The Open Biology Journal

Content list available at: https://openbiologyjournal.com/

REVIEW ARTICLE

Medicinal Properties of Fenugreek: A Review

Himanshi Varshney[1] and Yasir Hasan Siddique[1,*]

[1]*Department of Zoology, Drosophila Transgenic Laboratory, Section of Genetics, Faculty of Life Sciences, Aligarh Muslim University, Aligarh 202002, Uttar Pradesh, India*

Abstract:

Background:

Due to its numerous health benefits, fenugreek (*Trigonella foenum-graecum L.*) is commonly used in Ayurvedic and Traditional Chinese medicine. Its leaves and seeds contain several compounds (*e.g.*, alkaloids, amino acids, coumarins, flavonoids, saponins, polyphenols, carbohydrates, vitamins, and other bioactive compounds). Fenugreek is used for reproductive health problems, hepatoprotective properties, and improved digestion. Studies have shown that it has anti-cancerous, cardioprotective, anti-sterility, antimicrobial, antiparasitic, anti-helminthic, and neuroprotective properties. Various studies have been carried out on animals and humans to show the effectiveness of fenugreek against various diseases.

Methods:

This review focuses on studies and clinical trials to examine the effects of fenugreek on various diseases from 1990 to 2022, using popular databases, such as Google Scholar, PubMed, and Scopus.

Results:

By altering the activity of metabolic enzymes, fenugreek stimulates insulin secretion, reduces blood sugar, and controls cholesterol synthesis. It enhances SOD, glutathione peroxidase, glutathione-S-transferase, and catalase activity to protect cellular organelles from oxidative stress. Fenugreek improves the gastric mucosa lining and secretion, which improves gastric ulcers and digestion. Fenugreek ameliorates menstrual cramps and significantly increases sperm cell counts and testosterone levels in males.

Conclusion:

Studies and clinical trials have shown the beneficial effects of fenugreek. Therefore, it could be used as a therapeutic agent against various disorders.

Keywords: Fenugreek, Medicinal properties, Diseases, Therapeutic agent, Pharmacology, Disorders.

Article History	Received: August 02, 2022	Revised: January 23, 2023	Accepted: February 08, 2023

1. INTRODUCTION

Trigonella foenum graecum (fenugreek) belongs to the family Fabaceae. It is a medicinal herb used to treat various diseases, such as diabetes, inflammation, cancer, hypercholesteremia, reproductive dysfunction, and neurodegenerative disorders. For centuries, fenugreek seeds have been used as carminative, demulcent, expectorant, laxative, and stomachic agents [1]. It originated in Eastern Europe but is now grown all over the world. It has a variety of phytochemicals, such as flavonoids, alkaloids, coumarins, vitamins, carbohydrates (Galactomannan), saponins, trigonelline, diosgenin, and soluble fibers, which are responsible for the pharmacological effects. Numerous clinical and pre-clinical studies have revealed its anti-diabetic, anti-sterility, and anti-fertility effects. Moreover, it regulates the production of enzymes that control blood sugar levels and help in reducing cholesterol [2]. The hypoglycemic action of fenugreek corresponds to physiological requirements and is mediated by Glucogen-like peptide-1 levels [3]. Furthermore, it also regulates antioxidant and detoxifying enzymes to reduce oxidative stress. The flavonoids and saponins present in fenugreek prevent tumor formation by blocking carcinogen-DNA adduct formation [4]. Flavonoids and alkaloids are well known for their neuroprotective and

* Address correspondence to this author at the Department of Zoology, Drosophila Transgenic Laboratory, Section of Genetics, Faculty of Life Sciences, Aligarh Muslim University, Aligarh 202002, Uttar Pradesh, India; Tel: 0571-2700920-3447; E-mail:yasir_hasansiddique@rediffmail.com

antioxidative effects [5, 6]. The active components of fenugreek, *i.e.*, 4-hydroxyisoleucine (4-OH-Ile) and galactomannan, have been reported to reduce blood glucose levels and improve lipid metabolism *in vivo* [7]. Trigonelline regulates ß cell regeneration, insulin secretion, enzymes involved in glucose metabolism, and neuron excitability [8]. Diosgenin suppresses tumor necrosis factor-induced invasion, suppresses proliferation, and enhances apoptosis. Fenugreek seeds are effective in boosting both total and free testosterone, sperm cells count, and sperm motility, thus promoting physical and sexual health [9]. Research studies have confirmed the traditional use of fenugreek in treating various health problems, such as diabetes, reno-protective properties in diabetic complications, and gastric ulcers. It is also recommended to be used as a protein supplement (about 20-30%) as it contains a high level of protein [10].

2. HISTORY OF FENUGREEK USAGE

Fenugreek can be grown in all seasons and has medicinal values known from ancient times. Its seeds, leaves, and stems have been used for various purposes. The seeds are popularly known as *methi dana,* which is commonly used as a spice in Indian curries and pickles and also as a flavoring agent in baking bread, cheese, syrups, *etc.* Its leaves and young plants are cooked as winter dishes. Earlier, Romans and Greeks used it for cattle food. In Egypt, it was used to ease labor and enhance milk flow. Many Egyptian women used it to reduce menstrual pain. Its medicinal properties are extensively documented in Ayurveda, Chinese, Arabic, Greek, and Latin pharmacopoeia [10].

3. MEDICINAL PROPERTIES OF FENUGREEK

Scientists have reported several therapeutic uses of fenugreek. It has shown anti-diabetic, hypoglycaemic, anti-hyperlipidemic, anti-fertility, anti-cancer, anti-microbial, anti-parasitic, lactation stimulant, galactagogue, hypocholesterolemic, immunomodulatory, anti-carcinogenic, anti-helminthic, anti-nociceptive, anti-oxidant, anti-microbial, anti-ulcer, gastroprotective, and hepatoprotective properties Table **1**. Overnight-soaked seeds of fenugreek are used for hair and skin for a soft and smooth effect. It reduces the risk of myocardial damage and abnormal blood clotting linked with heart attacks and strokes [10.] It helps in reducing weight and heals inflammations. A number of studies have revealed that it also possess anti-carcinogenic property and neuroprotective effects. It is a rich source of iron, calcium, sulphur, chlorine, and vitamins A and C. Earlier, fenugreek has been used as a tonic for the treatment of weakness and edema of the legs. It is commonly used to treat menstrual cramps and acts as a lactation stimulant [11]. Its pharmacological properties against diseases have been identified by experimental evidence and clinical studies [12, 13]. The active constituents of fenugreek have been reported to have protective effects against diseases, such as diabetes, neurodegenerative disorders, various heart complications, cancer, hypolipidemic, gastroprotective effects, arthritis, *etc*. (Fig. **1**).

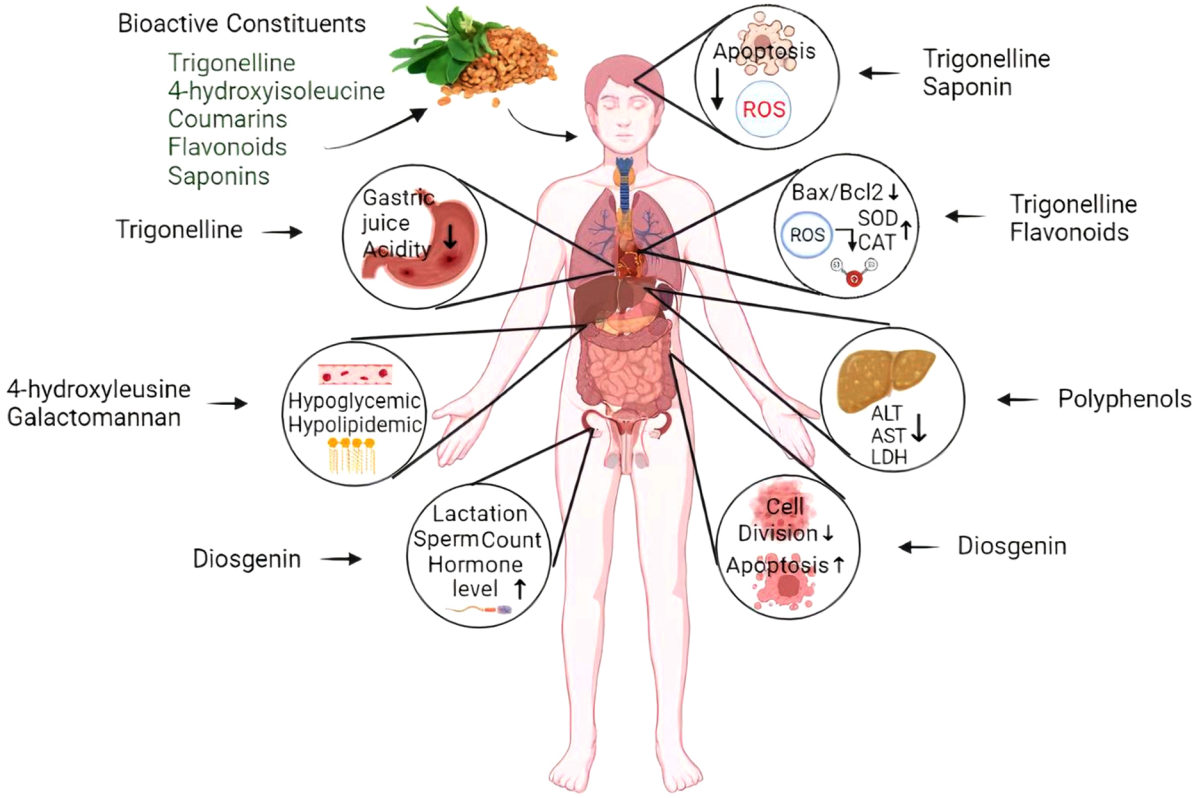

Fig. (1). Pharmacological effects of bioactive components of fenugreek

4. PHARMACOLOGICAL PROPERTIES OF FENUGREEK

4.1. Anti-diabetic Effects

The bioactive components of fenugreek, like galactomannan, saponins, trigonella, diosgenin, and 4-hydroxyisoleucine, have been reported to exert positive effects on diabetes. Several components have been isolated, and various studies have revealed their action on blood sugar [14]. Fenugreek controls diabetes *via* multi-physiological pathways, such as restoring pancreatic β-cell function and inhibiting sucrase as well as alpha-amylase activities. 4-Hydroxyisoleucine directly induces insulin secretion from pancreatic β-cells. Fenugreek saponin extract has shown anti-diabetic, hepatoprotective, and hypolipidemic effects [2, 15 - 17]. Fenugreek saponins regulate glycogen enzyme activities in the intestine and liver of rats, enhance hepatic glycogen content, lower blood glucose levels, and improve oral glucose tolerance [18]. In a study, 15 diabetic patients were given fenugreek seed powder for 10 days, which resulted in a significant reduction of fasting glucose level, LDL, and VLDL cholesterol and improved glucose tolerance. This also led to a 64% reduction in 24 hr urinary glucose excretion [19]. Galactomannan, one of the components of fenugreek, exhibits protection against diabetes. A group of 32 patients (type-2 diabetic) were given galactomannan and compared with the control (32 patients placebo). The study revealed a notable decrease in fasting blood glucose, HbA1c, total cholesterol, triglycerides, and low-density lipoprotein. Overall, galactomannan could be a good candidate for hyperglycemia and hypolipidemia. Diosgenin, a glycan in fenugreek, boosted glucose metabolism by stimulating adipocytes, inhibiting inflammation in adipose tissue, and lowering triglycerides in the plasma of obese diabetic mice. In research, it was observed that 10 gm/40 ml of liquid fenugreek extract could reduce the glucose level of blood. It was found that its liquid dosage is better than crushed and powdery forms [2].

Table 1. Therapeutic uses of fenugreek.

	Non-communicable Diseases	Model	Conclusion	References
-	**Anti-diabetic Effect**	-	-	-
1.	Effect of fenugreek seeds on blood glucose and serum lipids in type I diabetes.	Human	Fenugreek diet notably decreased fasting blood sugar and improve glucose tolerance test.	[71]
2.	Effect of fenugreek seeds on non-insulin dependent diabetic subjects	Human	Fenugreek lowers fasting blood glucose levels and enhance glucose tolerance test.	[72]
3.	Effect of fenugreek and lupine seeds on the development of experimental diabetes	Rat	Diabetic animals supplement with fenugreek showed reduction in hyperglycemia, free fatty acids, and cholesterol and triglycerides levels.	[73]
4.	Effects of a fenugreek seed extract on feeding behaviour	Rat	Administration of fenugreek seed extract displayed hyperinsulinemia as well as hypercholesterolemia effect.	[74]
5.	Effect of steroid saponins from fenugreek seeds on feeding behaviour and plasma cholesterol	Rat	Saponins lower down plasma cholesterol levels in rats.	[75]
6.	Effect of fenugreek seeds on blood lipid peroxidation and antioxidants levels	Rat	Fenugreek seed supplementation in the diet showed regulation in the free radical metabolism in diabetic animals	[76]
7.	Effect of *Trigonella foenum graecum* (fenugreek) seed powder on glucose homeostasis	Rat	*Trigonella*seed powder treatment altered glucose and lipid metabolising enzyme activities to normal values	[77]
8.	Effect of fenugreek seed aqueous extract of on alloxan diabetic males	Rat	Fenugreek seed aqueous extract display antioxidant property which decrease the biochemical and histopathological alteration caused by alloxan.	[78]
9.	Effects of fenugreek seed powder on type 2 diabetic patients	Human	Fenugreek seeds powder notably reduce serum lipid profile in type 2 diabetic patients.	[12]
10.	Effects of fenugreek alkaloid extract on streptozotocin induced hyperglycemia	Rat	Fenugreek suppressed lipid profile and oxidative stress via converting liver and kidney pathology caused by diabetes to normal level.	[79]
11.	Effect of *Trigonella foenum-graecum* (fenugreek) extract on streptozotocin-induced diabetes	Rat	*Trigonella foenum-graecum* extract decrease blood glucose, blood lipid levels and enhance hemorheological properties	[80]
12.	Effect of fenugreek on Type 2 diabetic Patients	Human	Fenugreek seeds notably control pathology of diabetic patients if used as an adjuvant in type 2 diabetes mellitus.	[14]
13.	Effect of fenugreek saponins on Diabetes	Rat	Fenugreek saponins reduce the absorption of LDL-cholesterol and increase the HDL-cholesterol level.	[18]
14.	Effect of fenugreek galactomannan on digestive enzymes	Rat	Fenugreek galactomannan hamper diabetes-induced kidney injury and creatinine content in plasma.	[19]

(Table 1) contd.....

15.	Effect of fenugreek oil on alloxan-induced diabetes	Rat	Fenugreek oil maintained hematological status, and renal toxicity by acting on immunomodulatory activity and stimulate insulin action.	[81]
16.	Effect of Omega-3 fattyacid and fenugreek essential oil on diabetes	Rat	Fenugreek oil regulates starch and glucose oral tolerance and drops down triglycerides and total cholesterol level	[82]
17.	Effect of *Trigonella foenum graecum* (fenugreek) on alloxan induced diabetes	Rat	Fenugreek aqueous seed extract and ethanol extract combination remarkably reduced the increased level of blood glucose and increased the levels of serum insulin.	[83]
18.	Effect of fenugreek on STZ-induced diabetic nephropathy	Rat	Diabetic rats significantly reduced the renal dysfunction, pathological alteration, and oxidative stress by fenugreek treatment.	[84]
19.	Effect of cinnamon, fenugreek and their combination on patients with type 2 diabetes	Human	Daily supplementation of cinnamon, fenugreek or their combination to patients effectively lowering HbA1C and 2 h PPG (postprandial glucose) in type 2 diabetic patients	[16]
20.	Effect of fenugreek (*Trigonella foenum-graecum*L.) intake on glycemia: a meta-analysis of clinical trials	Human	Fenugreek treatment lower down the glucose levels in treated patients.	[13]
21.	Effect of fenugreek (*Trigonella foenum-graecum*) on experimentally induced diabetes mellitus	Rabbit	Total lipids and serum sugar level is notably attenuated by fenugreek in experimentally induced diabetes mellitus in rabbit.	[85]
22.	Effect of fenugreek seeds on Type 2 diabetes	Type-2 diabetic Patients	Fenugreek seeds regulate glucose metabolism, serum lipid profile and adiponectin levels in studied patients.	[86]
23.	Effect of *Trigonella foenum-graecum*(Fenugreek) seed on glucose homeostasis	U2OS cell line	Fenugreek bioactive component bind with GLP-1 and stimulate GLP-1 signalling and show hypoglycaemic effect.	[15]
24.	Effect of Fenugreek on type 2 diabetes mellitus in prediabetes	Human	It results reduction in fasting plasma glucose (FPG), postprandial plasma glucose (PPPG) and low density lipoprotein cholesterol (LDLc) and increament in blood insulin by fenugreek.	[87]
25.	Effect of fenugreek in Type2 diabetes	Humans	Fenugreek liquid dosage form of 10gm/40ml notably reduced blood sugar level in diabetic patients.	[88]
26.	Effect of *Trigonella foenum graecum* (fenugreek) on diabetes	Rat	TFG seed extractshowed more antiperoxidative activity than leaves extract of it.	[89]
27.	Effect fenugreek seed (*Trigonella foenum-graecum*) extract (FenfuroTM) in patients with type 2 diabetes	Human	Fenugreek supplement leads to reduction in both fasting plasma and post-prandial blood sugar levels.	[90]
28.	Effect of fenugreek-based bio-nanocomposite on renal dysfunction	Rat	Fenugreek-based bio-nanocomposite enhance kidney function marker contents in the blood and improve renal dysfunction	[91]
29.	Effect of fenugreek compound (N55) in treating type-2 diabetes	Mice	N55 decreases plasma glucose by enhancing the response of physiological levels of GLP-1 and affect glucose tolerance.	[3]
30.	Effect of fenugreek seeds powder (*Trigonella foenum-graecum*L.) on experimental induced hyperlipidemia	Rabbit	Fenugreek seeds powder had a significant hypolipidemic effect in experimentally-induced hyperlipidemic rabbits.	[92]
31.	Effect of fenugreek (*Trigonella foenum-graecum*L.) seeds on insulin sensitivity and mitochondrial functions	3T3-L1 cells	Polyphenol stilbenes from the fenugreek kill scavenge reactive oxygen species (ROS).	[93]
32.	Effect of flavonoid glycosides from fenugreek seeds on 3T3-L1 adipocytes *in vitro*	3T3-L1 cells	It lowers glucose and insulin-resistance-improving agent for the treatment of diabetes	[17]
33.	Effect of fenugreek seed extract on type 2 diabetes mellitus	Human	Type 2 diabetes patients display lower level of HbA1c and require lower dose of insulin per day due to the uptake of fenugreek.	[94]
34.	Effects of fenugreek on high fat fed dyslipidemia	Rat	Fenugreek seems to be an effective hypolipidemic agent to control the increasing risk of dyslipidemia.	[95]
35.	Effect of fenugreek polysaccharides on type-2 diabetes	Human	Galactomannan notably reduce fasting blood glucose, HbA1c,total cholesterol,triglycerideand low-density lipoprotein.	[2]
36.	Effect of *Trigonellafoenum graecum* on streptozotocin induced diabetic complications	Rat	Fenugreek improved the biochemicall and histological parameters of diabetic complications	[96]

(Table 1) contd.....

37.	Effect of fenugreek (Trigonella foenum graecum) seed aqueous extract in streptozotocin-induced diabetes	Rat	Fenugreek treatment control blood glucose, lipid profile, liver, and kidney function	[97]
38.	Effect of fenugreek seed powder solution (*Trigonella foenum-graecum L.*) on hyperlipidemia in Diabetes	Human	*Trigonella foenum-graecum*seed powder solution ameliorates lipid metabolism of type II diabetic patients.	[98]
39.	Effect of fenugreek seeds in alloxan-induced diabetes	Rat	Fenugreek seeds showed hypoglycemic and hypolipidemic properties.	[99]
40.	Effects of fenugreek alkaliod extract on alloxan induced hyperglycemia	Rat	Treatment with alkaloid extract of fenugreek dried seeds displayed reduction of blood glucose and increase in serum insulin	[100]
41.	Effect of Fenugreek and Buckthorn as antioxidant and antidiabetic agent	Rat	Aqueous extract of fenugreek and buckthorn seed was more effective than leaves extract.	[101]
	Anti-cancerous effect			
42.	*Trigonella foenum* seed extract as an anti-neoplastic agent	Mice	*Trigonella foenum graecum* show anti-inflammatory and anti-neoplastic property.	[102]
43.	Effect of fenugreek on 1,2- dimethylhydrazine-induced hepatic oxidative stress during colon carcinogenesis	Rat	Fenugreek reduced circulatory lipidperoxidation and increased antioxidant levels.	[103]
44.	Effect of diosgenin, a steroid saponin of *Trigonella foenum graecum* on azoxymethane-induced aberrant crypt foci formation.	Rat and HT-29 Human Colon Cancer Cells	Fenugreek seed and diosgenin are helpful in preventing colon cancer. Diosgenin stops cell proliferation and initiate apoptosis in HT-29 human colon cancer cell lines.	[104]
	Effects of Trigonella foenum graecum (fenugreek) seed on colon cancer	Rat and HT-29 human colon cancer cell lines	It significantly induced apoptosis in HT-cells cells.	
45.	Effect of diosgenin on adenocarcinoma cells	HCT-116 cells	Diosgenin significantly decrease the expressions of β-catenin, peroxisome proliferator-activated receptor (PPAR) –γ and inhibit adenocarcinoma cells by targeting different cholesterol biosynthetic pathways	[105]
46.	Effect of diosgenin, a steroidal saponin constituent of fenugreek as chemoprotectant	Rat	Diosgenin significantly repressed both invasive and non-invasive colon tumor incidence upto 60%.	[106]
47.	Effect of diosgenin on 3-hydroxy-3-methylglutaryl CoA reductase expression	HCT-116 cells	Diosgenin suppressed growth and induced apoptosis in human colon carcinoma cells	[107]
48.	Effect of fenugreek seeds on 1,2-dimethylhydrazine-induced hepatic oxidative stress during colon carcinogenesis.	Rat	Fenugreek modulate DMH- induced oxidative stress	[4]
49.	Effect of traditional medicines thymoquinone and diosgenin as antineoplastic and apoptotic agent	Human SCC A431, Hep2 and RPMI 2650 cells	Thymoquinone and diosgenin suppress cell division and cytotoxicity in A431 and Hep2 cells.	[30]
50.	Effect of *Trigonella Foenum-Graecum* on cytotoxic anti-cancer properties	T-cell lymphoma (TCP), B-cell lymphomas, Thyroid Papillary carcinoma (FRO) and breast cancer (MCF7	Fenugreek has selective cytotoxic effects against cancer cellsand cell lines induce apoptosis.	[32]
51.	Effect of diosgenin on Akt-mediated prosurvival signalling	MCF-7 (ER1), MDA 231 (ER2) and MCF-10A cells	*In vivo* tumour studies shows diosgenin remarkably inhibits tumour growth in both MCF-7 and MDA231 xenografts in nude mice.	[31]
52.	Effect of *Trigonella foenum*(Fenugreek) on hepatocellular carcinoma	Hep G2 cells	FCE act as a promising non-toxic herbal drug induce apoptosis and upregulates caspase-3 dependent pathway.	[108]
53.	Effects of Trigonella foenum graecum methanol and ethyl acetate extracts, against cancer cell lines	Mice	There are significant anticancer and neuroprotective properties of both amurensin and cosmosiin derived from *T. foenum* extracts.	[109]
Hepatoprotective effect				
54.	Effect of fenugreek steroid saponins and sapogenins on hypocholesterolemia condition	Dog	Saponins present in the seed, reduced hypercholesterolemia and hypertriglyceridemia of alloxan-diabetic dogs.	[110]
55.	Hypolipidaemic effect of fenugreek seeds	Human	Fenugreek powder resulted in a significant reduction in the serum total cholesterol, LDL and VLDL cholesterol and triglyceride levels.	[111]
56.	Effect of fenugreek seeds on non-insulin dependent diabetic patients	Human	Fenugreek seed powder resulted in a significant reduction of total cholesterol, LDL and VLDL cholesterol and triglyceride levels	[23]

(Table 1) contd.....

57.	Effect of fenugreek oil on the efficiency of ovarian and liver tissues	Rat	Administration with fenugreek oil at 0.1 and 0.15 ml/mouse increased the totalnumber of cumulus-oocyte complexes as well as improved their quality.	[21]
58.	Effect of fenugreek seed (*Trigonella foenum graecum*) on ethanol-induced collagen and lipid accumulation	Rat	Administration of FPEt to alcohol-fed rats significantly improved lipid profile and reduced collagen content	[112]
59.	Effect of fenugreek (*Trigonella foenum graecum*) seed polyphenols on alchohol toxicity	Rat	Increased hepatocyte viability and reduced apoptotic nuclei were observed in FPEt-treated rats.	[20]
60.	Effect of fenugreek (*Trigonella foenum graecum*) seed polyphenols on alcohol-induced protein and lipid damage	Rat	FPEt ameliorates the pathological liver changes induced by chronic ethanol feeding	[113]
61.	Effect of dietary fenugreek seeds (Trigonella foenum-graecum) as antilithogenic herb	Mice	Fenugreek increased antioxidant enzyme activity and reduced hepatic lipid peroxidises.	[114]
62.	Effect of fenugreek seeds on fat accumulation and upregulation of LDL receptor	Mice	Hypolipidemic effect of TEFS is due to inhibition of fat accumulation and upregulation of LDLR	[115]
63.	Effect of fenugreek on diet-induced metabolic disorders	Rat	Fenugreek dose-dependently reduced the hepatic triglyceride and total cholesterol levels.	[116]
64.	Effect of fenugreek seeds extract against carbon tetrachloride induced liver toxicity	Rat	Fenugreek seeds extract as a good candidate to be used against drug induced hepatotoxicity	[117]
65.	Effect of fenugreek against metabolic disorders	Rat	FRB (1.2 ~ 4.8%) prevents diet-induced metabolic disorders such as insulin resistance, dyslipidemia and fatty liver.	[7]
66.	Effect of *Trigonella foenum-graecum L.* (Fenugreek) on liver enzymes in Ischemia-Reperfusion injury	Rat	*Trigonella foenum-graecum* L. (Fenugreek) treatment protects the rat liver against hepatic ischemia-reperfusion injury	[22]
67.	Effect of fenugreek seeds on adipogenesis and lipolysis	Rat	Fenugreek seed inhibits formation of new differentiated adipocytes from precursor cells through an anti-proliferative effect on preadipocytes	[118]
68.	Effects of fenugreek,*Nigella* and termis seeds on non-alcoholic fatty liver in obese diabetic albino rats	Rat	Considerable improvement in the liver of experimental animals was observed.	[119]
69.	Effect of combined extracts of red yeast rice and fenugreek on lipotoxicity	HepG2 hepatocytes	Combined extracts of red yeast rice and fenugreek, as low as 10–3 μg/ml, suppressed lipid content and apoptosis	[120]
70.	Effect of fenugreek in acetaminophen induced hepatotoxicity	Rat	FEN has a protective role against acetaminophen - induced hepatotoxicity by enabling hepatocyte regeneration and supressing inflammatory activity	[121]
71.	Effect of fenugreek (*Trigonella foenum graecum* Linn) in cirrhotic ascitic patients	Human	First human trial of fenugreek is safe and tolerable, no side-effects were observed.	[122]
72.	Effect of fenugreek seed supplementation on patients with type 2 diabetes mellitus	Human	Fenugreek seed has beneficial effects on fasting plasma glucose, systolic blood pressure, and liver and kidney function.	[123]
73.	Effect of fenugreek seeds extract supplementation on thioacetamide induced liver damage	Rat	Fenugreek seeds extract supplementation significantly increased plasma glucose and HDL level and remarkably decreased triglyceride, cholesterol, LDL, VLDL	[124]
74.	Effect of fenugreek (*Trigonella foenum-graecum*L.) seeds on liver antioxidant defense systems	Mice	The dietary supplementation of fenugreek seed showed a positive effect on the activities of the hepatic antioxidant defence enzymes in the aged mice.	[125]
75.	Effect of phytochemicals present in fenugreek on metabolic inflammation	Mice	Fenugreek seed suppressed metabolic inflammation via the mediation of gut microbiota.	[126]
Cardioprotective effect				
76.	Effect of fenugreek on isoproterenol-induced myocardial infarction in rats	Rat	Fenugreek displays cardioprotective effect on lipid peroxidation and antioxidant defense system during isoproterenol-induced myocardial infarction in rats.	[24]
77.	Effect of trigonelline from fenugreek seed on isoproterenol-induced myocardial injury	Rat	Its administration increases serum level of cardiac markers for cardiac dysfunctioning	[127]
78.	Effect of dietary fenugreek (*Trigonella foenum*-graecum) seeds and garlic (Allium sativum) on experimental myocardial infarction	Rat	Together fenugreek seeds with garlic offered significant changes in lipid profiling of cardiac tissue	[128]

(Table 1) contd.....

79.	Dietary effect of fenugreek (*Trigonella foenum-graecum*) seeds and garlic (*Allium sativum*) in experimental myocardial infarction	Rat	Combine dietary effect of garlic and fenugreek seeds reflect higher cardioprotective properties.	[129]
80.	Effect of fenugreek (*Trigonella foenum-graceum*) seed extract on streptozotocin induced diabetic rats as cardioprotectant agent	Rat	It lowers the metabolic abnormalities, oxidative stress and regulates apoptosis.	[25]
Gastroprotective effect				
81.	Effect of fenugreek seeds (*Trigonella foenum graecum*) on experimental gastric ulcer	Rat	Fenugreek seed decrease the mucosal injury by increasing antioxidant potential of thegastric mucosa.	[27]
82.	Effect of honey in combination with fenugreek seed extract on experimental gastric ulcer	Rat	Honey combination with fenugreek seed extract proved to be protective against lesion formation.	[26]
83.	Effect of aqueous *Trigonella feonum-gracum* and *Linum ussitatissimum* seed extracts as gastroprotective agents	Mice	*T. foenum-gracum* and *L. usitatissimum* posses anti-ulcer effect and reduce oxidative damage	[29]
84.	Effect of fenugreek seeds (*Trigonella foenum graecum*) on experimental gastric ulcer	Rat	Fenugreek seed prevent gastric ulcers and lesion formation.	[28]
85.	Effect of aqueous extracts of barley and Fenugreek on ulcer induction	Rat	Showed gastroprotective effect by lowering stomach lesion and GSH enzyme concentration.	[130]
86.	Effect of fenugreek, ginger, peppermint oil on experimentally induced gastric ulcer	Rat	Fenugreek oil notably reduced the gastric ulcer and possess gastroprotective property.	[131]
87.	Effect of fenugreek against indomethacin induced ulcer	Wistar rat	Sugaheal provide protection against oxidative damage and posses gastroprotecion property.	[8]
88.	Effect of fenugreek seed extract on gastric ulcers	AGS cells and Rat	Phytoconstituents like flavonoids and saponins, exhibit antioxidant and gastroprotective activity in the extract	[132]
89.	Effect of fenugreek seed extract in experimentally induced gastric ulcer	Wistar rats	Group fed with fenugreek showed a notable reduction in ulcer index, volume of gastric juice and acidity.	[133]
Anti-sterility and anti-fertility effect				
90.	Effect of fenugreek oil on the efficiency of ovarian and liver tissues	Mice	0.10-0.15ml/mouse dose displayed notable changes in number and quality of cumulus-oocyte complexes.	[21]
91.	Effect of fenugreek seeds in male and female on fertility	Rabbit	Treated animal showed proliferative changes of endometrial glands and histopathology changes of testis tissue	[134]
92.	Effects of aspirin and fenugreek seed on the testes	Mice	Fenugreek seed reversed the structural changes occurred in the testis of mice caused by aspirin	[135]
93.	Effect of hydro-alcoholic extract of fenugreek seeds on female reproductive hormones	Mice	Fenugreek significantly increases the progesterone level and reduction in folliculogenesis.	[136]
94.	Effect of fenugreek seed extract on carbendazim-inhibited spermatogenesis	Rat	Fenugreek significantly reduced testicular toxicity of carbendazim.	[137]
95.	Effect of fenugreek seeds extracton cyclophosphamide-induced changes in testes	Mice	Fenugreek seed extract decreased testis damage induced by cyclophosphamide.	[138]
96.	Effect of steroidal extract of fenugreek on reproductive functions	Mice	Fenugreek notably improve reproductive parameters in male mice	[139]
97.	Effect of fenugreek seed extract on cytotoxicity and testicular alterations	Rat	Activity of catalase (CAT) and superoxide dismutase (SOD) increased in the testis of treated animals	[140]
98.	Effect of fenugreek on menstrual disorders	Human	Fenugreek helped in managing menstrual disorders by relieving pelvic congestion, breast tenderness and improve reproductive health.	[11]
99.	Effect of fenugreek on reproductive, cytological and biochemical toxicity	Mice	Total sperm count and sperm motility increased in fenugreek treated mice.	[141],
100.	Effect of combination of fenugreek with insulin and Glimepiride on male reproductive system	Rat	Fenugreek in combination with insulin and glimepiride showed improvement in reproductive parameters of diabetic rats.	[142]
101.	Effect of novel extract of fenugreek husk (FenuSMART™): A Randomized, Double-Blind, Placebo-Controlled study on postmenopausal symptoms and hormonal balance	Human	FHE supplementation was also found to have a beneficial effect in the management of healthy serum calcium levels	[143]
102.	Efficacy of Furosap™, a novel*Trigonella foenum-graecum*seed extract on testosterone level and sperm profile	Human	It improved the sex hormone level in volunteers and modulate sperm morphology positively.	[9]
103.	Effect of fenugreek extract with docosahexaenoic acid in attenuating learning and memory deficits in ovariectomized rats	Rat	Fenugreek with acid supplementation could be used to improve menopause induce memory and learning impairment.	[144]

(Table 1) contd.....

104.	Effect of diosgenin on testicular damage	Rat	Diosgenin improved testosterone level and prevent testicular apoptosis.	[145]
105.	Effect of fenugreek seeds aqueous extract on ovarian hyperstimulation syndrome	Rat	Fenugreek seed extract decrease serum estradiol level in rat.	[34]
106.	Effects of the fenugreek seeds' powder and its aqueous and oil extracts on male reproductive system	Rat	Fenugreek seed showed significant changes in sperm viability and sperm count in rat.	[35]
107.	Effect of *Trigonella foenum-graecum*seed extract in male volunteers	Human	Sperm motility, reflex erection score, mood and mental alertness incresead in the male volunteers.	[146]
108.	Effect of fenugreek on menopause induced memory loss, BDNF and dendritic arborization in ovariectomized rats	Rat	Combination of fenugreek with choline-docosahexaenoic acid could be helpful in improving memory deficit.	[147]
109.	Effect of fenugreek on reproductive health	Human	Fenugreek improved reproductive health of women	[148]
Antibacterial property				
110.	Effect of fenugreek seed oil	*Escherichia coli, Staphylococcus aureus,* and *Salmonella typhimurium* and *Aspergillus niger*	The highest antimicrobial activity was recorded against *E.coli* as compared to others	[36]
111.	Antibacterial effect of fenugreek seed extract	*Bacillus subtilis, Staphylococcus aureus,* and *Escherichia coli*	Fenugreek extract from germinating seeds recorded highest antimicrobial property compared to ethanolic and methanolic extract	[149]
112.	Antibacterial effect of fenugreek extracts	*Escherichia coli, Pseudomonas aeruginosa* , and *Serratia marcescens,* and *Bacillus cereus*	*T. foenum-graecum* leaves extracts showed notable antibacterial effect with maximum activity against *Serratia marcescens*	[42]
113.	Effect of fenugreek seed gum based nanocomposites	*Listeria monocytogenes*, *Escherichia coli, Staphylococcus aureus* and *Bacillus cereus*	Fenugreek seed gum based clay nanocomposite films showed strong antimicrobial property against foodborne payhogens	[150]
114.	Effect of fenugreek seed extract showing antibacterial property	*Escherichia coli, Pseudomonas aeruginosa, Salmonella Typhi, Streptococcus pyogenes* and *Staphylococcus aureus*	Fenugreek seed extract might show antibacterial property at the concentration of 50-100 mg/ml	[151]
115.	Effect of fenugreek seeds and shoots extract	*Staphylococcus aureus* and *Pseudomonas aeruginosa*	Fenugreek shoots extract have strong antimicrobial property compared to its seeds extract	[152]
116.	Effect of fenugreek seed extract as antibacterial agent	*Staphylococcus aureus, Pseudomonas aeruginosa, Proteus mirabilis, Salmonella typhi, Escherichia coli,* and *Vibrio parahaemolyticus*.	Highest antibacterial activity was recorded with *Staphylococcus aureus* and *Pseudomonas aeruginosa* (22 mm and 17 mm diameter of inhibition zones respectively)	[37]
117.	Effect of fenugreek seeds' phytoconstituents	*S. aureus, E. coli, Citrobacter freundii,* and *Pseudomonas aeruginosa*	Extract showed an activity index of 1 to 1.25 with Gram-positive bacterial strains and 1 to 1.21 activity index with Gram-negative bacterial strains	[40]
118.	Effect of si;ver nano particle synthesized using fenugreek leaves extract	*S. aureus, E. coli, P. aeruginosa* and *V. cholera*	Highest inhibitory activity was found againstP.aeruginosacompared to other bacteria.	[39]
119.	Effect of fenugreek oil nanoemulsion	*Escherichia coli*,*Bacillus subtilis*,*Staphylococcus aureus*, and *Pseudomonas aeruginosa*	Nanoemulsion recorded antimicrobial effect against Gram positive and Gram negative bacterial strains used in the study	[153]
Antifungal property				
120.	Effect of fenugreek as antifungal agent	*Candida species (C. albicans, C. glabrata, C. parapsilosis).*	Fenugreek extract found to have antifungal activity against human pathogenic fungal strains	[43]
121.	Effect of seed and callus extract of fenugreek	*Aspergillus niger* and *Candida albicans*	Petroleum ether extract of *T.foenum- graecum* seeds have higher antimicrobial activity than methanoilc extract.	[41]
122.	Effect of novel defensin-like antifungal peptide from fenugreek	*Fusarium oxysporum*,*Fusarium solani*, and*Rhizoctonia solani*.	Defensin-like antifungal peptide (Tf-AFP)isolated from fenugreek seed possess antifungal property.	[45]

(Table 1) contd.....

123.	Effect of silver nano particle by using fenugreek seed extract as antifungal agent	*Candida Albicans*	Silver nanoparticle synthesized using fenugreek showed antifungal property against *Candida* species	[46]
Immunological property				
124.	Effect of fenugreek extract as immunomodulator	Mice	Fenugreek stimulates the immune function by up-regulating immune related genes	[47]
125.	Effect of aqueous extract of fenugreek (*Trigonella foenum-graecum*L.) on immune response	Hen	Fenugreek extract dose of 15 ml/l added to the drinking water improved inmmune responses of treated model	[51]
126.	Effect of fenugreek combined with prebiotics on immune system of treated model	*Sparus aurata*	Fenugreek combined with prebiotic strains enhance humoral immunity	[50]
127.	Effect of fenugreek on immune status of gilthead seabream	*Sparus aurata*	Inclusion of fenugreek seeds in the diet at 5% or 10% enhanced humoral and cellular immune activities	[48]
128.	Effect of fenugreek on immune functions	*Sparus aurata*	Fenugreek supplemented diet at higher inclusion dose upregulate skin mucosal immunity responses	[49]
129.	Effect of fenugreek on hematological parameters	Rat	Fenugreek enhanced Hb, RBC and WBC count at a dose of 400 mg/kg body weight.	[53]
130.	Effect of fenugreek on immune system	Humans	Diet combined with fenugreek impoved haematological status of treated obese women	[52]

4.2. Hepatoprotective Effects

Impairments of the liver can be favorably cured or controlled by the supplementation of antioxidants. Components like diosgenin, saponins, flavonoids, and polyphenol possess antioxidant, hypolipidemic, and hypocholesterolemic properties. In one study, fenugreek improved lipid profile and collagen content in the hepatotoxic Wistar rats at a dose of 200 mg/kg per day [20]. In another study, fenugreek reduced lipid aggregation in the liver by increasing lipid excretion in feces. Serum total cholesterol, low-density lipoproteins, very low-density lipoproteins, cholesterol, and triglycerides were also significantly reduced. However, the high-density lipoprotein and cholesterol fraction remained unchanged [21]. Active components of fenugreek, such as 4-hydroxyisoleucine and galactomannan, lowered blood glucose levels and improved lipid metabolism. Metabolic and hepatic damage that occurred after ischemia-reperfusion could be prevented by fenugreek. Fenugreek was found to be effective in reducing damage caused by ischemia-reperfusion. It has been shown that polyphenols and flavonoids are helpful in treating hepatic ischemia. The exposure of fenugreek extract to rats showed that the levels of plasma serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH) levels were significantly reduced, thus showing the hepatoprotective effects [22].

4.3. Cardioprotective Effects

Studies have revealed that fenugreek seeds are effective in lowering cholesterol levels and thus may also act as a cardioprotective agent [23]. The constituents of fenugreek, such as saponins, diosgenin, galactomannan, coumarin, fenugreekine, nicotinic acid, sapogenins, phytic acid, scopoletin, and trigonelline, have pharmacological properties. The effect of fenugreek was studied on isoproterenol-induced myocardial infarction in rats. The study revealed the cardioprotective effect of fenugreek in rats by increasing the activities of both enzymatic and non-enzymatic antioxidants (SOD, CAT, GPx, and GSH) [24]. Fenugreek strongly regulates blood lipid levels; hence, it is effective against atherosclerosis by lowering cholesterol, triglycerides, and LDL levels and raising HDL levels [12]. Fenugreek, a good anti-oxidant, protects the myocardial tissue from oxidative stress and improves metabolic abnormalities. One of the studies demonstrated the protective effect of the hydro-alcoholic extract of fenugreek seeds in STZ-induced diabetic rats. The results showed that fenugreek seed extract has the potential to treat diabetic cardiomyopathy by altering the expression of genes involved in apoptosis. It was reported that the expression of pro-apoptotic *Bax* gene and intercellular adhesion molecule was downregulated, and the anti-apoptotic gene *BCl2* was upregulated, indicating the anti-oxidant and anti-apoptotic property of fenugreek [25].

4.4. Gastroprotective Effects

Lifestyle and unhealthy diet style result in abdominal discomfort, loss of appetite, nausea, vomiting, gastric ulcer, and peptic ulcer. There are several studies reporting the beneficial role of fenugreek against gastrointestinal diseases. It possesses anti-ulcer, anti-inflammatory, gastroprotective, antioxidant as well as anti-secretory properties. The study on Albino rats revealed that when fenugreek seeds were orally given to rats, the severity of ulcers reduced significantly compared to the untreated group of rats [26]. Mucosal damage, hyperaemia, submucosal oedema, and severe congestion of vessels marked by HCl-ethanol induced in rats were significantly lowered in pre-treated rats with fenugreek seeds [27]. The fenugreek seed gel fractions of 700 mg/rat given orally proved anti-ulcerogenic. Gel fraction showed significantly less lesion formation, altered gastric secretion, reduced lipid peroxidation, and increased antioxidant capacity of the gastric mucosa [28]. Sugaheal®, the 4-hydroxyisoleucine and trigonelline enriched fraction (TF4H 28%), a well-known anti-diabetic drug possesses good antioxidant properties. In a study, sugaheal given to Wistar rats showed the beneficial property against gastric ulcers. Microscopic analysis of the stomach wall revealed a reduction in ulcer spots. A 100 mg/kg body weight (BW) dose of sugaheal displayed maximum protection against ROS damage mediated by a 48 mg/kg BW dose of indomethacin in a rat's stomach [8]. The polyphenols present in fenugreek are responsible for treating gastric and acute gastric injuries induced by chemicals [29]. Fenugreek seeds improve appetite

and gastric discomfort, and their oral administration enhances salivary flow as well as lactase activity [26].

4.5. Anti-cancerous Effects

Fenugreek contains a bioactive compound, 'diosgenin,' which is an anti-cancer agent [30]. Several studies have shown the benefit of fenugreek against cancerous cells by inducing apoptosis. Diosgenin arrests the G1 phase of the cell cycle (in both MCF-7 and MDA-231 cells) by downregulation of cyclin D1 and cdk-2. Treatment with diosgenin showed upregulation of p21 without involving p53 in the treated cells. It was also found to be involved in the up- and down-regulation of the protein involved in the apoptosis of cells (*in vivo* as well as *in vitro*) [31]. Levels of Bcl2 decreased in the breast cancer (BCa) cells, and the activity of caspase 3 increased in the treated cells compared to control cells. The results showed that diosgenin influences the apoptotic pathway in cancerous cells. Akt-mediated signaling, crucial for the progression of breast cancer cells, was downregulated by the treatment of diosgenin [31]. Thymoquinone and diosgenin possess anti-neoplastic property as they increase the expression of apoptotic genes and caspase activity, inhibit Akt and JNK phosphorylations, and thus prevents cell division. These two bioactive components possess synergistic effects and anti-proliferative properties [30]. A study showed that intraperitoneal administration of the fenugreek seed extract caused 70% inhibition of tumor cell growth compared to control and modulated 1,2-dimethylhydrazine-induced hepatic oxidative stress during colon carcinogenesis by increasing catalase, superoxide dismutase, glutathione-s-transferase activities in the liver of treated animal [4]. Fenugreek possesses a cytotoxic property, which has shown to be useful in the prevention and treatment of cancer [32]. According to a study, treatment with 10-15 ug/ml of FE for 72 hr showed inhibition of tumor growth in breast, pancreatic, and prostate cancer cell lines (PCa) [33].

4.6. Anti-sterility and Anti-fertility Effects

Reproductive health benefits of fenugreek include regulation of sex hormones, sperm viability, sperm count, and other sexual dysfunction in both genders. Bioactive components of fenugreek, such as steroidal saponins (Diosgenin and yamogenin), possess anti-sterility and anti-androgenic effects. According to some studies, saponin binds to estradiol receptors and modulates the activity of E2 in the rat model of Ovarian Hyperstimulation Syndrome [34]. Diosgenin regulates sexual activity by stimulating growth hormones from the pituitary [35]. Diosgenin is a precursor used for the majority of commercially available cortisone, pregnenolone, progesterone, and other steroids. Rats exposed to fenugreek powder, oil extract, and aqueous extract altered sex hormone levels, sperm count, and sperm viability [35].

4.7. Anti-Bacterial Property

The antimicrobial property of fenugreek has become popular among various herbal extracts. The effectiveness of fenugreek against many bacteria has been studied. Sulieman *et al*. [36] studied the antimicrobial property of fenugreek against *Staphylococcus aureus*, *Escherichia coli*, *Salmonella typhimurium,* and *Aspergillus niger*. They reported that the 100% concentrated fenugreek oil showed maximum inhibition against *Escherichia coli* rather than *Salmonella typhimurium* and *Staphylococcus aureus*. Ethanolic extract of fenugreek seed was also tested on 6 bacterial strains, including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Salmonella typhi*, *Escherichia coli,* and *Vibrio parahaemolyticus*, with low to moderate activity except on *Staphylococcus aureus* and *E. coli* [37]. Phytochemical analysis showed the antibacterial properties of fenugreek seed extracts due to the presence of alkaloids, flavonoids, tannins, saponins, terpenoids, and steroids [38]. The antibacterial activity of AgNPs synthesized using fenugreek leaves extract was tested against *S. aureus, E. coli, P. aeruginosa* and *V. cholera,* with an inhibition zone of 6, 12, 11, and 6 mm, respectively. Fenugreek leaves contain bioactive components, such as flavonoids, including quercetin, vitexin, and kaempferol and glycosides, phenolic compounds, and ascorbic acid, which act as a bioactive source or reducing agent for the synthesis of silver nanoparticles [39]. Phytoconstituents, particularly polyphenols, showed low to strong effects on most tested strains, with a strong antibacterial effect of fenugreek compared to aqueous extracts [40]. An *in vitro* study on methanolic and petroleum ether extracts of seeds and callus extracted from hypocotyls and cotyledons explants of fenugreek against standard microorganisms, *Bacillus, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Aspergillus niger*, and *Candida albicans* reported antimicrobial activity of petroleum ether extract with inhibition zones of 17±0.33mm and 15±0.57mm against *Escherichia coli* and *Staphylococcus aureus,* respectively, which were higher than methanolic extract [41]. The minimum inhibitory concentration (MIC) recorded was 6.25 to 25 mg/ml of *Trigonella foenum-graecum* leaf extract, showing significant antibacterial properties that could be therapeutic for a wide range of drug-resistance microorganisms with minimal or no side effects [42].

4.8. Antifungal Property

Multi-drug resistant strains of pathogenic fungi have led to the utilization of medicinal plants and compounds isolated from them for their antifungal property. Extract of fenugreek was proved to be effective against pathogenic fungi strains of *Candida* species [43]. A study on ethanolic extract of fenugreek showed the highest zone of inhibition of 16.510+ 0.85 mm and 38.395% of mycelial inhibition using 100 µl of concentration against *Microsporum gypseum*. Such antifungal property of fenugreek is due to the presence of secondary metabolites, such as flavonoids, saponins, alkaloids, steroids, and tannins [44]. Maximum zone of inhibition, *i.e.*, 20±0.88 mm against *Aspergillus niger* by concentration 250 mg/ml and 17±0.57mm of inhibition zone against *Candida albicans* by concentration 250 mg/ml have been recorded by petroleum ether extract of fenugreek seeds [41]. A novel defensin-like antifungal peptide (Tf AFP) of molecular mass 10.3 kDa has been isolated from *Trigonella foenum graecum* (fenugreek) and demonstrated antifungal properties against *Fusarium oxysporum, Fusarium solani,* and *Rhizoctonia solan* fungal species [45]. Elsidding *et al*. [46] synthesized silver nanoparticles using fenugreek extract as an antifungal agent against *Candida albicans*. Three different concentrations of silver nitrate were mixed with fenugreek extract, which served as a reducing agent and generated silver nanoparticles.

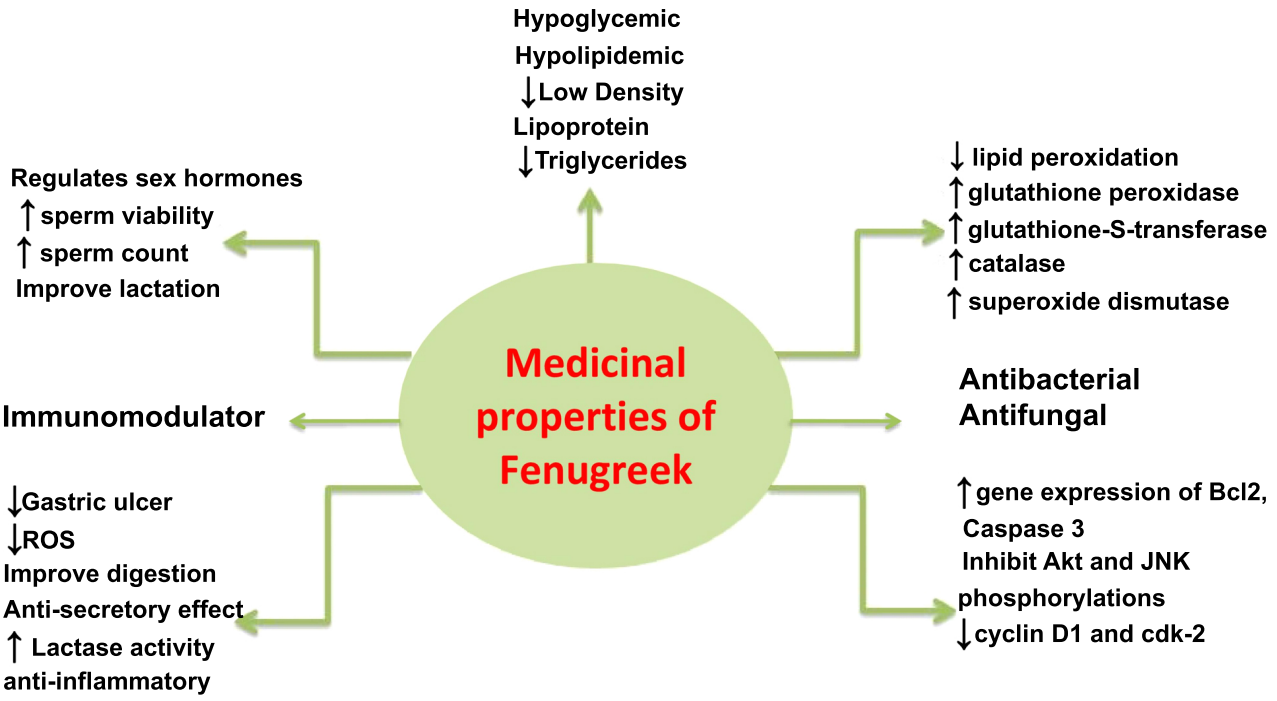

Fig. (2). Medicinal properties of fenugreek.

4.9. Immunological Property

Several studies reported the immunomodulatory activity of fenugreek on immune functions, including humoral immunity, leucocytic count, phagocytic index, serum globulins, and related genes. Mice treated with three different doses of aqueous extract of fenugreek showed increased activity of humoral immunity at 100 mg and delayed hypersensitivity. The phagocytic index and phagocytic capacity of macrophages were significantly elevated in the treated mouse model [47]. The dietary supplement action of fenugreek (*Trigonella foenum graecum*) with gilt-head seabream (*Sparus aurata* L.) was found to stimulate the immune system by up-regulating immune-related genes along with significant improvement in the hematological parameters [48] and enhance skin mucosal immunity response by increasing some enzymatic activities [49]. Fenugreek combined with prebiotic strains showed a significant rise in the expression of immune-related genes (*igm*, *tcr-β*, *csfr1,* and *bd*) and the growth performance of the species [50]. In addition, fenugreek extract refined the immune system of egg-laying hens and production performance [51]. Ebrahimi *et al*. [52] reported remarkable improvement in the levels of immunoglobulins (IgG), lymphocytes, and leukocytes in obese women after 6 weeks of regular, intense training and fenugreek supplementation. Hematological parameters analysis revealed that the extract notably (p<0.05) enhanced Hb, RBC, and WBC count at a dose of 400 mg/kg body weight in the rodent model [53]. Therefore, the efficacy of fenugreek on hematological parameters could be used to strengthen the immune system.

CONCLUSION

For ages, the plant extract and its products have been proven to be successful in treating various ailments associated with diseases or drugs in humans and available experimental models [54 - 70]. Fenugreek has been used for centuries to treat various diseases due to a wide range of properties, including anti-diabetic, hepatoprotective, cardioprotective, anti-cancerous, anti-androgenic effects, and anti-sterility effects. Results obtained from *in vivo* and *in vitro* studies on fenugreek have shown beneficial effects not only on diabetes, reproductive issues, and hypolipidemic conditions but also on immune functions. It has several properties, including anticancer properties, antimicrobial, gastroprotective, cardioprotective, antioxidative, antinociceptive, antimicrobial properties, anthelmintic, anti-arthritic, and vascular protective effects (Fig. **2**). However, more studies are required on its interaction with other drugs. Furthermore, its diverse chemical composition attributes for future application as therapeutic agents. The consumption of fenugreek is safe and proved to be a necessary ingredient of our daily diet to drive health benefits. A comprehensive investigation based on clinical trials is required to investigate the role of fenugreek in the treatment of numerous ailments.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The author that confirmed all the sources for the data search are mentioned in the manuscript.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Sun W, Shahrajabian MH, Cheng Q. Fenugreek cultivation with emphasis on historical aspects and its uses in traditional medicine and modern pharmaceutical science. Mini Rev Med Chem 2021; 21(6): 724-30. [http://dx.doi.org/10.2174/18755607MTEx4OTAn5] [PMID: 33245271]

[2] Rashid R, Ahmad H, Ahmed Z, Rashid F, Khalid N. Clinical investigation to modulate the effect of fenugreek polysaccharides on type-2 diabetes. Bioactive Carbohyd Diet Fibre 2019; 19: 100194. [http://dx.doi.org/10.1016/j.bcdf.2019.100194]

[3] Chou IW, Cheng YH, Chen YR, Hsieh PCH, King K. Fenugreek Compound (N55) lowers plasma glucose through the enhancement of response of physiological glucagon-like peptide-1. Sci Rep 2017; 7(1): 12265. [http://dx.doi.org/10.1038/s41598-017-12290-x] [PMID: 28947828]

[4] Devasena T, Venugopal Menon P. Fenugreek seeds modulate 1,2-dimethylhydrazine-induced hepatic oxidative stress during colon carcinogenesis. Ital J Biochem 2007; 56(1): 28-34. [PMID: 17511351]

[5] Rahul , Siddique YH. Neurodegenerative diseases and flavonoids: special reference to kaempferol. CNS Neurol Disord Drug Targets 2021; 20(4): 327-42. [http://dx.doi.org/10.2174/1871527320666210129122033] [PMID: 33511932]

[6] Varshney H, Siddique YH. Role of natural plant products against Alzheimer's disease. CNS Neurol Disord Drug Targets 2021; 20: 904-41. [http://dx.doi.org/10.2174/1871527320666210420135437]

[7] Muraki E, Chiba H, Taketani K, *et al.* Fenugreek with reduced bitterness prevents diet-induced metabolic disorders in rats. Lipids Health Dis 2012; 11(1): 58. [http://dx.doi.org/10.1186/1476-511X-11-58] [PMID: 22642742]

[8] Ghosal N, Firdaus SB, Naaz S, *et al.* Gastroprotective effect of Fenugreek 4-hydroxyisoleucine and trigonelline enriched fraction (TF4H (28%)) Sugaheal® against indomethacin induced ulcer in male wistar rats. J Pharm Res 2016; 10: 351-64.

[9] Maheshwari A, Verma N, Swaroop A, *et al.* Efficacy of FurosapTM, a novel *Trigonellafoenum-graecum* seed extract, in enhancing testosterone level and improving sperm profile in male volunteers. Int J Med Sci 2017; 14(1): 58-66. [http://dx.doi.org/10.7150/ijms.17256] [PMID: 28138310]

[10] Al-Asadi JN. Therapeutic uses of fenugreek (*Trigonella foenum-graecum L.).* Am J Soc Issues Hum 2014; 2: 21-36.

[11] Yassin SA. Herbal remedy used by rural adolescent girls with menstrual disorders. J Am Sci 2012; 8: 467-73.

[12] Moosa AS, Rashid MU, Asadi AZS, *et al.* Hypolipidemic effects of fenugreek seed powder. Bangladesh J Pharmacol 2006; 1: 64-7.

[13] Neelakantan N, Narayanan M, de Souza RJ, van Dam RM. Effect of fenugreek (*Trigonella foenum-graecumL.)* intake on glycemia: a meta-analysis of clinical trials. Nutr J 2014; 13(1): 7. [http://dx.doi.org/10.1186/1475-2891-13-7] [PMID: 24438170]

[14] Kassaian N, Azadbakht L, Forghani B, Amini M. Effect of fenugreek seeds on blood glucose and lipid profiles in type 2 diabetic patients. Int J Vitam Nutr Res 2009; 79(1): 34-9. [http://dx.doi.org/10.1024/0300-9831.79.1.34] [PMID: 19839001]

[15] King K, Lin NP, Cheng YH, Chen GH, Chein RJ. Isolation of positive modulator of glucagon-like peptide-1 signaling from *Trigonellafoenum-graecum* (fenugreek) seed. J Biol Chem 2015; 290(43): 26235-48. [http://dx.doi.org/10.1074/jbc.M115.672097] [PMID: 26336108]

[16] Ahmed J, LuAl-Adaban R, Mansour A. Evaluation of the effectiveness of cinnamon, fenugreek and their combination on patients with type 2 diabetes in Basrah. Med J Basrah Univ 2014; 32: 15-21. [http://dx.doi.org/10.33762/mjbu.2014.94443]

[17] Luan G, Wang Y, Wang Z, *et al.* Flavonoid glycosides from fenugreek seeds regulate glycolipid metabolism by improving mitochondrial function in 3T3-L1 adipocytes *in vitro*. J Agric Food Chem 2018; 66(12): 3169-78. [http://dx.doi.org/10.1021/acs.jafc.8b00179] [PMID: 29526086]

[18] Hamden K, Jaouadi B, Salami T, Carreau S, Bejar S, Elfeki A. Modulatory effect of fenugreek saponins on the activities of intestinal and hepatic disaccharidase and glycogen and liver function of diabetic rats. Biotechnol Bioprocess Eng; BBE 2010; 15(5): 745-53. [http://dx.doi.org/10.1007/s12257-009-3159-0]

[19] Hamden K, Jaouadi B, Carreau S, Bejar S, Elfeki A. Inhibitory effect of fenugreek galactomannan on digestive enzymes related to diabetes, hyperlipidemia, and liver-kidney dysfunctions. Biotechnol Bioprocess Eng; BBE 2010; 15(3): 407-13. [http://dx.doi.org/10.1007/s12257-009-3037-9]

[20] Kaviarasan S, Sundarapandiyan R, Anuradha CV.

[21] Hassan AM, Khalil WK, Ahmed KA. Genetic and histopathology studies on mice: Effect of fenugreek oil on the efficiency of ovarian and liver tissues. Afr J Biotechnol 2006; 5: 477-83.

[22] Taha Mohammed M. Effect of *TrigonellaFoenum-Graecum L.*(Fenugreek) on liver enzymes in ischemia-reperfusion injury. Iraqi Postgrad Med J 2013; 12: 69-74.

[23] Sharma RD, Sarkar A, Hazra DK, *et al.* Hypolipidaemic effect of fenugreek seeds: A chronic study in non-insulin dependent diabetic patients. Phytother Res 1996; 10(4): 332-4. [http://dx.doi.org/10.1002/(SICI)1099-1573(199606)10:4<332::AID-PTR827>3.0.CO;2-J]

[24] Manju V, Murugesan M, Revathi R. Cardioprotective effect of fenugreek on isoproterenol-induced myocardial infarction in rats. Indian J Pharmacol 2011; 43(5): 516-9. [http://dx.doi.org/10.4103/0253-7613.84957] [PMID: 22021992]

[25] Bafadam S, Mahmoudabady M, Niazmand S, Rezaee SA, Soukhtanloo M. Cardioprotective effects of Fenugreek (*Trigonella foenum-graceum*) seed extract in streptozotocin induced diabetic rats. J Cardiovasc Thorac Res 2021; 13(1): 28-36. [http://dx.doi.org/10.34172/jcvtr.2021.01] [PMID: 33815699]

[26] Mahmood AA, Sidik K, Salmah I. Anti-ulcer and gastro protective effects of honey in combination with *Trigonellafoenum-graecum* seed extract on experimental gastric ulcer in rats. Int J Mol Med Adv Sci 2005; 1: 225-9.

[27] Suja Pandian R, Anuradha CV, Viswanathan P. Gastroprotective effect of fenugreek seeds (*Trigonella foenum graecum*) on experimental gastric ulcer in rats. J Ethnopharmacol 2002; 81(3): 393-7. [http://dx.doi.org/10.1016/S0378-8741(02)00117-4] [PMID: 12127242]

[28] Thirunavukkarasu V, Anuradha CV. Gastroprotective effect of fenugreek seeds (*Trigonellafoenum graecum*) on experimental gastric ulcer in rats. J Herbs Spices Med Plants 2007; 12(3): 13-25. [http://dx.doi.org/10.1300/J044v12n03_02]

[29] Mequanente S, Makonnen E, Debella A. Gastroprotective effect of aqueous *Trigonellafeonum-gracum* and linumussitatissimum seed extracts in mice. Pharmacol Online 2006; 2: 324-34.

[30] Das S, Dey KK, Dey G, *et al.* Antineoplastic and apoptotic potential of traditional medicines thymoquinone and diosgenin in squamous cell carcinoma. PLoS One 2012; 7(10): e46641. [http://dx.doi.org/10.1371/journal.pone.0046641] [PMID: 23077516]

[31] Srinivasan S, Koduru S, Kumar R, Venguswamy G, Kyprianou N, Damodaran C. Diosgenin targets Akt-mediated prosurvival signaling in human breast cancer cells. Int J Cancer 2009; 125(4): 961-7. [http://dx.doi.org/10.1002/ijc.24419] [PMID: 19384950]

[32] Alsemari A, Alkhodairy F, Aldakan A, *et al.* The selective cytotoxic anti-cancer properties and proteomic analysis of *TrigonellaFoenum-Graecum.* BMC Comple Alt Med 2014; 14: 1-9.

[33] Shabbeer S, Sobolewski M, Anchoori RK, *et al.* Fenugreek: A naturally occurring edible spice as an anticancer agent. Cancer Biol Ther 2009; 8(3): 272-8. [http://dx.doi.org/10.4161/cbt.8.3.7443] [PMID: 19197146]

[34] Ben Hameid A, Al-Sindi T, Allow A, Nafie E, Alahmad B, Faisal G. Substantial effect of fenugreek seeds aqueous extract on serum estradiol level in ovarian hyperstimulation syndrome rat model. Oman Med J 2019; 34(3): 238-43. [http://dx.doi.org/10.5001/omj.2019.45] [PMID: 31110632]

[35] Mansour AB, AbouElghait A, Abo-youssef A, Abdelwahab N, Helaly H. A comparative study on the effects of the fenugreek seed's powder and its peroductive system in Albino Rats.Bull Pharm Sci. Assiut 2021; 44: 593-605.

[36] Sulieman AM, Ahmed HE, Abdelrahim AM. The chemical composition of fenugreek (*Trigonellafoenum graceum L.*) and the antimicrobial properties of its seed oil. Gezira J Eng Appl Sci 2008; 3: 52-71.

[37] Al-Timimi LAN. Antibacterial and anticancer activities of fenugreek seed extract. Asian Pac J Cancer Prev 2019; 20(12): 3771-6. [http://dx.doi.org/10.31557/APJCP.2019.20.12.3771] [PMID: 31870120]

[38] Alwhibi MS, Soliman DA. Evaluating the antibacterial activity of fenugreek (*Trigonella foenum-graecum*) seed extract against a selection of different pathogenic bacteria. J Pure Appl Microbiol 2014; 8: 817-21.

[39] Ghoshal G, Singh M. Characterization of silver nano-particles synthesized using fenugreek leave extract and its antibacterial activity. Mater Sci Energy Technol 2022; 5: 22-9. [http://dx.doi.org/10.1016/j.mset.2021.10.001]

[40] Benyagoub E, Nabbou N, Aguid A, Alkhudhairy MK, Bendada F. *In vitro* antibacterial activity of fenugreek seeds' phytoconstituents from Taghit Region (Southwest of Algeria) against the bacterial strains responsible for UTI. Curr Bioact Compd 2021; 17(4): 339-55. [http://dx.doi.org/10.2174/1573407216999200703123154]

[41] ElNour ME, Ali AM, Saeed BE. Antimicrobial activities and phytochemical screening of callus and seeds extracts of fenugreek (*Trigonella foenum-graecum*). Int J Curr Microbiol Appl Sci 2015; 4: 147-57.

[42] Dharajiya D, Jasani H, Khatrani T, Kapuria M, *et al.* Evaluation of antibacterial and antifungal activity of fenugreek (*Trigonella foenum-graecum*) extracts. Int J Pharm Pharm Sci 2016; 8: 212-7.

[43] Jasim AS, Kumar YA, Benjamin JC, Masih HA. Studies on antifungal properties of some plant extracts (garlic, fenugreek, ginger) against of clinical isolate *Candida* species. Int J Sci Eng Technol Res 2013; 2: 2180-5.

[44] Puneet Sudan , Manish Goswami , Jitender Singh . Antifungal potential of Fenugreek seeds (*Trigonella foenum-graecum*) crude extracts against Microsporum gypseum. Int J Res Pharm Sci 2020; 11(1): 646-9. [http://dx.doi.org/10.26452/ijrps.v11i1.1870]

[45] Oddepally R, Guruprasad L. Isolation, purification, and characterization of a stable defensin-like antifungal peptide from *Trigonella foenum-graecum* (fenugreek) seeds. Biochemistry 2015; 80(3): 332-42. [http://dx.doi.org/10.1134/S0006297915030086] [PMID: 25761687]

[46] Elsiddig ES. Green Synthesis of Silver Nano-particles by Using Fenugreek Seeds Extract and Application as Antifungal Agent. : Doctoral dissertation, Sudan University of Science & Technology

[47] Bin-Hafeez B, Haque R, Parvez S, Pandey S, Sayeed I, Raisuddin S. Immunomodulatory effects of fenugreek (*Trigonella foenum graecum L.*) extract in mice. Int Immunopharmacol 2003; 3(2): 257-65. [http://dx.doi.org/10.1016/S1567-5769(02)00292-8] [PMID: 12586606]

[48] Guardiola FA, Bahi A, Esteban MA. Effects of dietary administration of fenugreek seeds on metabolic parameters and immune status of gilthead seabream (*Sparus aurata L*). Fish Shellfish Immunol 2018; 74: 372-9. [http://dx.doi.org/10.1016/j.fsi.2018.01.010] [PMID: 29337247]

[49] Guardiola FA, Bahi A, Jiménez-Monreal AM, Martínez-Tomé M, Murcia MA, Esteban MA. Dietary administration effects of fenugreek seeds on skin mucosal antioxidant and immunity status of gilthead seabream (*Sparus aurata L*). Fish Shellfish Immunol 2018; 75: 357-64. [http://dx.doi.org/10.1016/j.fsi.2018.02.025] [PMID: 29462748]

[50] Bahi A, Guardiola FA, Messina C, *et al.* Effects of dietary administration of fenugreek seeds, alone or in combination with probiotics, on growth performance parameters, humoral immune response and gene expression of gilthead seabream (*Sparus aurata L*). Fish Shellfish Immunol 2017; 60: 50-8. [http://dx.doi.org/10.1016/j.fsi.2016.11.039] [PMID: 27856325]

[51] Zadeh JB, kor NM, Olfati A. The effects of different levels aqueous extract of fenugreek (*Trigonella foenum-graecum* L.) on performance and immune response of laying hens. J Essent Oil-Bear Plants 2015; 18(6): 1476-81. [http://dx.doi.org/10.1080/0972060X.2014.981594]

[52] Ebrahimi K, Mogharnasi M. The effect of six weeks of high-intensity interval training and fenugreek supplementation on indicators of immune system in overweight and obese women. Medical journal of mashhad university of medical sciences 2022; 65(1): 193-207.

[53] Chourasiya A, Sahu RK, Khan MA. Anti-Anemic and haemopoietic evaluation of *Trigonella foenum-graecum* (Fenugreek) in rodent model. J Drug Deliv Ther 2019; 9(4-s): 332-7. [http://dx.doi.org/10.22270/jddt.v9i4-s.3335]

[54] Ali F, Rahul , Naz F, Jyoti S, Siddique YH. Health functionality of apigenin: A review. Int J Food Prop 2017; 20(6): 1197-238. [http://dx.doi.org/10.1080/10942912.2016.1207188]

[55] Ali F, Siddique YH. Bioavailability and pharmaco-therapeutic potential of luteolin in overcoming Alzheimer's disease. CNS Neurol Disord Drug Targets 2019; 18(5): 352-65. [http://dx.doi.org/10.2174/1871527318666190319141835] [PMID: 30892166]

[56] Beg T, Jyoti S, Naz F, *et al.* Protective effect of kaempferol on the transgenic *Drosophila* model of Alzheimer's disease. CNS Neurol Disord Drug Targets 2018; 17(6): 421-9. [http://dx.doi.org/10.2174/1871527317666180508123050] [PMID: 29745345]

[57] Siddique YH, Naz F, Jyoti S. Effect of curcumin on lifespan, activity pattern, oxidative stress, and apoptosis in the brains of transgenic *Drosophila* model of Parkinson's disease. BioMed Res Int 2014; 2014: 1-6. [http://dx.doi.org/10.1155/2014/606928] [PMID: 24860828]

[58] Siddique YH, Beg T, Afzal M. Antigenotoxic effect of apigenin against anti-cancerous drugs. Toxicol. *In Vitro* 2008; 22(3): 625-31. [http://dx.doi.org/10.1016/j.tiv.2007.12.002] [PMID: 18206345]

[59] Ali F, Rahul , Jyoti S, *et al.* Therapeutic potential of luteolin in transgenic Drosophila model of Alzheimer's disease. Neurosci Lett 2019; 692: 90-9. [http://dx.doi.org/10.1016/j.neulet.2018.10.053] [PMID: 30420334]

[60] Siddique YH, Naz F, Jyoti S, *et al.* Protective effect of Geraniol on the transgenic *Drosophila* model of Parkinson's disease. Environ Toxicol Pharmacol 2016; 43: 225-31. [http://dx.doi.org/10.1016/j.etap.2016.03.018] [PMID: 27026137]

[61] Rahul , Naz F, Jyoti S, Siddique YH. Effect of kaempferol on the transgenic *Drosophila* model of Parkinson's disease. Sci Rep 2020; 10(1): 13793. [http://dx.doi.org/10.1038/s41598-020-70236-2] [PMID: 32796885]

[62] Siddique YH, Afzal M. Antigenotoxic effect of apigenin against mitomycin C induced genotoxic damage in mice bone marrow cells. Food Chem Toxicol 2009; 47(3): 536-9. [http://dx.doi.org/10.1016/j.fct.2008.12.006] [PMID: 19121640]

[63] Siddique YH, Mujtaba SF, Jyoti S, Naz F. GC–MS analysis of Eucalyptus citriodora leaf extract and its role on the dietary supplementation in transgenic *Drosophila* model of Parkinson's disease. Food Chem Toxicol 2013; 55: 29-35. [http://dx.doi.org/10.1016/j.fct.2012.12.028] [PMID: 23318758]

[64] Siddique YH, Ara G, Jyoti S, Afzal M. The dietary supplementation of nordihydroguaiaretic acid (NDGA) delayed the loss of climbing ability in *Drosophila* model of Parkinson's disease. J Diet Suppl 2012; 9(1): 1-8. [http://dx.doi.org/10.3109/19390211.2011.630716] [PMID: 22432798]

[65] Dahiru D, William ET, Nadro MS. Protective effect of Ziziphus mauritiana leaf extract on carbon tetrachloride-induced liver injury. Afr J Biotechnol 2005; 4(10)

[66] Colle D, Arantes LP, Gubert P, *et al.* Antioxidant properties of Taraxacum officinale leaf extract are involved in the protective effect against hepatoxicity induced by acetaminophen in mice. J Med Food 2012; 15(6): 549-56. [http://dx.doi.org/10.1089/jmf.2011.0282] [PMID: 22424457]

[67] Sreelatha S, Padma PR, Umadevi M. Protective effects of Coriandrum sativum extracts on carbon tetrachloride-induced hepatotoxicity in rats. Food Chem Toxicol 2009; 47(4): 702-8. [http://dx.doi.org/10.1016/j.fct.2008.12.022] [PMID: 19146910]

[68] Sharma N, Trikha P, Athar M, Raisuddin S. Protective effect of Cassia occidentalis extract on chemical-induced chromosomal aberrations in mice. Drug Chem Toxicol 1999; 22(4): 643-53. [http://dx.doi.org/10.3109/01480549908993173] [PMID: 10536754]

[69] Lee YK, Yuk DY, Kim TI, *et al.* Protective effect of the ethanol extract of Magnolia officinalis and 4-O-methylhonokiol on scopolamine-induced memory impairment and the inhibition of acetylcholinesterase activity. J Nat Med 2009; 63(3): 274-82. [http://dx.doi.org/10.1007/s11418-009-0330-z] [PMID: 19343477]

[70] Heidarian E, Rafieian-Kopaei M. Protective effect of artichoke (*Cynara scolymus*) leaf extract against lead toxicity in rat. Pharm Biol 2013; 51(9): 1104-9. [http://dx.doi.org/10.3109/13880209.2013.777931] [PMID: 23745593]

[71] Sharma RD, Raghuram TC, Rao NS. Effect of fenugreek seeds on blood glucose and serum lipids in type I diabetes. Eur J Clin Nutr 1990; 44(4): 301-6. [PMID: 2194788]

[72] Sharma RD, Raghuram TC. Hypoglycaemic effect of fenugreek seeds in non-insulin dependent diabetic subjects. Nutr Res 1990; 10(7): 731-9. [http://dx.doi.org/10.1016/S0271-5317(05)80822-X]

[73] Riyad MA, Abdul-Salam SA, Mohammad SS. Effect of fenugreek and lupine seeds on the development of experimental diabetes in rats.

Planta Med 19S88; 54: 286-90.
[http://dx.doi.org/10.1055/s-2006-962434]

[74] Petit P, Sauvaire Y, Ponsin G, Manteghetti M, Fave A, Ribes G. Effects of a fenugreek seed extract on feeding behaviour in the rat: Metabolic-endocrine correlates. Pharmacol Biochem Behav 1993; 45(2): 369-74.
[http://dx.doi.org/10.1016/0091-3057(93)90253-P] [PMID: 8327543]

[75] Petit PR, Sauvaire YD, Hillaire-Buys DM, *et al.* Steroid saponins from fenugreek seeds: Extraction, purification, and pharmacological investigation on feeding behavior and plasma cholesterol. Steroids 1995; 60(10): 674-80.
[http://dx.doi.org/10.1016/0039-128X(95)00090-D] [PMID: 8539775]

[76] Ravikumar P, Anuradha CV. Effect of fenugreek seeds on blood lipid peroxidation and antioxidants in diabetic rats. Phytother Res 1999; 13(3): 197-201.
[http://dx.doi.org/10.1002/(SICI)1099-1573(199905)13:3<197::AID-PTR413>3.0.CO;2-L] [PMID: 10353156]

[77] Raju J, Gupta D, Rao AR, Yadava PK, Baquer NZ. *Trigonellafoenum graecum* (fenugreek) seed powder improves glucose homeostasis in alloxan diabetic rat tissues by reversing the altered glycolytic, gluconeogenic and lipogenic enzymes. Mol Cell Biochem 2001; 224(1/2): 45-51.
[http://dx.doi.org/10.1023/A:1011974630828] [PMID: 11693199]

[78] Khalil EAM. Biochemical and histopathological studies on the influence of aqueous extract of fenugreek seed (*Trigonella foenum graecum*) on alloxan diabetic male rats. Egypt J Hosp Med 2004; 15(1): 83-94.
[http://dx.doi.org/10.21608/ejhm.2004.18189]

[79] Abou El-Soud NH, Khalil MY, Hussein JS, Oraby FS, Farrag AH. Antidiabetic effects of fenugreek alkaliod extract in streptozotocin induced hyperglycemic rats. J Appl Sci Res 2007; 3: 1073-83.

[80] Xue WL, Li XS, Zhang J, Liu YH, Wang ZL, Zhang RJ. Effect of *Trigonella foenum-graecum* (fenugreek) extract on blood glucose, blood lipid and hemorheological properties in streptozotocin-induced diabetic rats. Asia Pac J Clin Nutr 2007; 16(Suppl. 1): 422-6.
[PMID: 17392143]

[81] hamden K, Masmoudi H, Carreau S, elfeki A. Immunomodulatory, β-cell, and neuroprotective actions of fenugreek oil from alloxan-induced diabetes. Immunopharmacol Immunotoxicol 2010; 32(3): 437-45.
[http://dx.doi.org/10.3109/08923970903490486] [PMID: 20100065]

[82] Hamden K, Keskes H, Belhaj S, Mnafgui K, feki A, Allouche N. Inhibitory potential of omega-3 fatty and fenugreek essential oil on key enzymes of carbohydrate-digestion and hypertension in diabetes rats. Lipids Health Dis 2011; 10(1): 226.
[http://dx.doi.org/10.1186/1476-511X-10-226] [PMID: 22142357]

[83] Rajarajeswari A, Vijayalakshmi P, Sadiq AM. Influence of *Trigonellafoenum graecum* (fenugreek) in alloxan induced diabetic rats. Bioscan 2012; 7: 395-400.

[84] Jin Y, Shi Y, Zou Y, Miao C, Sun B, Li C. Fenugreek prevents the development of STZ-induced diabetic nephropathy in a rat model of diabetes. Evid Based Complement Alternat Med 2014; 2014: 1-11.
[http://dx.doi.org/10.1155/2014/259368] [PMID: 25057273]

[85] Salih NA. Effect of fenugreek (*Trigonellafoenum-graecum*) on experimentally induced diabetes mellitus in male rabbits. Al-QadisiyahJ Med Sci 2014; 13: 33-8.

[86] Rafraf M, Malekiyan M, Asghari-Jafarabadi M, Aliasgarzadeh A. Effect of fenugreek seeds on serum metabolic factors and adiponectin levels in type 2 diabetic patients. Int J Vitam Nutr Res 2014; 84(3-4): 0196-205.
[http://dx.doi.org/10.1024/0300-9831/a000206] [PMID: 26098483]

[87] Gaddam A, Galla C, Thummisetti S, Marikanty RK, Palanisamy UD, Rao PV. Role of Fenugreek in the prevention of type 2 diabetes mellitus in prediabetes. J Diabetes Metab Disord 2015; 14(1): 74.
[http://dx.doi.org/10.1186/s40200-015-0208-4] [PMID: 26436069]

[88] Hasan M, Rahman M. Effect of Fenugreek on Type2 diabetic patients. Int JSci Res Publications 2016; 6: 251-5.

[89] Bhaskar A, Vidhya VG. Effect of *TrigonellaFoenum Graecum* (Fenugreek) on diabetes induced oxidative stress and tissue antioxidants in streptozotic diabetic rats. Biosci Biotechnol Res Asia 2016; 7: 419-24.

[90] Verma N, Usman K, Patel N, *et al.* A multicenter clinical study to determine the efficacy of a novel fenugreek seed (*Trigonella foenum-graecum*) extract (Fenfuro™) in patients with type 2 diabetes. Food Nutr Res 2016; 60(1): 32382.
[http://dx.doi.org/10.3402/fnr.v60.32382] [PMID: 27733237]

[91] Konopelniuk VV, Goloborodko II, Ishchuk TV, *et al.* Efficacy of Fenugreek-based bionanocomposite on renal dysfunction and endogenous intoxication in high-calorie diet-induced obesity rat model—comparative study. EPMA J 2017; 8(4): 377-90.
[http://dx.doi.org/10.1007/s13167-017-0098-2] [PMID: 29209440]

[92] Sharma MS, Choudhary PR. Effect of fenugreek seeds powder (*Trigonellafoenum-graecum L.*) on experimental induced hyperlipidemia in rabbits. J Diet Suppl 2017; 14(1): 1-8.
[http://dx.doi.org/10.3109/19390211.2016.1168905] [PMID: 27070043]

[93] Li G, Luan G, He Y, *et al.* Polyphenol stilbenes from fenugreek (*Trigonellafoenum-graecum L.)* seeds improve insulin sensitivity and mitochondrial function in 3T3-L1 adipocytes. Oxid Med Cell Longev 2018; 2018: 1-9.
[http://dx.doi.org/10.1155/2018/7634362]

[94] Kandhare A, Phadke U, Mane A, Thakurdesai P, Bhaskaran S. Add-on therapy of herbal formulation rich in standardized fenugreek seed extract in type 2 diabetes mellitus patients with insulin therapy: An efficacy and safety study. Asian Pac J Trop Biomed 2018; 8(9): 446.
[http://dx.doi.org/10.4103/2221-1691.242288]

[95] Chennappaneskar H, Lathadevi GV. Hypolipidemic effects of fenugreek and atorvastatin-comparative study on high fat fed dyslipidemic rats. J Clin &Diagnos Res 2018; p. 12.

[96] Elghazaly NA, Zaatout HH, Radwan EH, Elghazaly MM, Elsheikha EA. *Trigonellafoenum graecum* extract benefits on hematological, biochemical and male reproductive system as a complementary therapy with glimepiride in treating streptozotocin induced diabetic rats. J Bioinform Diab 2019; 1(3): 45-59.
[http://dx.doi.org/10.14302/issn.2374-9431.jbd-19-2613]

[97] Al-Chalabi SM, Abdul-Lattif RF, Al-Mahdawi FA, Abud HN. Effect of fenugreek (*Trigonellafoenum graecum*) seed aqueous extract on blood glucose, lipid profile and some hormonal assay in streptozotocin-induced diabetic male albino rats. Int J DrugDeliv Technol 2019; 9: 19-25.

[98] Geberemeskel GA, Debebe YG, Nguse NA. Antidiabetic effect of fenugreek seed powder solution (*Trigonellafoenum-graecum L.*) on hyperlipidemia in diabetic patients. J Diabetes Res 2019; 2019: 1-8.
[http://dx.doi.org/10.1155/2019/8507453] [PMID: 31583253]

[99] Saadh MJ. Hypoglycemic and hypolipidemic activity of combined milk thistle and fenugreek seeds in alloxan-induced diabetic albino rats. Vet World 2020; 13(8): 1732-6.
[http://dx.doi.org/10.14202/vetworld.2020.1732-1736] [PMID: 33061252]

[100] Patil PB, Tote MV, Mutha SS, Bhosale AV. Antidiabetic effects of fenugreek alkaliod extract in alloxan induced hyperglycemic rats. Int J Pharm Tech Res 2009; 1(3): 588-97.

[101] Alsieni MA, El Rabey HA, Al-Sieni AI, Al-Seeni MN. Comparison between the antioxidant and antidiabetic activity of fenugreek and buckthorn in streptozotocin-induced diabetic male rats. BioMed Res Int 2021; 2021: 1-12.
[http://dx.doi.org/10.1155/2021/7202447] [PMID: 34497854]

[102] Sur P, Das M, Gomes A, *et al. Trigonella foenum graecum* (fenugreek) seed extract as an antineoplastic agent. Phytother Res 2001; 15(3): 257-9.
[http://dx.doi.org/10.1002/ptr.718] [PMID: 11351364]

[103] Devasena T, Menon VP. Enhancement of circulatory antioxidants by fenugreek during 1,2-dimethylhydrazine-induced rat colon carcinogenesis. J Biochem Mol Biol Biophys 2002; 6(4): 289-92. [PMID: 12186747]

[104] Raju J, Patlolla JMR, Swamy MV, Rao CV. Diosgenin, a steroid saponin of *Trigonella foenum graecum* (Fenugreek), inhibits azoxymethane-induced aberrant crypt foci formation in F344 rats and induces apoptosis in HT-29 human colon cancer cells. Cancer Epidemiol Biomarkers Prev 2004; 13(8): 1392-8.
[http://dx.doi.org/10.1158/1055-9965.1392.13.8] [PMID: 15298963]

[105] Raju J, Patlolla JM, Swamy MV, Rao CV. Colon cancer preventive effects of *Trigonellafoenum graecum* (fenugreek) seed and its constituent diosgenin using *in vitro* and *in vivo* models. In: Amer Assoc Cancer Res 2004; pp. 731-1.

[106] Malisetty VS. Chemoprevention of colon cancer by diosgenin, a steroidal saponin constituent of fenugreek. Cancer Res 2005; 65(9_Supplement): 580.

[107] Raju J, Bird RP. Diosgenin, a naturally occurring furostanol saponin suppresses 3-hydroxy-3-methylglutaryl CoA reductase expression and induces apoptosis in HCT-116 human colon carcinoma cells. Cancer Lett 2007; 255(2): 194-204.
[http://dx.doi.org/10.1016/j.canlet.2007.04.011] [PMID: 17555873]

[108] Khalil MI, Ibrahim MM, El-Gaaly GA, *et al. Trigonellafoenum*

(Fenugreek) induced apoptosis in hepatocellular carcinoma cell line, HepG2, mediated by upregulation of p53 and proliferating cell nuclear antigen. BioMed Res Int 2015; 2015: 914645.

[109] Ahmed SI, Hayat MQ, Zahid S, *et al.* Isolation and identification of flavonoids from anticancer and neuroprotective extracts of *Trigonella foenum graecum*. Trop J Pharm Res 2017; 16(6): 1391-8. [http://dx.doi.org/10.4314/tjpr.v16i6.25]

[110] Sauvaire Y, Ribes G, Baccou JC, Loubatieres-Mariani M-M. Implication of steroid saponins and sapogenins in the hypocholesterolemic effect of fenugreek. Lipids 1991; 26(3): 191-7. [http://dx.doi.org/10.1007/BF02543970] [PMID: 2046485]

[111] Sharma RD, Raghuram TC, Rao VD. Hypolipidaemic effect of fenugreek seeds. A clinical study. Phytother Res 1991; 5(3): 145-7. [http://dx.doi.org/10.1002/ptr.2650050313]

[112] Kaviarasan S, Viswanathan P, Anuradha CV. Fenugreek seed (*Trigonella foenum graecum*) polyphenols inhibit ethanol-induced collagen and lipid accumulation in rat liver. Cell Biol Toxicol 2007; 23(6): 373-83. [http://dx.doi.org/10.1007/s10565-007-9000-7] [PMID: 17453353]

[113] Kaviarasan S, Anuradha CV. Fenugreek (*Trigonella foenum graecum*) seed polyphenols protect liver from alcohol toxicity: A role on hepatic detoxification system and apoptosis. Pharmazie 2007; 62(4): 299-304. [PMID: 17484288]

[114] Reddy R. Biochemical studies on the antilithogenic effect of dietary fenugreek seeds *Trigonellafoenum-graecum*. Med Plants 2019; 11(2): 117-26.

[115] Vijayakumar MV, Pandey V, Mishra GC, Bhat MK. Hypolipidemic effect of fenugreek seeds is mediated through inhibition of fat accumulation and upregulation of LDL receptor. Obesity 2010; 18(4): 667-74. [http://dx.doi.org/10.1038/oby.2009.337] [PMID: 19851306]

[116] Muraki E, Hayashi Y, Chiba H, Tsunoda N, Kasono K. Dose-dependent effects, safety and tolerability of fenugreek in diet-induced metabolic disorders in rats. Lipids Health Dis 2011; 10(1): 240. [http://dx.doi.org/10.1186/1476-511X-10-240] [PMID: 22188728]

[117] Said AM, Al-Khashali D, Al-Khateeb E, Al-Wakeel N. The hepatoprotective activity of Fenugreek seeds' extract against carbon tetrachloride induced liver toxicity in rats. Al-Mustansiriyah J Pharm Sci 2011; 9: 94-103. [http://dx.doi.org/10.32947/ajps.v9i1.275]

[118] Ghorbani A, Hadjzadeh MAR, Rajaei Z, Zendehbad SB. Effects of fenugreek seeds on adipogenesis and lipolysis in normal and diabetic rats. Pak J Biol Sci 2014; 17(4): 523-8. [http://dx.doi.org/10.3923/pjbs.2014.523.528] [PMID: 25911840]

[119] Mohamed WS, Mostafa AM, Mohamed KM, Serwah AH. Effects of fenugreek, Nigella, and termis seeds in nonalcoholic fatty liver in obese diabetic albino rats. Arab J Gastroenterol 2015; 16(1): 1-9. [http://dx.doi.org/10.1016/j.ajg.2014.12.003] [PMID: 25670619]

[120] Chen TC, Lo HC, Su RC, Shen SY. The efficacy of combined extracts of red yeast rice and fenugreek on attenuating lipotoxicity in human HepG2 hepatocytes. FASEB J 2016; 30: lb297-7.

[121] Ibrahim AA, Osman AA. Fenugreek downregulating caspase-3 and VEGF expression as a therapeutic agent in acetaminophen induced hepatotoxicity in male rats. Merit Res J Med Sci 2017; 5: 177-86.

[122] El-Nawasany SA, Shalaby SI, El Badria FA, Magraby GM, Gupta N. Diuretic effect of fenugreek (*Trigonellafoenum-graecum Linn*) in cirrhotic ascitic patients. J Pharmacogn Phytochem 2017; 185: 185-9.

[123] Hadi A, Arab A, Hajianfar H, *et al.* The effect of fenugreek seed supplementation on serum irisin levels, blood pressure, and liver and kidney function in patients with type 2 diabetes mellitus: A parallel randomized clinical trial. Complement Ther Med 2020; 49: 102315. [http://dx.doi.org/10.1016/j.ctim.2020.102315] [PMID: 32147060]

[124] Fatima Zaidi SN, Masood J. The protective effect of fenugreek seeds extract supplementation on glucose and lipid profile in thioacetamide induced liver damage in rats. Pak J Pharm Sci 2020; 33(5): 2003-8. [PMID: 33824107]

[125] Tewari D, Jóźwik A, Łysek-Gładysińska M, *et al.* Fenugreek (*Trigonella foenum-graecum* L.) seeds dietary supplementation regulates liver antioxidant defense systems in aging mice. Nutrients 2020; 12(9): 2552. [http://dx.doi.org/10.3390/nu12092552] [PMID: 32846876]

[126] Su Q. Phytochemicals in fenugreek seed prevent high fat diet induced metabolic inflammation and NAFLD *via* the mediation of Akkermansiamuciniphila. Proc Nutr Soc 2020; 79(OCE2)

[127] Panda S, Biswas S, Kar A. Trigonelline isolated from fenugreek seed protects against isoproterenol-induced myocardial injury through down-regulation of Hsp27 and αB-crystallin. Nutrition 2013; 29(11-12): 1395-403. [http://dx.doi.org/10.1016/j.nut.2013.05.006] [PMID: 24103517]

[128] Mukthamba P, Srinivasan K. Hypolipidemic influence of dietary fenugreek (*Trigonella foenum-graecum*) seeds and garlic (Allium sativum) in experimental myocardial infarction. Food Funct 2015; 6(9): 3117-25. [http://dx.doi.org/10.1039/C5FO00240K] [PMID: 26220304]

[129] Mukthamba P, Srinivasan K. Dietary fenugreek (*Trigonella foenum-graecum*) seeds and garlic (*Allium sativum*) alleviates oxidative stress in experimental myocardial infarction. Food Sci Hum Wellness 2017; 6(2): 77-87. [http://dx.doi.org/10.1016/j.fshw.2017.04.001]

[130] Al-dalain S, El-kutry MS, Ibrahim HS. Inhibitory effect of aqueous extracts of barley and fenugreek on ulcer induction in rats. World Appl Sci J 2008; 5: 332-9.

[131] Kamel MA, Hamza RZ, Abdel-Hamid NE, Mahmoud FA. Anti-ulcer and gastro protective effects of fenugreek, ginger and peppermint oils in experimentally induced gastric ulcer in rats. J Chem Pharm Res 2014; 6: 451-68.

[132] Figer B, Pissurlenkar R, Ambre P, *et al.* Treatment of gastric ulcers with fenugreek seed extract; *in vitro*, *in vivo* and *in silico* approaches. Indian J Pharm Sci 2017; 79(5): 724-30. [http://dx.doi.org/10.4172/pharmaceutical-sciences.1000285]

[133] Sankarapillai J, Chandrakumari AS, Sinha P. Effect of *Trigonellafoenum gracecum* (Fenugreek) seed extract in experimentally induced gastric ulcer in wistar rats. Pharmacogn J 2018; 10(6): 1169-73.

[134] Kassem A, Al-Aghbari A, AL-Habori M, Al-Mamary M. Evaluation of the potential antifertility effect of fenugreek seeds in male and female rabbits. Contraception 2006; 73(3): 301-6. [http://dx.doi.org/10.1016/j.contraception.2005.08.020] [PMID: 16472574]

[135] Chaloob AK, Qasim HM, Gassim MH. The effects of aspirin and fenugreek seed on the testes of white mice. J Fac Med Baghdad 2010; 52: 349-51.

[136] c Modaresi M, Mahdian B, Jalalizand A. The effect of hydro-alcoholic extract of fenugreek seeds on female reproductive hormones in mice. Int Conf Appl Life Sci 2012; 12: 437-.

[137] Lamfon H. Effect of fenugreek seed extract on carbendazim-inhibited spermatogenesis in albino rats. J Appl Pharm Sci 2012; 2: 09-13. [http://dx.doi.org/10.7324/JAPS.2012.2423]

[138] Sakr SA, Mahran HA, Abo-El-Yazid SM. Effect of fenugreek seeds extract on cyclophosphamide-induced histomorphometrical, ultrastructural and biochemical changes in testes of albino mice. Toxicol Ind Health 2012; 28(3): 276-88. [http://dx.doi.org/10.1177/0748233711412427] [PMID: 21949087]

[139] Ahamed SK. Effect of the steroidal extract of fenugreek (*Trigonellafoenum graecum*) seeds on some aspects of reproductive functions in male mice. Al-Anbar J Vet Sci 2012; 5: 123-8.

[140] Sakr SA, El-shenawy SM, Al-Shabka AM. Aqueous fenugreek seed extract ameliorates adriamycin-induced cytotoxicity and testicular alterations in albino rats. Reprod Sci 2012; 19(1): 70-80. [http://dx.doi.org/10.1177/1933719111413301] [PMID: 22051850]

[141] Al-Yahya A. Reproductive, cytological and biochemical toxicity of fenugreek in male Swiss albino mice. Afr J Pharm Pharmacol 2013; 7(29): 2072-80. [http://dx.doi.org/10.5897/AJPP2013.3449]

[142] Reddy AG, Reddy YR, Kumar A. Effect of combination of fenugreek with insulin and Glimepiride on male reproductive system in Streptozotocin-induced diabetic rats. Indian J Nat Prod Resour 2015; 6: 156-61.

[143] Shamshad Begum S, Jayalakshmi HK, Vidyavathi HG, *et al.* A novel extract of fenugreek husk (FenuSMART™) alleviates postmenopausal symptoms and helps to establish the hormonal balance: A randomized, double-blind, placebo-controlled study. Phytother Res 2016; 30(11): 1775-84. [http://dx.doi.org/10.1002/ptr.5680] [PMID: 27406028]

[144] Anjaneyulu K, Rai KS, Rajesh T, Nagamma T, Bhat KM. Therapeutic efficacy of fenugreek extract or/and choline with docosahexaenoic acid in attenuating learning and memory deficits in ovariectomized rats. Ethiop J Health Sci 2018; 7: 10-20.

[145] Khosravi Z, Sedaghat R, Baluchnejadmojarad T, Roghani M. Diosgenin ameliorates testicular damage in streptozotocin-diabetic rats through attenuation of apoptosis, oxidative stress, and inflammation. Int Immunopharmacol 2019; 70: 37-46. [http://dx.doi.org/10.1016/j.intimp.2019.01.047] [PMID: 30785089]

[146] Sankhwar SN, Kumar P, Bagchi M, Rungta M, Bagchi D. Safety and

Efficacy of Furosap®, a Patented *Trigonellafoenum-graecum* seed extract, in boosting testosterone level, reproductive health and mood alleviation in male volunteers. J Am Coll Nutr 2023; 42(1): 27-35.

[147] Konuri A, Bhat KMR, Rai KS, Gourishetti K, Phaneendra M YS. Supplementation of fenugreek with choline–docosahexaenoic acid attenuates menopause induced memory loss, BDNF and dendritic arborization in ovariectomized rats. Anat Sci Int 2021; 96(2): 197-211. [http://dx.doi.org/10.1007/s12565-020-00574-8] [PMID: 32944877]

[148] Singh N, Yadav SS, Kumar S, Narashiman B. Ethnopharmacological, phytochemical and clinical studies on Fenugreek (*Trigonella foenum-graecum L*). Food Biosci 2022; 46: 101546. [http://dx.doi.org/10.1016/j.fbio.2022.101546]

[149] Fezea FA, Norziah MH, Bhat R, Ahmad M. Effect of extraction solvents on antioxidant and antimicrobial properties of fenugreek seeds (*Trigonella foenum-graecum L*). International Food Research Journal 2015; 22(3): 1261-71.

[150] Memiş S, Tornuk F, Bozkurt F, Durak MZ. Production and characterization of a new biodegradable fenugreek seed gum based active nanocomposite film reinforced with nanoclays. Int J Biol Macromol 2017; 103: 669-75. [http://dx.doi.org/10.1016/j.ijbiomac.2017.05.090] [PMID: 28536016]

[151] Babaei HA, Motamedifar M, Khalifat S, Mohammadi A, Khosrow Z, Motamedifar A. *In vitro* study of antibacterial property and cytotoxic effects of aqueous, ethanolic, methanolic, and hydroalcoholic extracts of fenugreek seed. Pak J Med Health Sci 2018; 12: 906-10.

[152] Baba WN, Tabasum Q, Muzzaffar S, *et al*. Some nutraceutical properties of fenugreek seeds and shoots (*Trigonella foenum-graecum L.*) from the high Himalayan region. Food Biosci 2018; 23: 31-7. [http://dx.doi.org/10.1016/j.fbio.2018.02.009]

[153] Mansuri A, Chaudhari R, Nasra S, Meghani N, Ranjan S, Kumar A. Development of food-grade antimicrobials of fenugreek oil nanoemulsion—bioactivity and toxicity analysis. Environ Sci Pollut Res Int 2022; 1-2. online ahead of print [http://dx.doi.org/10.1007/s11356-022-19116-y] [PMID: 35150423]