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Review Article

Comparative overview of phytoconstituents and pharmacological potential of *Trigonella foenum-graecum* leaves and seeds

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Abstract

Background: *Trigonella foenum-graecum*, commonly known as Fenugreek is a plant found extensively in semi-arid regions. In Indian subcontinents, leaves and seeds of fenugreek are consumed as food and spice respectively. Fenugreek plant as a whole have different ethnomedicinal values. Analysis revealed presence of multiple bioactive phytoconstituents in the seeds and leaves of Fenugreek. The scientific knowledge of comparative correlation of phytoconstituents in leaves and seeds of Fenugreek and their traditional medicinal importance is mostly unexplored. Objective: This review aims to compare the phytoconstituent composition and pharmacological activities of the leaves and seeds of Fenugreek. Results: The phytoconstituent present in leaves and seeds differ widely. Seeds are rich in components like Galactomannan, free peptide 4-hydroxy isoleucine and alkaloids like Trigonelline and Fenugreekine. These compounds reduce glucose and lipid absorption and enhanced metabolism, thus showing anti-diabetic and anti-hyperlipidemic activity, whereas the Fenugreek leaves show more potent anti-microbial activity including anti-dandruff, anti-fungal and anti-amebicidal activities due to high saponin content. Both the parts of the plant are safe for topical application and show anti-inflammatory effect and strengthens hair follicle reducing hair fall. Conclusion: Understanding the correlation between phytochemistry and modern Pharmacology of Fenugreek leaves and seeds is crucial for optimizing therapeutic applications and developing targeted pharmaceutical formulations. In future, bio-active derivatization of the phytoconstituents of fenugreek can be carried out to enhance the pharmacological activities of Fenugreek.

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Introduction

The existence of human mankind has been invaded by several diseases. Different sources either natural or artificial have been examined for investigating their potential activities against specific diseases since traditional time. In fact, for several diseases human beings used to identify the appropriate natural sources for their treatment based on folklore uses. The extracts of leaves, fruits or specific part of different plant either administered topically or orally were used to identify their potential health benefits (1). Once the activity of the plant extract against specific disease was found, it was used for generations.

The uses of natural product to treat diseases traditionally were practiced without the knowledge of the mechanism of action shown by the specific components of the plant. A specific plant could have activity against several diseases and these properties are usually characteristics of the leaves, stem, bark or roots of the particular plant. For example, Cinchona bark were used to treat malaria; Tulsi leaves to treat cough; Turmeric rhizome for treatment of cold and clove buds were used to treat toothaches (2–6).

One of the important plants used by human beings to ameliorate several diseases is fenugreek. Fenugreek, which belongs to Fabaceae family is one of the most widely traditionally used medicinal plant. This plant is native to Asia, parts of Europe, Africa, Australia, and North and South America. The leaves and seeds of fenugreek are used to make extracts and powders for medicinal purposes. Fenugreek or *Trigonella foenum-graecum*, belongs to the family Fabaceae. Traditionally fenugreek seeds showed potential effect in treatment of polyuruia (7). Polyuria, as described in Aryurveda as *Prameha* is a condition when the patient urinates for multiple times (8). It is a hallmark for one of the most concerning disease, diabetes. Thus, since ancient time fenugreek seeds were important anti-diabetic agent, which have been established by different literature survey. Similarly, fenugreek leaves were effective in protection of liver in several diseases like jaundice, which is called *sudha paitika roga* in Ayurveda (9). Fenugreek has also been reported to be a digestive aid, appetizer and increase milk production in lactating mothers (10). It is also said to be rasayana implicating its ability to rejuvenate and regenerate energy in body. Fenugreek leaves were often used in cooking as herbs. This was because of its gastro-protective activity (11). These phytoconstituents in human body act as bioactive compounds and bio-markers to treat different

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diseases. Images of fenugreek leaves and seeds are shown in Figure 1.

Fenugreek possesses diverse ethnomedicinal values, but a direct comparison of phytoconstituents in seeds and leaves, and their respective pharmacological importance, remains underexplored. Direct comparison between seeds and leaves is essential because of difference of their medicinal applications. Seeds being more effective for managing metabolic disorders, while leaves possess antimicrobial and nutraceutical benefits. Understanding these differences ensures rational selection for dietary and clinical use.

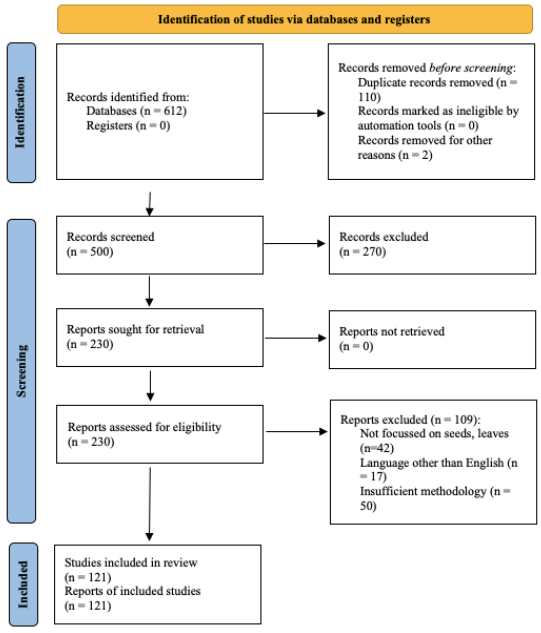
This review aims to compare the phytoconstituent and Pharmacological activity profiling of leaves and seeds of Fenugreek. Thus, this work highlights the different therapeutic importance of fenugreek seeds and leaves to provide guidance in targeted use and nutraceutical formulation development of these parts of Fenugreek plant.

Figure 1: Fenugreek seeds, leaves and entire plant

Methodology

The review was conducted using PRISMA 2020 methodology to ensure reproducibility, transparency and comprehensiveness of Literature review. Initially 612 literatures were screened to conduct the review work. Detailed PRISMA methodology is shown in Figure 2.

Figure 2: Detailed methodology following PRISMA 2020



Strategy of Search

Literatures from renowned journals and indexing platforms like PubMed, Web of Science, Scopus, Elsevier, Taylor and Francis, MDPI and Wiley were referred to collect information. Keywords like 'Fenugreek', 'seed', 'leaf', 'ethnomedicinal uses', 'pharmacology', 'health benefits', '*Trigonella foenum-graecum*' were searched to screen suitable journals. The search covered literature published from 1993 to April 2025 followed by manual screening of relevant articles.

Inclusion Criteria

The articles were screened manually to collect information. Studies encompassing *in vitro*, *in vivo*, or clinical studies investigating fenugreek seeds or leaves and published in English with full paper available were included for Literature review. Only peer-reviewed articles were included in the search. To make the search more explicit, articles published in span of 30 years were included.

Exclusion Criteria

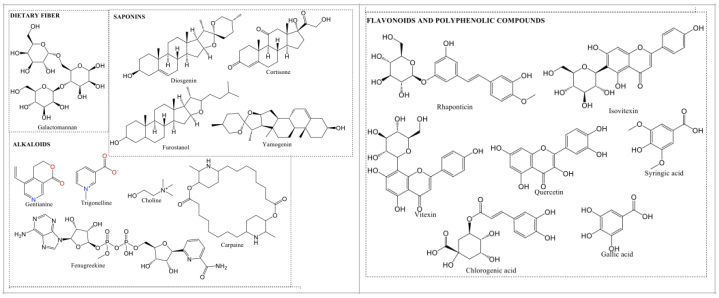
The articles published in languages other than English were not considered. Studies on other plant parts (roots, stem, flowers) were not considered. Editorial, commentaries and conference abstracts were not selected.

Phytoconstituents profiling of Fenugreek leaves and seeds

Phytoconstituents elicits different responses in human body by interacting with different receptors. While both seeds and leaves share common classes of phytoconstituents, the variation in concentration explains their distinct pharmacological effects. Similarly, the leaves and seeds of Fenugreek plant have quite similarity in major classes of phytoconstituents present in them but vary in concentration of individual phytoconstituent. Table 1 given below deals with the different phytocomponents present in the leaves and the seeds of Fenugreek.

Phytoconstituent profiling from different literature reveals presence of various saponins, alkaloids, dietary fiber, phenolic compounds and flavonoids in seeds and leaves of fenugreek. The important phytoconstituents as listed in Table 1 are shown in Figure 3.

Figure 3: Phytoconstituents present in Fenugreek leaves and seeds



Pharmacological activities

The biological activity shown by a specific chemical component is called its Pharmacological activity. Plant extracts are composed of several phytoconstituent and mineral. Thus, when administered in human body, each molecule act differently to different receptors present in the human body, showing multiple biological activity. This is the reason of plant extracts of specific part to have multiple biological activities. Plant parts differ in concentration of phytoconstituents present in them which affects their biological activity. Fenugreek seeds demonstrate better anti-diabetic and hepatoprotective effects due to high levels of galactomannan, trigonelline, and 4-hydroxyisoleucine. On the other hand, leaves are richer in saponins and flavonoids and show higher antimicrobial and anti-dandruff activities.

Table 1: Phytoconstituents present in Fenugreek leaves and seeds

Sl. No.	Components		Fenugreek seeds	Fenugreek leaves	References
1	Saponins	Total Saponin	4.63 – 6mg Diosgenin eq./g	8% mg Diosgenin eq./g	(12, 13)
		Diosgenin ($C_{27}H_{42}O_3$)	0.1–0.9% Total saponin	0.1–2.2% Total saponin	(12, 14)
		Cortisone ($C_{21}H_{28}O_5$)	Trace amount	Trace amount	(14, 15)
		Furostanol ($C_{27}H_{46}O_2$)	0.1-2.2mg Furostanol eq/g DW	Absent	(15, 16)
		Graecunins (A-G)	0.2-0.6% Total saponin	Trace amount	(12, 17)
		Fenugrin B ($C_{35}H_{60}O_7$)	0.1-0.4% Total saponin	0.02% Total saponin	(16)
		Yamogenin ($C_{27}H_{42}O_3$)	0.3-0.9% Total saponin	Absent	(15)
2	Alkaloids	Total alkaloid	35 mg Atropine eq./g	21 mg Atropine eq./g	(18)
		Trigonelline ($C_7H_7NO_2$)	0.12-0.25mg Trigonelline/g	Trace amounts	(13, 15)
		Fenugreekine ($C_{21}H_{27}N_7O_{14}P$)	0.6-0.9%	Trace amounts	(12, 16)
		Gentianine ($C_{10}H_9NO_2$)	Trace content	Trace amount	(18)
		Carpaine ($C_{28}H_{50}N_2O_4$)	0.1-03%	Trace amount	(19)
		Choline ($C_5H_{14}NO$)	Trace amount	0.05-0.09%	(19)
3	Polyphenolic compounds	Total polyphenolics (TPC)	30-42 mg Gallic acid eq/g	10-11 mg Gallic acid eq/g	(20)
		Rhaponticin ($C_{21}H_{24}O_9$)	2-6% TPC	1-4% TPC	
		Isovitexin ($C_{21}H_{20}O_{10}$)	4-10% TPC	5-6% TPC	
		Quercetin ($C_{15}H_{10}O_7$)	2-3% TPC	1-2.5% TPC	
		Syringic acid ($C_9H_{10}O_5$)	0.4-0.9% TPC	1-2% TPC	
		Chlorogenic acid ($C_{16}H_{18}O_9$)	2-5% TPC	1.2-2.4% TPC	
		Gallic acid ($C_7H_6O_5$)	3.5-3.8% TPC	0.6-0.8% TPC	
4	Fiber	Total Fiber	32% DW	1.1% DW	(12)
		Galactomannan ($C_{18}H_{32}O_{16}$)	25-27% Total fiber	0.7-0.9% Total fiber	(21)
5	4-hydroxyisoleucine (4-OH-Ile)		80% TFAA	1-2% TFAA	(18)
6	Minerals	Iron (Fe)	1.5 mg/100g	2.5mg/100g	(12)
		Calcium (Ca)	0.5g/100g	3.5 g/100g	
		Magnesium (Mg)	0.2g/100g	0.4 g/100g	
		Phosphorous (P)	0.4g/100g	0.9 g/100g	
		Potassium (K)	0.1g/100g	0.5 g/100g	
		Zinc (Zn)	Trace amount	Trace amount	

TPC: Total Phenolic Content; TFAA: Total Free Amino Acids; DW: Dry Weight; FW: Fresh Weight.

Table 2: Antidiabetic activity of Fenugreek seeds and leaves

Sl. No.	Experiment subject and experiment conditions	Experiment Observations	Mechanism of action	References
	Anti-diabetic activity of Fenugreek seeds			
1	*In-vivo (*Human beings) Subjects after 12 hours fasting performed rapid exercise; then administered with glucose and 4-OH Ile (of fenugreek seeds) [1.8g/kgBW; 2.0mg/kgBW)	Insulin synthesis; muscle glycogen synthesis; glycosylated hemoglobin (after 4 hrs)	Increases peripheral glucose uptake, upregulate liver glycogen formation, glycogenosis and reduce glycogenolysis. Reduces the glucose absorption from gastrointestinal tract by delayed gastric emptying (31). Trigonelline shows increased the levels of glucose kinase and glucose-6-phosphate enzyme ratio. 4-OH Ile, or 4-Hydroxy isoleucine increases blood glucose response; has insulinotropic activity and upregulates the glucose tolerance. It also	(32)
2	*In- vivo* (Wistar Rats) Streptozotocin induced diabetic rats were administered 4-OH Ile (50mg/kg BW) IV route	restored glucose-induced insulin response; insulin secretion; glucose tolerance; basal hyperglycemia; basal insulinemia		(33)
3	*In- vivo* (Wistar Rats) Streptozotocin induced diabetic rats were subjected to oral administration of 0.44 – 1.74g/kg BW fenugreek seed powder for six weeks	HbA1c levels fasting glucose levels 2-h Plasma glucose level Insulin level		(34)
4	*In- vivo* (Wistar Rats) Soluble dietary fiber fraction of fenugreek seeds, administered to diabetic mice for 28 days at a dose of 0.5g/kg body weight	Glycogen conc. In liver Gycogenesis Gastric emptying time Serum glucose levels		(35)
5	*In-vivo* (Albino rats) Streptozotocin induced diabetic rats, with dose of fenugreek powder administered was 300mg/kg body weight for 21 days	69.4% blood glucose level; 20% diabetic weight loss; Serum insulin level		(36)
6	*In-vivo* (Albino rats) Streptozotocin induced diabetic rats, were administered with 200 mg/kg BW aqueous seed extract per day for 21 days.	Serum glucose and blood glucose level; HbA1c		(37)

7	*In-vivo* (Albino rats) Diabetic and non-diabetic rats were administered with Fenugreek ethanolic extract (0.1-0.5g/kg BW) and glibenclamide (600 µg/kg)	Serum glucose level in diabetic rat compared to control group The glucose level reduction is comparable to reduction shown by glibenclamide. Slight increase in insulin level	stimulates glycogen re-synthesis (29)	(38)
Anti-diabetic activity of fenugreek leaves				
1	*In-vivo* (Human beings) Sixty diabetic patients were divided into three groups and were observed for 12 week. a) Positive control receives 5mg glipizide once daily. b) Test group receives 500mg/kg BW fenugreek once daily. c) Test 2 group receives 2.5mg glipizide and 500mg/kg BW fenugreek extract once a day	Fasting blood glucose level such that reduction in glucose level of group A< C < B HbA1c level with highest reduction in group C (P<0.0001)	Fenugreek leaves are potent inhibitors of -amylase and -glucosidase activity. Thus, these adipocytes prevent amylolysis and reduced SGLT-1 mediated glucose absorption due to presence of alkaloids like Trigonelline in it (39–44).	(45)
2	*In-vivo* (Albino rats) Streptozotocin induced diabetic rats, were administered with 200 mg/kg BW aqueous leaves extract per day for 21 days.	Serum glucose and blood glucose level (but less than seeds); HbA1c (but less than seeds)		(37)

Anti-diabetic agent

Fenugreek since ancient time is a widely used common plant used to treat diabetes. In Ayurveda, it is mentioned that Fenugreek seeds can treat Prameha or polyurea (22). There are various mechanisms by which natural products act as anti-hyperglycemic agents. Insulin-mimetic actions are the primary mechanism of anti-diabetic action. Regeneration of pancreatic -cell also increases insulin secretion. Alteration of glucose metabolism including gluconeogenesis, glycolysis, glycogenesis, glycogenolysis and inhibition of enzymes like -amylase, -glucosidase. (23–26). Fenugreek seeds are more potent anti-hyperglycemic agents than the leaves. It showed potent decrease in blood glucose level in various animal models (27,28). The main anti-diabetic activity of Fenugreek seeds is due to the various components present in it. Dietary fiber galactomannan and different alkaloids like fenugreekine and trigonelline are some of the most important bioactive phytoconstituents. 4-Hydroxy isoleucine is an important peptide which also act in several mechanism to show hypoglycemic effects (29). The alkaloid rich fraction is potent anti-diabetic agent since it stimulates -cells of islets of Langerhans of Pancreas by elevating the calcium influx which increase in insulin synthesis. Moreover, it inhibits the action of pro-inflammatory cytokines like TNF-α (30). Phytoconstituents of Fenugreek seeds act only on -cell of pancreas, since alteration in insulin level was found without any change in levels of glucagon and somatropin (29). Seeds are superior for managing diabetes by influencing both insulin secretion and glucose metabolism, while leaves act only at the carbohydrate digestion stage.

The different studies of anti-diabetic effect on animal model and human subject is shown in Table 2.

Anti-hyperlipidemic agent

Hyperlipidemia is another metabolic disorder common in today's world. Increased lipid content in blood leads to multiple health hazards (46). Hypercholesterolemia can be indicated by the following hallmarks: increase in total cholesterol level, reduction in HDL-C level, increase in LDL and VLDL level, increase in triglycerides (TG) and Non-HDL-C levels (47,48). Different enzymes are involved in the lipid metabolism and formation. Lipoprotein lipase is a primary enzyme involved in the metabolism of lipoproteins. LPL forms fatty acids from VLDL and triglycerides present in chylomicrons so that it can be taken up by the cells (49). Diosgenin, present in fenugreek leaves extract inhibit the action of LPL and thus reduces the formation of LDL and VLDL.

Studies were conducted to elucidate the mechanistic approach of anti-hyperlipidemic action of fenugreek seeds and leaves. Both leaves and seeds show anti-hyperlipidemic effect, with leaves showing lesser effect than seeds because of lesser concentration of alkaloids and dietary fiber. The animal model which were used to demonstrate the lipid lowering activity of Fenugreek seeds and leaves are represented in Table 3. The basic action of fenugreek seeds as anti-hyperlipidemic agent is represented in Figure 4A.

Table 3: Lipid lowering activities of fenugreek leaves and seeds

Sl. No.	Experiment Condition	Experiment Observations	Mechanism of action	References
Anti-hyperlipidemic actions of fenugreek seeds				
1	*In- vivo* (Hamster) Dislipidemic hamster model was administered with 0.5mg/kg BW 4-OH Ile of fenugreek seed extract	33% plasma triglyceride; 22% Total cholesterol; 14% free fatty acid; 39% HDL level	Fenugreek seeds prevents the expression of Sterol regulatory element binding proteins, required for lipogenesis and reduces FFA and TG in human body (50); inhibition of expression of CETP inhibits the progression of formation of HDL from LDL (51)	(53)
2	*In-vivo* (Human volunteers) Newly diagnosed Type II diabetes patient were administered with 25g Fenugreek seed powder orally twice daily	13.16% total cholesterol level 23.53% serum triglyceride level 23.4% LDL level; 21.7% HDL-C level		(54)
3	*In-vivo* (Albino Rats) Streptozotocin induced rats were administered with 200mg/ml fenugreek seed extract for 21 days	Total Cholesterol level, Triglycerides, LDL, VLDL HDL level (Similar activity of leaves and seeds)		(37)

4	*In-vivo* (Rabbit) Treatment of positive control group of rabbits with 2ml aqueous atorvastatin solution (0.5mg/kg BW) and test group with 2ml of aqueous fenugreek extract (500mg/kg BW).	HDL-C level for both groups (Positive control group > test group) Total cholesterol level for test extract but lesser than positive control	of HDL from LDL (54). Increase fatty acid metabolism by activating PPAR- (52). Fenugreek seeds increase in regulation of CCAT element binding proteins - and fatty acid binding protein aP2.	(55)
5	*In-vivo* (Albino rats) Diabetic and non-diabetic rats were administered with Fenugreek ethanolic extract (0.1-0.5g/kg BW)	Serum triglyceride and LDL level Total cholesterol level (P<0.05) No effect on triacylglycerol in non-diabetic rat		(38)
Anti-hyperlipidemic actions of fenugreek leaves				
1	*In-vivo* (Human beings) Sixty diabetic patients were divided into three groups and were observed for 12 week. a) Positive control receives 5mg glipizide once daily. b) Test group receives 500mg/kg BW fenugreek once daily. c) Test 2 group receives 2.5mg glipizide and 500mg/kg BW fenugreek extract once a day	Total cholesterol level in group B and C significantly Triglyceride, LDL level in group B and C HDL-C level but non-significant in groups A and C.	Saponins increase the bile salt production and excretion of the bile salts thus regulating the lipid level in human body (56). Fenugreek leaves enhances the expression of LDL receptor for uptake of LDL to reduce level of LDL in blood (57).	(45)

Galactagogue effect

Traditionally fenugreek seeds were consumed by lactating mothers to increase the production of breast milk for feeding their new born babies. Studies shown that the activity of increase in milk secretion is mainly by Trigonelline (58). This not only increases the secretion of milk by the mammary glands, but also increases the content of micronutrient and macronutrient in the milk. Studies reveal that the main lactogenic hormone, Igf1r was increased by the action of fenugreek seeds (59). Fenugreek increases the macronutrient content of milk because of its increase in expression of genes involved in their uptake. (59). Fenugreek seeds induces insulin/GH/IGF-1 axis, initiates a cascade of events and thereby promotes lactose synthesis (59,60). The entire pathway is mediated through oxytocin induced lactose synthesis. The mechanism of lactation inducing capability of fenugreek seed is illustrated in Figure 4B. Animal study involving the same is represented in Table 5.

Table 5: Galactagogue activity of fenugreek seeds

Sl. No.	Experiment Condition	Experiment Observations	Mechanism of action	References
1	72 pregnant rats were selected and divided into groups: Control: Normal protein diet Test group: Normal protein and fenugreek seeds (1g/kg/day) for entire gestation period	Significant increase in the Total milk production by 16% in fenugreek treated group	Trigonelline and the polyphenol increase *Cs, Mtco1* gene responsible for energy metabolism in mammary gland; increase milk synthesis regulatory factors (*Akt-1, Pparg, Stat-5*); lactose synthesis involving genes (*B4galt1, Lalba*) Glucose uptake was increased by increase in regulation of glucose by GLUT-1, galactose by *Pgm1, Ugp2* and lactose by *B4galt1, Lalba* (59), (61)	(62)
2	16 rats were selected for the study and were divided into two groups. 8 rats received normal food along with saline water as vehicle while fenugreek treated group received 1g/kg BW fenugreek seed extract for 15 days	Increase in different hormones and genes were found. Increased growth hormone (GH), insulin-like growth factor 1 (IGF-1) and oxytocin levels in fenugreek treated group. Increased β-casein and α-lactalbumin (enzymes responsible for milk synthesis); improved expression of glucose transporter 1 (GLUT1) and acetyl-CoA carboxylase (ACC); prolactin receptor (PRLR) and oxytocin receptor (OXTR) genes		(63)

Hepatoprotective actions

Liver is the largest organ of our body and have multiple functions to maintain the normal physiology of human beings (64). The main role of liver is to metabolize different molecules and thus detoxify endogenous and exogenous substances. Different absorbed compounds either drug or nutrient in liver gets metabolized to form simpler water soluble products to facilitate urinary elimination (65). Endogenous substances like glucose, lipids are metabolized by liver. It stores vitamins and secretes bile (66). Natural products have proved to be important hepatoprotective agents due to presence of multiple phytoconstituents present in them. Fenugreek is one of the important natural products which has hepatoprotective action.

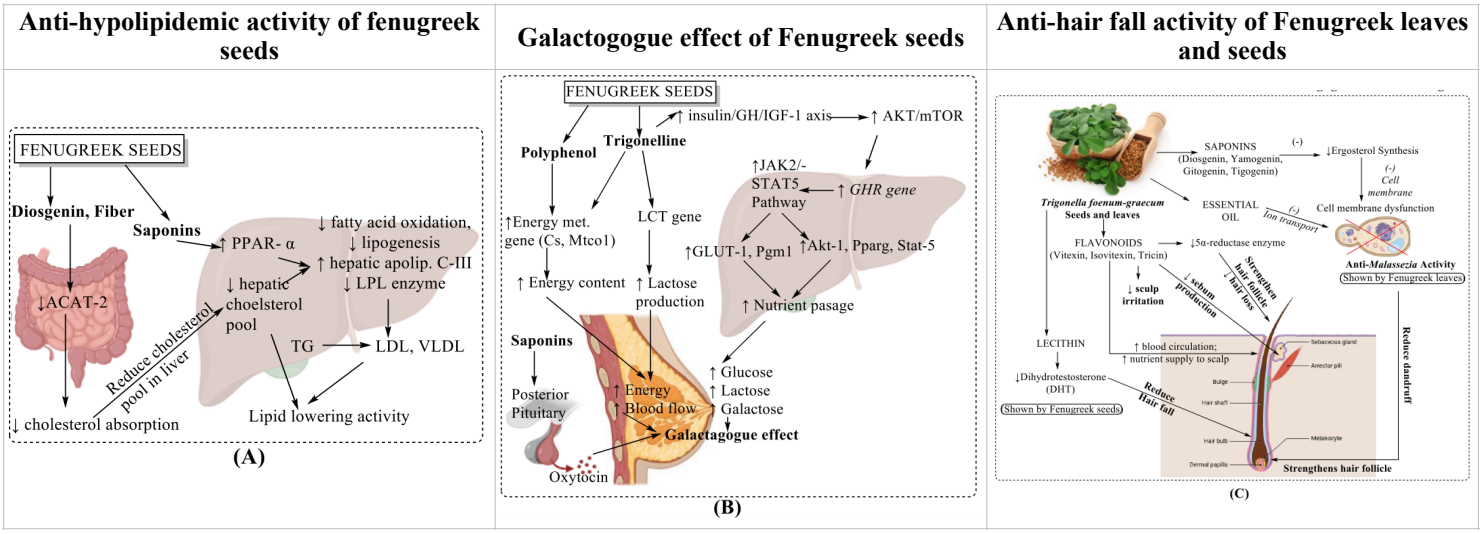
It is found that two main components of fenugreek seeds and leaves diosgenin and trigonelline are hepatoprotective in nature (67). Fenugreek leaves and seeds are equally hepatoprotective in nature. Fenugreek seed extract shows to increase the liver weight by 22.9% with P<0.01 (68).

The different studies conducted to produce evidence for hepatoprotective action of fenugreek leaves and seeds are shown in Table 6.

Table 6: Hepatoprotective activities of fenugreek leaves and seeds

Sl. No.	Experiment Condition	Experiment Observations	Mechanism of action	References
Hepatoprotective actions of Fenugreek Seeds				
1	*In-vivo* (Wistar rats) 40 female Wistar rats were divided into four groups a) Control (300 L saline/ day) b) Negative control: $NaNO_2$ (80mg/kg) c) Test: $NaNO_2$ (80mg/kg) + fenugreek seed extract (150mg/kg)	Negative control group showed mild to severe intermittent liver hemorrhage Test group showed: TNF- , IL-6 in Group C Proinflammatory cytokine in Group D AST, ALT, urea, creatinine in Group C 32% AST, 81% ATL in Group D 82% hepatotoxicity	Fenugreek seeds increases the hepatic cell viability; reduces liver oxidative stress and ROS, reduces necrosis and inflammation in liver tissue; reduces pro-inflammatory cytokines like IL-6, TNF , IL-1 and apoptotic protein like CDK5.	(71)
2	*In-vivo* (Wistar rats) Diabetic and non-diabetic rats were administered with Fenugreek ethanolic extract (0.1-0.5g/kg BW)	Levels of creatinine, urea, uric acid more in diabetic rat than non-diabetic rats AST and ALT levels	It also reduces the activity of Caspase 3 and 4, further reducing apoptosis. (68). Increase activity of alcohol dehydrogenase, lactate dehydrogenase.	(38)
3.	*In-vivo* (Albino rats) Streptozotocin induced diabetic rats with fasting blood glucose level more than 200mg/dl, was administered with 200mg/ kg leaves extract	anti-oxidant enyzme like catalase, GST, SOD, where activity of seeds>> leaves Lipid peroxidation (P<0.05) leaves> seeds.	Increases activity of CAT, GSH, SOD and reduces action of AST, ALT and GGC (69). It antagonizes harmful action of $AlCl_3$ (70)	(37)
Hepatoprotective actions of Fenugreek Leaves				
1	*In-vivo* (Human beings) Non-insulin dependent diabetic human were given with 100g fenugreek seed powder for 10 days in blinded randomized cross over study	Serum LDL level, total cholesterol Triglyceride level No effect on HDL level	Reduce the action of lipid peroxidase and thus reduces lipid peroxidation (72).	(73)

Figure 4: Pharmacological activities shown by Fenugreek seeds and leaves



Anti-microbial activity

Besides several significant activity, both fenugreek seed and leaves have prominent ethnomedicinal anti-microbial health effects. Anti-bacteria, anti-fungal, anti-dandruff, anti-amebae and anti-protozoal activities are shown by different parts of fenugreek. These activities are due to the presence of different components in fenugreek leaves and seeds such as Saponins (Diosgenin, Yamogenin, Gitogenin, Tigogenin); Flavonoids (Vitexin; Tricin); α,β-pienine; Alkaloids (Trigonelline, Choline, Gentianine) and Terpenoids (Cadinene, Eudesmol, Germacrone) (74)

Among the different anti-microbial activity, one of the established effects of fenugreek seeds and leaves is anti-hairfall activity. Traditionally, fenugreek seeds and leaves were boiled with oil and were applied topically on scalp to prevent hair loss and reduce dandruff. The mechanism of fenugreek seeds in strengthening hair follicle is different from that of fenugreek leaves as represented in Figure 4C.

Fenugreek seeds stimulates and strengthens hair follicles by increasing the blood circulation to scalp and nutrients to hair roots. Trigonelline and Diosgenin have prominent anti-inflammatory effects on scalp and shows antioxidant protection to follicles. Fenugreek leaves on the other hand shows anti-hairfall activity due to their anti-dandruff activity (75,76).

Table 7: Given below represents the different *in-vitro* and *in-vivo* anti-microbial activity of fenugreek seeds and leaves

Table 7: In-vitro activities of anti-microbial activities of fenugreek seeds and leaves

Sl. No.	Experiment Condition	Experiment Observations	Mechanism of actions	References
1	Ethanolic extract of fenugreek seeds were made (1mg/ml). 5ml of it was mixed with Carbopol and CMC (1:1) to form gel. This gel was added to agar plate of *Streptococcus mutans, Lactobaillus, Enterococcus, C. albicin*	Zone of inhibition formed for all the extracts. Zone for 100 g/ml was greater than zone formed by doxycycline	Cell membrane disruption Metabolic interference Protein synthesis inhibition Prevent cell wall formation by inhibiting the action of penicillin binding proteins. Effective against *Streptococcus mutans, Lactobacillus, Enterococcus faecalis* (77).	(78)
1	Fenugreek ethanolic and aqueous extracts diluted with DMSO and methanol. Applied in 1ml – 5ml in agar plates of *S.aureus, P. aeruginosa, P.mirabilis, E.coli, S. typhi)*	Ethanolic extract shows anti-bacterial activity against *S.aureus, P. aeruginosa* (G+ and G- respectively) Ethanolic extract have no effect on *E.coli* Low – moderate Zone of inhibition for all except *E.coli, S.aureus*	Alkaloids: Interfere with peptidoglycan synthesis; reduces chitin synthesis; disrupts cell wall integrity; Polyphenolic compounds reduces lipid biosynthesis, electron transport chain, hyphae formation (79,80).	(81)
2	Ethanolic and alcoholic extract of fenugreek leaves were made a) Test: Disc diffusion method agar plate of dandruff causing fungus, *M. furfur*. b) Positive Control: 2%w/v ketoconazole extract was given as positive control Extract added to agar plate of *A. niger*, *C. albicins*	Zone of inhibition formed in control and fenugreek treated *M. furfur* plate ($P<0.01$) Zone of inhibition of 0.1ml>> 0.2ml >0,3ml 0.3ml zone of inhibition is comparable to Positive Control Ethanolic extract forms zone of inhibition in plate of *A. niger* and no response for *C. albicins*	Saponins: Anti-*Malassezia* Activity; disrupt the fungal cell membrane; prevent ergosterol synthesis Essential oil disrupts ion transport in fungal cell membrane Flavonoids: inhibits 5α-reductase enzyme; sebaceous gland action in scalp Local anti-inflammatory effect in scalp (82,83).	(82)
3	Ethanolic extract of fenugreek leaves was added to non-nutritive agar plates of *Acanthamoeba castellanii, E.coli* at 1-32 g/ml and was observed for 3, 24, 32, 48, 72, 96, 102 hr	Zone of inhibition was formed highest for 32 g/ml extract of fenugreek leaves	Saponin binds to membrane cholesterol, form cell membrane pore and lysis of cell; Trophozoite Inhibition by polyphenols; Reduces nucleic acid, protein synthesis (84,85)	(85)

4.6.Other Pharmacological actions

Apart from the main Pharmacological actions, traditional uses and modern Pharmacological studies shows that the fenugreek seeds are good gastroprotective agents, anti-ulcer agents, anti-inflammatory, immunomodulatory and anti-oxidant agents. The mechanistic insights and the phytoconstituents responsible for these effects are shown in Table 8.

Table 8: Mechanistic insight of few Biological activities shown by Fenugreek seeds

Sl. No.	Biological activity	Phytoconstituent responsible	Mechanistic insight	References
Pharmacological actions of seeds of Fenugreek				
1	Anti-inflammatory agent	Diosgenin; Flavonoids (Quercetin, Kampeferol); mucilage	Cyclooxygenase and Lipoxygenase thiobarbituric acid reactive substance (TBARS) Inflammatory mediators (TNF- , IL-6, IL-) Reduces cytokine production Activity of anti-oxidant enzyme Suppresses NF-κB pathway	(86, 87)
2	Anti-oxidant agent	Polyphenolic compounds (Rhaponticin; Isovitexin; Chlorogenic Acid)	Polyphenols donate H atoms to free radicals Scavenges free radicals Protects against oxidative damage Cellular antioxidant systems SOD and catalase activity Reduces lipid peroxidation	(72, 88, 89)
3	Gastro-protective agent	Galactomannan, mucilage, alkaloids	protective mucus layer on the GI membrane acid secretion in parietal cell Anti-*H. pylori* activity mucosal wound healing opening of cardiac sphincter and prevent bloating Regulate intestinal microflora lipid peroxidation in GI mucous layer	(90, 91)
4	Anti-ulcer agent	Flavonoids (vitexin-7-O-glucoside, isovitexin, orientin), saponins	Enhances mucosal defense Increases prostaglandin synthesis Antioxidant effects H^+/K^+ ATPase receptor Prevent lesion formation and is as effective as ranitidine	(91–93)

6	Immuno-modulatory agent	Saponins, fiber; Flavonoids (Quercetin, Kampeferol)	immune functions; Enhances T-cell; modulates cytokine production antibody production; delayed type of hypersensitivity; phagocytic index phagocytic capacity of macrophages cellular and humoral immune mechanism	(94, 95)

Discussion

Due to excessive use of Fenugreek for its ethnomedicinal health benefits, the quest to identify the reasons and mechanism of its therapeutic potential by different researchers was initiated. Traditional records and modern studies highlight the pharmacological significance of both fenugreek seeds and leaves and quantify the bioactive components present in fenugreek seeds and leaves which act as biomarkers in human body.

Apart from conventional extraction technique like maceration using ethanol (96,97), hydroalcoholic mixture, chloroform (98) and non-polar solvent systems like petroleum ether (99), some modern techniques are also used for extraction of bioactive components from fenugreek leaves and seeds. This includes Ultrasonic-assisted extraction (100); Soxhlet extraction using petroleum ether or ethanol; galactomannan extraction using 5% NaCl solution and Isopropyl alcohol (101); Subcritical Butane Extraction (102); Supercritical fluid extraction using carbon dioxide or propane (103) and Precipitation-Based Gum Extraction (104). This results in extraction of wide range of compounds in high purity.

Comparative approach of activities shown by fenugreek leaves and seeds is essential because though derived from the same plant, they are consumed and applied differently in diet and medicine. Seeds are used for metabolic disorders like diabetes and hyperlipidemia, whereas leaves show antimicrobial and gastroprotective effects. These differences justify the need for direct comparison to optimize their targeted applications.

Phytochemical analysis determined that alkaloids like trigonelline, choline and fenugreekine were present in both Fenugreek seeds and leaves but the content of alkaloid in seeds are much more than that of the leaves. Fenugreek seeds contain near about 32% dietary fiber like galactomannan, which is almost 30 times of that found in fenugreek (56). Saponins on the other hand is present in a much higher concentration in leaves (8%). This results in several important anti-microbial activity of leaves of fenugreek. One of the most important and unique constituent of fenugreek seeds and leaves are 4-OH Ile, which is a free peptide and is responsible for eliciting the anti-diabetic activity of fenugreek seeds (105,106). Fenugreek seeds contains almost 35% alkaloid, which is a huge considerable amount (56).

4-OH Ile, fenugreekine and trigonelline increases the glucose metabolism in liver and reduces gluconeogenesis and increase cellular uptake of glucose (107). Galactomannan being dietary fiber is excreted without being absorbed. This delays the gastric emptying time and absorption of carbohydrates. This further reduces the effect of hunger hormone 'ghrelin' (108,109). Thus, fenugreek seeds, which contains higher concentration of alkaloid and dietary fiber are excellent anti-diabetic agent. Lower concentration of these phytoconstituents in fenugreek leaves make them insufficient in treating metabolic disorders.

Streptozotocin induced rats and mice when treated with fenugreek seeds and leaves extract showed activities like reduced blood sugar level, reduced LDL and total cholesterol level and increased activity of catalase, Superoxide dismutase and other enzymes. These activities conclude anti-diabetic, anti-hyperlipidemic and hepatoprotective activities of fenugreeks seeds and leaves as shown in Table 2. These activities are attributed to Diosgenin, Trigonelline, 4-OH Ile and Fenugreekine, which are more abundant in fenugreek seeds than in fenugreek leaves. Fenugreek seeds also increase the expression of Cholesterol-7-alpha hydroxylase which increases bile synthesis and thus enhances elimination of cholesterol (7,30,34,52,54,73,110,111).

Fenugreek seeds were traditionally considered to promote lactation. The galactagogue effect is attributed by the presence of polyphenolic compounds and trigonelline alkaloids, which increased the activity of several pathways including induction of insulin/GH/IGF-1 axis, which results in increase in blood flow to mammary gland and increased production of lactose and milk with higher content of energy, glucose, galactose and nutrient. Increased oxytocin level by fenugreek seeds increases the lactation (21,59,112).

Fenugreek leaves and seeds are potent in preventing hair fall. This is due to the activity of multiple components present in them. Vitexin and isovitexin which are polyphenolic components present in fenugreek seeds and leaves increases the blood flow to the scalp which strengthens the hair follicle. Essential oils and Saponins causes lysis of fungus *Malassezia*, which is dandruff causing fungus by destroying its cell membrane integrity This correlates to the traditional use of fenugreek, where fenugreek leaves and seeds were boiled with oil and applied tropically on scalp to induce hair growth, nourish the hair and prevent hair fall (75,82,113).

Fenugreek seeds and leaves are extensively used in human diet specially in Indian subcontinent. But excessive use of fenugreek seeds and leaves have certain disadvantages and side effects. The side effects shown by fenugreek seeds are more than those shown by fenugreek leaves. Since fenugreek seeds contain high amount of dietary fiber, excess consumption might cause gastrointestinal disorders like bloating and gas formation. At typically high doses diarrhea can also occur. Seeds might have possible interference with hormone-sensitive conditions due to diosgenin content (114–117). Fenugreek seeds are also seen to interact with anti-coagulant drugs like warfarin. While fenugreek seed when administered with amlodipine shows better reduction in blood pressure (118,119). Fenugreek leaves have lower incidence to gastro-intestinal disorders but might induce allergic reactions like skin irritation, inflammation, wheezing, sneezing etc. (120,121).

Thus, this review gives a detailed insight of different ethnomedicinal uses of Fenugreek leaves and seeds and correlate these uses with the phytoconstituents present in them and the mechanism of action of these bioactive phytoconstituent in eliciting the pharmacological actions.

Conclusion

Fenugreek is an extensively used and consumed plant in Indian subcontinent due to its rich ethnomedicinal uses. The comparative analysis reveals fenugreek seeds and leaves are complementary resources, seeds being more effective for diabetes and

hyperlipidemia because of higher content of alkaloids, galactomannan, and 4-hydroxyisoleucine. Leaves are stronger antimicrobial and nutritional benefits due to rich saponin content. Hence both the parts are incorporated in diet traditionally. In future, molecular studies to identify more bioactive compounds by metabolomics can be done. The mechanism of action of these molecules in human body can also be investigated. Clinical research can be conducted to establish the bio-efficacy of fenugreek leaves and seeds to ameliorate different diseases by using proper standardized dosing protocols.

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Abbreviations

TNF-α – Tumor Necrosis Factor-alpha
SGLT – Sodium-Glucose Linked Transporter
GLUT – Glucose Transporter
TG – Triglyceride
HDL – High-Density Lipoprotein
LPL – Lipoprotein Lipase
VLDL – Very Low-Density Lipoprotein
LDL – Low-Density Lipoprotein
CETP – Cholesteryl Ester Transfer Protein
LDLR – Low-Density Lipoprotein Receptor
PPAR – Peroxisome Proliferator-Activated Receptor
CCAT – CCAAT (a DNA sequence motif)
IL-6 – Interleukin-6
IL-1β – Interleukin-1 Beta
CDK5 – Cyclin-Dependent Kinase 5
GSH – Glutathione
AST – Aspartate Aminotransferase
ALT – Alanine Aminotransferase
GGC – Gamma-Glutamyl Cysteine
LDH – Lactate Dehydrogenase
LPO – Lipid Peroxidation
FSP – Fibroblast-Specific Protein
Cs – Citrate Synthase
Mtco1 – Mitochondrial Cytochrome c Oxidase Subunit 1
Akt-1 – Protein Kinase B Alpha
Pparg – Peroxisome Proliferator-Activated Receptor Gamma
Stat-5 – Signal Transducer and Activator of Transcription 5
B4galt1 – Beta-1,4-Galactosyltransferase 1
Lalba – Alpha-Lactalbumin
Pgm1 – Phosphoglucomutase 1
Ugp2 – UDP-Glucose Pyrophosphorylase 2
Insulin/GH/IGF-1 – Insulin/Growth Hormone/Insulin-like Growth Factor-1
AKT/mTOR – AKT/Mammalian Target of Rapamycin
GHR – Growth Hormone Receptor
JAK2/STAT5 – Janus Kinase 2/Signal Transducer and Activator of Transcription 5
BW – Body Weight
TBARS – Thiobarbituric Acid Reactive Substances
NF-κB – Nuclear Factor Kappa B
DHT – Dihydrotestosterone

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References

1. Sruthi D, Jishna JP, Dhanalakshmi M, Deepanraj SP, Jayabaskaran C. Medicinal Plant Extracts and Herbal Formulations: Plant Solutions for the Prevention and Treatment of COVID-19 Infection. Future Integrative Medicine. 2023 Dec 28;2(4):216–26.
2. García-Casal MN, Peña-Rosas JP, Malavé HG. Sauces, spices, and condiments: definitions, potential benefits, consumption patterns, and global markets. Ann N Y Acad Sci. 2016 Sep 6;1379(1):3–16.
3. Kunnumakkara AB, Sailo BL, Banik K, Harsha C, Prasad S, Gupta SC, et al. Chronic diseases, inflammation, and spices: how are they linked? J Transl Med. 2018 Dec 25;16(1):14.
4. Pradeep KU, Geervani P, Eggum BO. Common Indian spices: Nutrient composition, consumption and contribution to dietary value. Plant Foods for Human Nutrition [Internet]. 1993 Sep;44(2):137–48. Available from: http://link.springer.com/10.1007/BF01088378
5. Tapsell LC, Hemphill I, Cobiac L, Sullivan DR, Fenech M, Patch CS, et al. Health benefits of herbs and spices: the past, the present, the future. Medical Journal of Australia. 2006 Aug 21;185(S4).
6. Cobb MA. Spices in the Ancient World. In: Cobb MatheuA, editor. Oxford Research Encyclopedia of Food Studies. Oxford University Press; 2024.
7. Haber SL, Keonavong J. Fenugreek use in patients with diabetes mellitus. American Journal of Health-System Pharmacy. 2013 Jul 15;70(14):1196–203.
8. Sharma H, Chandola HM. *Prameha* in *Ayurveda* : Correlation with Obesity, Metabolic Syndrome, and Diabetes Mellitus. Part 1–Etiology, Classification, and Pathogenesis. The Journal of Alternative and Complementary Medicine. 2011 Jun;17(6):491–6.
9. Raghuvanshi D, Dhalaria R, Sharma A, Kumar D, Kumar H, Valis M, et al. Ethnomedicinal Plants Traditionally Used for the Treatment of Jaundice (Icterus) in Himachal Pradesh in Western Himalaya—A Review. Plants. 2021 Jan 25;10(2):232.
10. Khan TM, Wu DB, Dolzhenko A V. Effectiveness of fenugreek as a galactagogue: A network meta-analysis. Phytotherapy Research. 2018 Mar 30;32(3):402–12.
11. Pirintsos S, Panagiotopoulos A, Bariotakis M, Daskalakis V, Lionis C, Sourvinos G, et al. From Traditional Ethnopharmacology to Modern Natural Drug Discovery: A Methodology Discussion and Specific Examples. Molecules. 2022 Jun 24;27(13):4060.
12. Wani SA, Kumar P. Fenugreek: A review on its nutraceutical properties and utilization in various food products. Journal of the Saudi Society of Agricultural Sciences. 2018 Apr;17(2):97–106.
13. Faisal Z, Irfan R, Akram N, Manzoor HMI, Aabdi MA, Anwar MJ, et al. The multifaceted potential of fenugreek seeds: From health benefits to food and nanotechnology applications. Food Sci Nutr. 2024 Apr 10;12(4):2294–310.
14. Motevalli S, Hassani SB, Ghalamboran MR, Rezadoost Chahardeh H. Increase of diosgenin in fenugreek seedlings by cobalt nanoparticles. Rhizosphere. 2021 Jun;18:100335.
15. Dar TA. Fenugreek: A Miraculous Medicinal Herb. Journal of Complementary Medicine & Alternative Healthcare. 2018 Aug 24;7(2).
16. Żuk-Gołaszewska K, Wierzbowska J, Żuk-Gołaszewska K. Fenugreek: productivity, nutritional value and uses. J Elem. 2017 Jun 6;(3/2017).
17. Altuntaş E, Özgöz E, Taşer ÖF. Some physical properties of fenugreek (Trigonella foenum-graceum L.) seeds. J Food Eng. 2005 Nov;71(1):37–43.

18. Haxhiraj M, White K, Terry C. The Role of Fenugreek in the Management of Type 2 Diabetes. Int J Mol Sci. 2024 Jun 26;25(13):6987.
19. Afzal B, Pasha I, Zahoor T, Nawaz H. NUTRITIONAL POTENTIAL OF FENUGREEK SUPPLEMENTED BREAD WITH SPECIAL REFERENCE TO ANTIOXIDANT PROFILING. Pak J Agric Sci. 2016 Apr 1;53(01):217–23.
20. Salam SGA, Rashed MM, Ibrahim NA, Rahim EAA, Aly TAA, AL-Farga A. Phytochemical screening and in-vitro biological properties of unprocessed and household processed fenugreek (Trigonella foenum-graecum Linn.) seeds and leaves. Sci Rep. 2023 Apr 29;13(1):7032.
21. Nalbantova V, Benbassat N, Delattre C. Fenugreek Galactomannan and Its Versatile Applications. Polysaccharides. 2024 Sep 6;5(3):478–92.
22. Ranade M, Mudgalkar N. A simple dietary addition of fenugreek seed leads to the reduction in blood glucose levels: A parallel group, randomized single-blind trial. AYU (An international quarterly journal of research in Ayurveda). 2017;38(1):24.
23. Cheng J, Li J, Xiong RG, Wu SX, Xu XY, Tang GY, et al. Effects and mechanisms of anti-diabetic dietary natural products: an updated review. Food Funct. 2024;15(4):1758–78.
24. Rahman MdM, Dhar PS, Sumaia, Anika F, Ahmed L, Islam MdR, et al. Exploring the plant-derived bioactive substances as antidiabetic agent: An extensive review. Biomedicine & Pharmacotherapy. 2022 Aug;152:113217.
25. Wang T, Wang YY, Shi MY, Liu L. Mechanisms of action of natural products on type 2 diabetes. World J Diabetes. 2023 Nov 15;14(11):1603–20.
26. Hussain H. Editorial for Special Issue "Natural Products as Potential Source of Antidiabetic Compounds." Curr Issues Mol Biol. 2023 Mar 24;45(4):2699–702.
27. Kim J, Noh W, Kim A, Choi Y, Kim YS. The Effect of Fenugreek in Type 2 Diabetes and Prediabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Int J Mol Sci. 2023 Sep 12;24(18):13999.
28. Shabil M, Bushi G, Bodige PK, Maradi PS, Patra BP, Padhi BK, et al. Effect of Fenugreek on Hyperglycemia: A Systematic Review and Meta-Analysis. Medicina (B Aires). 2023 Jan 27;59(2):248.
29. Upaganlawar AB, Badole SL, Bodhankar SL. Antidiabetic Potential of Trigonelline and 4-Hydroxyisoleucine in Fenugreek. In: Bioactive Food as Dietary Interventions for Diabetes. Elsevier; 2013. p. 59–64.
30. Yoshinari O, Igarashi K. Anti-Diabetic Effect of Trigonelline and Nicotinic Acid, on KK-Ay Mice. Curr Med Chem. 2010 Jul 1;17(20):2196–202.
31. Anwar S, Desai S, Eidi M, Eidi A. Antidiabetic Activities of Fenugreek (Trigonella foenum-graecum) Seeds. In: Nuts and Seeds in Health and Disease Prevention. Elsevier; 2011. p. 469–78.
32. Ruby BC, Gaskill SE, Slivka D, Harger SG. The addition of fenugreek extract (Trigonella foenum-graecum) to glucose feeding increases muscle glycogen resynthesis after exercise. Amino Acids. 2005 Feb 25;28(1):71–6.
33. Broca C, Gross R, Petit P, Sauvaire Y, Manteghetti M, Tournier M, et al. 4-Hydroxyisoleucine: experimental evidence of its insulinotropic and antidiabetic properties. American Journal of Physiology-Endocrinology and Metabolism. 1999 Oct 1;277(4):E617–23.
34. 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.
35. Hannan JMA, Ali L, Rokeya B, Khaleque J, Akhter M, Flatt PR, et al. Soluble dietary fibre fraction of Trigonella foenum-graecum (fenugreek) seed improves glucose homeostasis in animal models of type 1 and type 2 diabetes by delaying carbohydrate digestion and absorption, and enhancing insulin action. Br J Nutr. 2007 Mar;97(3):514–21.
36. Laila O, Murtaza I, Muzamil S, Imtiyaz Ali S, Abid Ali S, Ahamad Paray B, et al. Enhancement of nutraceutical and anti-diabetic potential of fenugreek (Trigonella foenum-graecum). Sprouts with natural elicitors. Saudi Pharm J. 2023 Jan;31(1):1–13.
37. 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 Aug 27;2021:1–12.
38. Eidi A, Eidi M, Sokhteh M. Effect of fenugreek (Trigonella foenum-graecum L) seeds on serum parameters in normal and streptozotocin-induced diabetic rats. Nutrition Research. 2007 Nov;27(11):728–33.
39. Arooj M, Ahmed Z, Khalid N, Suleria HAR. Formulation and assessment of chickpea pulao using fenugreek seeds and Indian rennet to improve blood glycemic levels. Food Sci Nutr. 2024 Jun 18;12(6):4408–20.
40. Vijayakumar MV, Singh S, Chhipa RR, Bhat MK. The hypoglycaemic activity of fenugreek seed extract is mediated through the stimulation of an insulin signalling pathway. Br J Pharmacol. 2005 Sep 29;146(1):41–8.
41. Al-Habori M, Raman A, Lawrence MJ, Skett P. *In Vitro* Effect of Fenugreek Extracts on Intestinal Sodium-dependent Glucose Uptake and Hepatic Glycogen Phosphorylase A. J Diabetes Res. 2001 Jan 25;2(2):91–9.
42. Zhang H, Xu J, Wang M, Xia X, Dai R, Zhao Y. Steroidal saponins and sapogenins from fenugreek and their inhibitory activity against α-glucosidase. Steroids. 2020 Sep;161:108690.
43. Kwon S, Lee Y, Park HJ, Hahm DH. Coarse needle surface potentiates analgesic effect elicited by acupuncture with twirling manipulation in rats with nociceptive pain. BMC Complement Altern Med. 2017 Dec 3;17(1):1.
44. Sarker DK, Ray P, Dutta AK, Rouf R, Uddin SJ. Antidiabetic potential of fenugreek (*Trigonella foenum-graecum*): A magic herb for diabetes mellitus. Food Sci Nutr. 2024 Sep 5;
45. Singh A, Rai J, Mahajan D. Comparative evaluation of glipizide and fenugreek (Trigonella foenum-graecum) seeds as monotherapy and combination therapy on glycaemic control and lipid profile in patients with type 2 diabetes mellitus. Int J Basic Clin Pharmacol. 2016;942–50.
46. Berberich AJ, Hegele RA. A Modern Approach to Dyslipidemia. Endocr Rev. 2022 Jul 13;43(4):611–53.
47. Aparisi Á, Martín-Fernández M, Ybarra-Falcón C, Gil JF, Carrasco-Moraleja M, Martínez-Paz P, et al. Dyslipidemia and Inflammation as Hallmarks of Oxidative Stress in COVID-19: A Follow-Up Study. Int J Mol Sci. 2022 Dec 5;23(23):15350.
48. Kavoussi H, Ebrahimi A, Rezaei M, Ramezani M, Najafi B, Kavoussi R. Serum lipid profile and clinical characteristics of patients with xanthelasma palpebrarum. An Bras Dermatol. 2016 Aug;91(4):468–71.
49. Otarod JK, Goldberg IJ. Lipoprotein lipase and its role in regulation of plasma lipoproteins and cardiac risk. Curr Atheroscler Rep. 2004 Sep;6(5):335–42.

50. Moon JH, Kim K, Choi SH. Lipoprotein Lipase: Is It a Magic Target for the Treatment of Hypertriglyceridemia. Endocrinology and Metabolism. 2022 Aug 31;37(4):575–86.
51. Zhu L, Luu T, Emfinger CH, Parks BA, Shi J, Trefts E, et al. CETP Inhibition Improves HDL Function but Leads to Fatty Liver and Insulin Resistance in CETP-Expressing Transgenic Mice on a High-Fat Diet. Diabetes. 2018 Dec 1;67(12):2494–506.
52. Mohammad-Sadeghipour M, Afsharinasab M, Mohamadi M, Mahmoodi M, Falahati-pour SK, Hajizadeh MR. The Effects of Hydro-Alcoholic Extract of Fenugreek Seeds on the Lipid Profile and Oxidative Stress in Fructose-Fed Rats. J Obes Metab Syndr. 2020 Sep 30;29(3):198–207.
53. Narender T, Puri A, Shweta, Khaliq T, Saxena R, Bhatia G, et al. 4-Hydroxyisoleucine an unusual amino acid as antidyslipidemic and antihyperglycemic agent. Bioorg Med Chem Lett. 2006 Jan;16(2):293–6.
54. Geberemeskel GA, Debebe YG, Nguse NA. Antidiabetic Effect of Fenugreek Seed Powder Solution (Trigonella foenum-graecum L.) on Hyperlipidemia in Diabetic Patients. J Diabetes Res. 2019;2019:8507453.
55. Sharma MS, Choudhary PR. Hypolipidemic effect of fenugreek seeds and its comparison with atorvastatin on experimentally induced hyperlipidemia. J Coll Physicians Surg Pak. 2014 Aug;24(8):539–42.
56. Visuvanathan T, Than LTL, Stanslas J, Chew SY, Vellasamy S. Revisiting Trigonella foenum-graecum L.: Pharmacology and Therapeutic Potentialities. Plants. 2022 May 29;11(11):1450.
57. Vijayakumar M V, Pandey V, Mishra GC, Bhat MK. Hypolipidemic effect of fenugreek seeds is mediated through inhibition of fat accumulation and upregulation of LDL receptor. Obesity (Silver Spring). 2010 Apr;18(4):667–74.
58. Wani SA, Kumar P. Fenugreek: A review on its nutraceutical properties and utilization in various food products. Vol. 17, Journal of the Saudi Society of Agricultural Sciences. King Saud University; 2018. p. 97–106.
59. Sevrin T, Boquien CY, Gandon A, Grit I, de Coppet P, Darmaun D, et al. Fenugreek Stimulates the Expression of Genes Involved in Milk Synthesis and Milk Flow through Modulation of Insulin/GH/IGF-1 Axis and Oxytocin Secretion. Genes (Basel). 2020 Oct 16;11(10):1208.
60. Akers RM. Major Advances Associated with Hormone and Growth Factor Regulation of Mammary Growth and Lactation in Dairy Cows. J Dairy Sci. 2006 Apr;89(4):1222–34.
61. Osorio JS, Lohakare J, Bionaz M. Biosynthesis of milk fat, protein, and lactose: roles of transcriptional and posttranscriptional regulation. Physiol Genomics. 2016 Apr;48(4):231–56.
62. Sevrin T, Alexandre-Gouabau MC, Castellano B, Aguesse A, Ouguerram K, Ngyuen P, et al. Impact of Fenugreek on Milk Production in Rodent Models of Lactation Challenge. Nutrients. 2019 Oct 24;11(11):2571.
63. Sevrin T, Boquien CY, Gandon A, Grit I, de Coppet P, Darmaun D, et al. Fenugreek Stimulates the Expression of Genes Involved in Milk Synthesis and Milk Flow through Modulation of Insulin/GH/IGF-1 Axis and Oxytocin Secretion. Genes (Basel). 2020 Oct 16;11(10):1208.
64. Mahadevan V. Anatomy of the liver. Surgery (Oxford). 2020 Aug;38(8):427–31.
65. Esteves F, Rueff J, Kranendonk M. The Central Role of Cytochrome P450 in Xenobiotic Metabolism—A Brief Review on a Fascinating Enzyme Family. J Xenobiot. 2021 Jun 22;11(3):94–114.
66. Zaefarian F, Abdollahi MR, Cowieson A, Ravindran V. Avian Liver: The Forgotten Organ. Animals. 2019 Feb 15;9(2):63.
67. Mayakrishnan T, Nakkala JR, Jeepipalli SPK, Raja K, Khub Chandra V, Mohan VK, et al. Fenugreek seed extract and its phytocompounds- trigonelline and diosgenin arbitrate their hepatoprotective effects through attenuation of endoplasmic reticulum stress and oxidative stress in type 2 diabetic rats. European Food Research and Technology. 2015 Jan 14;240(1):223–32.
68. Prema A, Justin Thenmozhi A, Manivasagam T, Mohamed Essa M, Guillemin GJ. Fenugreek Seed Powder Attenuated Aluminum Chloride-Induced Tau Pathology, Oxidative Stress, and Inflammation in a Rat Model of Alzheimer's Disease1. Journal of Alzheimer's Disease. 2017 Sep 15;60(s1):S209–20.
69. Madhava Naidu M, Shyamala BN, Pura Naik J, Sulochanamma G, Srinivas P. Chemical composition and antioxidant activity of the husk and endosperm of fenugreek seeds. LWT - Food Science and Technology. 2011 Mar;44(2):451–6.
70. Belaïd-Nouira Y, Bakhta H, Haouas Z, Flehi-Slim I, Neffati F, Najjar MF, et al. Fenugreek seeds, a hepatoprotector forage crop against chronic AlCl3 toxicity. BMC Vet Res. 2013;9(1):22.
71. ATİLA USLU G, USLU H, ADALI Y. Hepatoprotective and nephroprotective effects of Trigonella foenum-graecum L. (Fenugreek) seed extract against sodium nitrite toxicity in rats. Biomedical Research and Therapy. 2019 May 30;6(5):3142–50.
72. Kaviarasan S, Naik GH, Gangabhagirathi R, Anuradha CV, Priyadarsini KI. In vitro studies on antiradical and antioxidant activities of fenugreek (Trigonella foenum graecum) seeds. Food Chem. 2007 Jan;103(1):31–7.
73. Sharma RD, Raghuram TC. Hypoglycaemic effect of fenugreek seeds in non-insulin dependent diabetic subjects. Nutrition Research. 1990 Jul;10(7):731–9.
74. Idris S, Mishra A, Khushtar M. Recent Therapeutic Interventions of Fenugreek Seed: A Mechanistic Approach. Drug Res. 2021 Apr 30;71(04):180–92.
75. Umar S, Carter MJ. A Multimodal Hair-Loss Treatment Strategy Using a New Topical Phytoactive Formulation: A Report of Five Cases. Case Rep Dermatol Med. 2021 Feb 4;2021:1–12.
76. Sharma A, Mohapatra H, Arora K, Babbar R, Arora R, Arora P, et al. Bioactive Compound-Loaded Nanocarriers for Hair Growth Promotion: Current Status and Future Perspectives. Plants. 2023 Oct 31;12(21):3739.
77. 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.
78. Sindhusha VB, Rajasekar A. Preparation and Evaluation of Antimicrobial Property and Anti-inflammatory Activity of Fenugreek Gel Against Oral Microbes: An Invitro Study. Cureus. 2023 Oct;15(10):e47659.
79. Omezzine F, Bouaziz M, Daami-Remadi M, Simmonds MSJ, Haouala R. Chemical composition and antifungal activity of Trigonella foenum-graecum L. varied with plant ploidy level and developmental stage. Arabian Journal of Chemistry. 2017 May;10:S3622–31.
80. Abbood MA, Attraqchi AAF AL, Sahib HB. Evaluation of The Effect of Crude Extracts of Fenugreek on Resistant Isolates of Candida species (In vitro study). Journal of Population Therapeutics and Clinical Pharmacology. 2023 Jan 1;30(3).

81. Al-Timimi LAN. Antibacterial and Anticancer Activities of Fenugreek Seed Extract. Asian Pac J Cancer Prev. 2019 Dec 1;20(12):3771–6.
82. Kulkarni M, Hastak V, Jadhav V, Date AA. Fenugreek Leaf Extract and Its Gel Formulation Show Activity Against Malassezia furfur. Assay Drug Dev Technol. 2020 Jan;18(1):45–55.
83. Angiolella L, Carradori S, Maccallini C, Giusiano G, Supuran CT. Targeting *Malassezia* species for Novel Synthetic and Natural Antidandruff Agents. Curr Med Chem. 2017 Aug 23;24(22).
84. Almatroodi SA, Almatroudi A, Alsahli MA, Rahmani AH. Fenugreek (Trigonella Foenum-Graecum) and its Active Compounds: A Review of its Effects on Human Health through Modulating Biological Activities. Pharmacognosy Journal. 2021 May 5;13(3):813–21.
85. Kaya Y, Baldemir A, Karaman Ü, Ildız N, Arıcı YK, Kaçmaz G, et al. Amebicidal effects of fenugreek (Trigonella foenum-graecum) against Acanthamoeba cysts. Food Sci Nutr. 2019 Feb;7(2):563–71.
86. Pundarikakshudu K, Shah D, Panchal A, Bhavsar G. Anti-inflammatory activity of fenugreek (Trigonella foenum-graecum Linn) seed petroleum ether extract. Indian J Pharmacol. 2016;48(4):441.
87. Sindhu G, Ratheesh M, Shyni GL, Nambisan B, Helen A. Anti-inflammatory and antioxidative effects of mucilage of Trigonella foenum graecum (Fenugreek) on adjuvant induced arthritic rats. Int Immunopharmacol. 2012 Jan;12(1):205–11.
88. Rababah TM, Hettiarachchy NS, Horax R. Total Phenolics and Antioxidant Activities of Fenugreek, Green Tea, Black Tea, Grape Seed, Ginger, Rosemary, Gotu Kola, and Ginkgo Extracts, Vitamin E, and *tert* -Butylhydroquinone. J Agric Food Chem. 2004 Aug 1;52(16):5183–6.
89. Dixit P, Ghaskadbi S, Mohan H, Devasagayam TPA. Antioxidant properties of germinated fenugreek seeds. Phytotherapy Research. 2005 Nov;19(11):977–83.
90. Suja Pandian R, Anuradha CV, Viswanathan P. Gastroprotective effect of fenugreek seeds (Trigonella foenum graecum) on experimental gastric ulcer in rats. J Ethnopharmacol. 2002 Aug;81(3):393–7.
91. Azari O, Kheirandish R, Shojaeepour S. Protective effect of fenugreek seeds (Trigonella foenum graecum) extract against experimental gastric ulcer in rats. Comp Clin Path. 2014 Nov 20;23(6):1743–8.
92. Figer B, Pissurlenkar R, Ambre P, Kalekar S, Munshi R, Gatne M, 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).
93. Afroz R, Rahman KA, Kamal AM, Lotus MJ, Yesmin S, Yeasmin N, et al. The Gastro Protective Effect of Trigonella Foenum Graecum Seed (Methi) and Omeprazole in Experimentally Induced Gastric illcer in Rats. Journal of Dhaka Medical College. 2018 Nov 18;26(2):126–31.
94. 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 Feb;3(2):257–65.
95. Huang H, Wang X, Yang L, He W, Meng T, Zheng K, et al. The Effects of Fenugreek Extract on Growth Performance, Serum Biochemical Indexes, Immunity and NF-κB Signaling Pathway in Broiler. Front Vet Sci. 2022 Jun 23;9.
96. Ahmad R, Alqathama A, Aldholmi M, Riaz M, Eldin SM, Mahtab Alam M, et al. Ultrasonic-assisted extraction of fenugreek flavonoids and its geographical-based comparative evaluation using green UHPLC-DAD analysis. Ultrason Sonochem. 2023 May;95:106382.
97. Eaknai W, Bunwatcharaphansakun P, Phungbun C, Jantimaporn A, Chaisri S, Boonrungsiman S, et al. Ethanolic Fenugreek Extract: Its Molecular Mechanisms against Skin Aging and the Enhanced Functions by Nanoencapsulation. Pharmaceuticals. 2022 Feb 20;15(2):254.
98. Pournamdari M, Mandegary A, Sharififar F, Zarei G, Zareshahi R, Asadi A, et al. Anti-Inflammatory Subfractions Separated from Acidified Chloroform Fraction of Fenugreek Seeds (*Trigonella foenum-graecum* L.). J Diet Suppl. 2018 Jan 2;15(1):98–107.
99. Pundarikakshudu K, Shah D, Panchal A, Bhavsar G. Anti-inflammatory activity of fenugreek (Trigonella foenum-graecum Linn) seed petroleum ether extract. Indian J Pharmacol. 2016;48(4):441.
100. Ahmad R, Alqathama A, Aldholmi M, Riaz M, Eldin SM, Mahtab Alam M, et al. Ultrasonic-assisted extraction of fenugreek flavonoids and its geographical-based comparative evaluation using green UHPLC-DAD analysis. Ultrason Sonochem. 2023 May;95:106382.
101. Rashid F, Hussain S, Ahmed Z. Extraction purification and characterization of galactomannan from fenugreek for industrial utilization. Carbohydr Polym. 2018 Jan;180:88–95.
102. Gu LB, Liu XN, Liu HM, Pang HL, Qin GY. Extraction of Fenugreek (Trigonella foenum-graceum L.) Seed Oil Using Subcritical Butane: Characterization and Process Optimization. Molecules. 2017 Feb 2;22(2):228.
103. Shi Y, Ma Y, Zhang R, Ma H, Liu B. Preparation and characterization of foxtail millet bran oil using subcritical propane and supercritical carbon dioxide extraction. J Food Sci Technol. 2015 May 6;52(5):3099–104.
104. Brummer Y, Cui W, Wang Q. Extraction, purification and physicochemical characterization of fenugreek gum. Food Hydrocoll. 2003 May;17(3):229–36.
105. Fuller S, Stephens JM. Diosgenin, 4-Hydroxyisoleucine, and Fiber from Fenugreek: Mechanisms of Actions and Potential Effects on Metabolic Syndrome. Advances in Nutrition. 2015 Mar;6(2):189–97.
106. Avalos-Soriano A, De la Cruz-Cordero R, Rosado J, Garcia-Gasca T. 4-Hydroxyisoleucine from Fenugreek (Trigonella foenum-graecum): Effects on Insulin Resistance Associated with Obesity. Molecules. 2016 Nov 22;21(11):1596.
107. Knott EJ, Richard AJ, Mynatt RL, Ribnicky D, Stephens JM, Bruce-Keller A. Fenugreek supplementation during high-fat feeding improves specific markers of metabolic health. Sci Rep. 2017 Oct 6;7(1):12770.
108. Mathern JR, Raatz SK, Thomas W, Slavin JL. Effect of Fenugreek Fiber on Satiety, Blood Glucose and Insulin Response and Energy Intake in Obese Subjects. Phytotherapy Research. 2009 Nov 23;23(11):1543–8.
109. Rouag F, Djemli S, Boussena M, Memouni R, Refes I, Ferhati H, et al. The effect of oral gavage (force-feeding) administration of fenugreek seeds (Trigonella foenum-graecum L.) on biochemical and neurobehavioural parameters in male Wistar rats. Journal of Animal Behaviour and Biometeorology. 2021;9(1):1–7.
110. Kassaee S. Ameliorative Effect Of Trigonella Foenum Graecum L. On Lipid Profile, Liver Histology and Ldl-Receptor Gene Expression in High Cholesterol-Fed Hamsters. Acta Endocrinologica (Bucharest). 2021;17(1):7–13.
111. Chiang JYL, Ferrell JM. Up to date on cholesterol 7 alpha-hydroxylase (CYP7A1) in bile acid synthesis. Liver Res. 2020 Jun;4(2):47–63.

112.Sevrin T, Alexandre-Gouabau MC, Castellano B, Aguesse A, Ouguerram K, Ngyuen P, et al. Impact of Fenugreek on Milk Production in Rodent Models of Lactation Challenge. Nutrients. 2019 Oct 24;11(11):2571.
113.Ruwali P, Pandey N, Jindal K, Singh RV. Fenugreek (Trigonella foenum-graecum): Nutraceutical values, phytochemical, ethnomedicinal and pharmacological overview. South African Journal of Botany. 2022 Dec;151:423–31.
114.Taj Eldin IM, Abdalmutalab MM, Bikir HE. An in vitro anticoagulant effect of Fenugreek (Trigonella foenum-graecum) in blood samples of normal Sudanese individuals. Sudan J Paediatr. 2013;13(2):52–6.
115.Dhull SB, Bamal P, Kumar M, Bangar SP, Chawla P, Singh A, et al. Fenugreek (*Trigonella foenum graecum*) gum: A functional ingredient with promising properties and applications in food and pharmaceuticals—A review. Legume Science. 2023 Sep 15;5(3).
116.Bruce-Keller AJ, Richard AJ, Fernandez-Kim SO, Ribnicky DM, Salbaum JM, Newman S, et al. Fenugreek Counters the Effects of High Fat Diet on Gut Microbiota in Mice: Links to Metabolic Benefit. Sci Rep. 2020 Jan 27;10(1):1245.
117.Ouzir M, El Bairi K, Amzazi S. Toxicological properties of fenugreek (Trigonella foenum graecum). Food and Chemical Toxicology. 2016 Oct;96:145–54.
118.Alam MA, Bin Jardan YA, Raish M, Al-Mohizea AM, Ahad A, Al-Jenoobi FI. Effect of Nigella sativa and Fenugreek on the Pharmacokinetics and Pharmacodynamics of Amlodipine in Hypertensive Rats. Curr Drug Metab. 2020 Jun 25;21(4):318–25.
119.Al-Jenoobi FI, Alam MA, Alkharfy KM, Al-Suwayeh SA, Korashy HM, Al-Mohizea AM, et al. Pharmacokinetic interaction studies of fenugreek with CYP3A substrates cyclosporine and carbamazepine. Eur J Drug Metab Pharmacokinet. 2014 Jun 11;39(2):147–53.
120.Kandhare AD, Thakurdesai PA, Wangikar P, Bodhankar SL. A systematic literature review of fenugreek seed toxicity by using ToxRTool: evidence from preclinical and clinical studies. Heliyon. 2019 Apr;5(4):e01536.
121.Patil SP, Niphadkar P V, Bapat MM. Allergy to Fenugreek (Trigonella foenum graecum). Annals of Allergy, Asthma & Immunology. 1997 Mar;78(3):297–300.

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