:283–286.
114. Tayyaba Z., Hasnain S.N., Hasan S.K(2001). Evaluation of the oral hypoglycemic effects of *Trigonella foenum graecum* L. (Methi) in normal mice. *J. Ethnopharmacol*;75:191–195.
115. Amin A., Alkaabi A., Al-Falasi S., Daoud S.A(2005). Chemopreventive activities of *Trigonella foenum graecum* (Fenugreek) against breast cancer. *Cell Biol. Int*; 8:687–694.