

BIOLOGICAL AND MEDICINAL SIGNIFICANCE OF *TRIGONELLA FOENUM-GRAECUM*: A REVIEW

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ABSTRACT: *Trigonella foenum-graecum* commonly known as Fenugreek is an annual herb belonging to family Fabaceae. It is cultivated all through the world as a semiarid crop and its seeds are rich sources of protein dietary fiber, iron B Vitamins and several other dietary minerals. It has many potential therapeutic applications in the health sector. It contains different kinds of bioactive compounds such as diosgenin, galactomannan, 3-hydroxy-4,5-dimethyl-2(5H) furanone (stolone), 4-hydroxy isoleucene etc. Fenugreek is one of the most ancient plants with bunch of medicinal uses such as anti-diabetic, antipyretic, anti-inflammatory, diuretic, antiradical, antibacterial activity etc. Fenugreek is also known to have hypocholesterolemic, digestive stimulant action, antioxidant potency and hepatoprotective effect. Numerous experiments have been conducted to see their effectiveness to cure diseases in different ways. This review presents the major medicinal and other beneficial uses of fenugreek discovered through last many years of research in animal and human subjects as well as in other experimental studies.

Keywords: *Trigonella foenum-graecum*, Phytochemical constituents, Morphology, Pharmacological activities

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INTRODUCTION: Herbal medicine is the oldest form of medical treatment. People used medicinal plants for different therapeutic purposes from the ancient time and now, it is the precursor of the modern pharmaceutical field. Seeds, berries, roots, leaves, bark or flowers of the medicinal plants are being utilized for medicinal purposes. *Trigonella foenum-graecum* L. (fenugreek) is widely used for its therapeutic properties everywhere throughout the world. More than 260 species of *Trigonella* are spread around the world¹.

The genus name *Trigonella* signifies 'tri-calculated', possibly in light of triangular state of its blossoms, while the species name *foenum-graecum* signifies 'Greek roughage'². It is a yearly harvest and dicotyledonous plant belonging to the family Fabaceae. It is mainly found in India, North American and certain regions of Africa and in a few sections of Australia.

It has been used as a medicinal plant since over 4000 years in different parts of world. It has wide therapeutic applications including aphrodisiac, carminative and lactation stimulant in women after child birth in traditional Chinese medicines and in Indian Ayurvedic medicines. Literature survey revealed that the whole plant possesses a lot of activities for treatment of diseases such as fresh leaves have been used for the treatment of flatulence, indigestion and the dried leaves have

	<p>QUICK RESPONSE CODE</p>
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<p>Article can be accessed online on: www.ijlsr.com</p>	
<p>DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.IJLSR.4(2).15-26</p>	

been utilized as a quality flavour for fish, meat and vegetable dishes³ while seeds are used to preserve foods in chutneys, pickles and other similar food products. As seeds are very hard and difficult to grind, seed extract is used in butterscotch, vanilla and rum flavouring⁴. Gargle which is made from the seeds is used for recurrent ordinary sore throat and mouth ulcers.

Main objective of the use of this plant is to cause improvement in the health quality of individuals as well as prevention of the diseases. There are numerous other folkloric uses of *Trigonella foenum-graecum* L., such as the treatment of indigestion and baldness⁵. Roasted Methi grain is used as a coffee-substitute, particularly in Africa. It has also been used for controlling insects in grain storages and perfume industries⁶. Trigonelline compound can be also used for the production of maple syrup and as an artificial flavour for vanilla, rum and butter scotch⁷.

Fenugreek seeds lower serum triglycerides, total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C) due to the presence of saponin, which increase excretion secretion of biliary cholesterol which leads to lowered serum cholesterol levels⁵. It has many effects e.g. anthelmintic, anti-cancer, anti-nociceptive, anti-bacterial, antidicer, gastro and hepatoprotective, immune-modulatory, etc. Its capacity to treat wounds and sore muscles had made its use wide in science⁸. It has antibacterial effect⁹ and also has anticancer effects¹⁰. It possesses antioxidative, anthelmintic, anti-diabetic, hypocholesterolaemic, hypoglycemic, hepato-protective and pain reducing properties¹¹⁻¹⁵. It is also used for treating weakness and edema of legs in traditional Chinese medicine¹⁶.

It contains phytochemicals like flavonoids, steroids and alkaloids and they are used as hormonal and therapeutic drugs. Trigonelline compound isolated from fenugreek can be used for the manufacture of maple syrup and as an artificial flavor¹⁷. The unsaponifiable portion of the fenugreek seed oil has lactation stimulating capacity¹⁸. Phenolic compounds offer greater protection against oxidation as compared to other extracts of fenugreek¹⁹. The following is a comprehensive and up-to-date review about the distribution, phytochemistry, and

pharmacological properties of *Trigonella foenum-graecum* L with an urge of further advancements in the medicinal uses of the herb worldwide.

Vernacular Names:

Hindi: Methi, Sag methi, Kasurimethi,

English: Fenugreek, Bird foot, Greek hayseed,

Bengali: Methis, Methi-shak, Methuka,

French: Trigonella Fenugrec,

Italian: Fieno Greco, Trigonella,

Punjabi: Metha, Shamli, Methi, Methini,

Gujrati: Methi, Methini, Bhaj

Botanical Classification:

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Fabales

Family: Fabaceae

Genus: *Trigonella*

Species: *foenum-graecum*

Botanical Description: *T. foenum-graecum* is a plant in Fabaceae family which completes its life cycle in one year. The name *Trigonella foenum-graecum* comes from two latin word the genus and *faenu-graecum*. The genus means “little triangle” and *faenu-graecum* means “Greek hay”²⁰. The flower of the *T. foenum-graecum* is triangle shaped and pale yellow in colour. The height of this plant is 30 to 60 cm²¹. It is found in Asia, Europe, and Middle East.

The seed and leaves are mainly used as several food and medicinal purpose. Leaves contain 89% water, 6% carbohydrates, 4% protein and less than 1% fat. Leaves are also rich in minerals, calcium (40%), iron (15%) and phosphorus (7%). Seeds contain 45-60% carbohydrates, 30% soluble and 20% insoluble fiber, 20-30% protein, oil (5-10%)²². Seeds are good source of calcium, magnesium, iron, phosphorus and Vitamins²³. 100 g of *Trigonella foenum-gracum* seeds contain almost 65% dietary fiber. Its protein is soluble at the pH of 11²⁴. Many literature surveys shows that *T. foenum-graecum* leaves are used as food flavour

and seeds are used in the preservation of several foods²⁵. As seeds are really hard to grind so its extract are used in flavouring butterscotch, vanilla etc.²⁶. Further, gargle is prepared from the seeds of

T. foenum-graecum-to prevent sore throat and mouth ulcer. Traditionally, it is used as laxative, demulcent, stimulant etc. and medicinally in preventing wounds, arthritis, ulcer etc.²⁷.



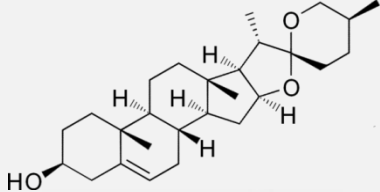
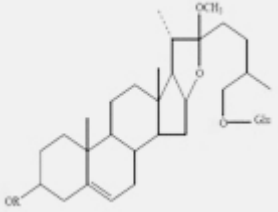
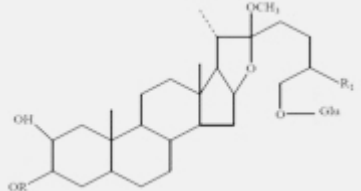
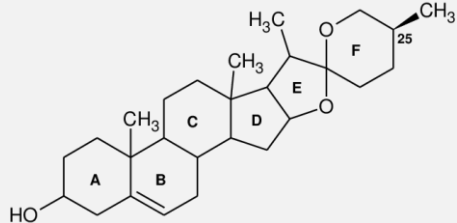
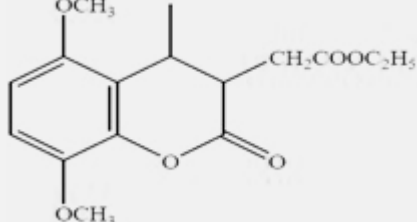
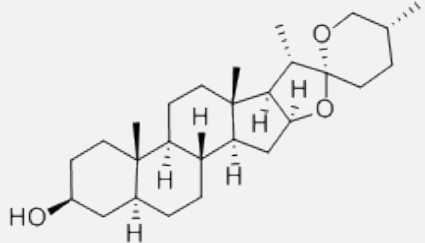
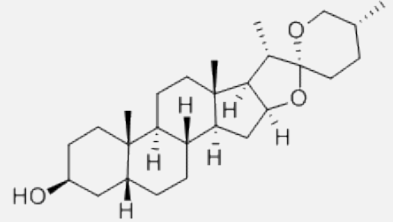
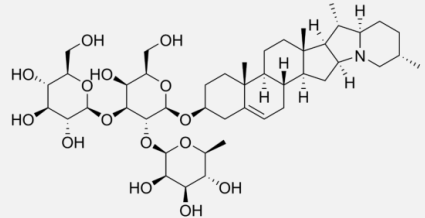
FIG. 1: TRIGONELLA FOENUM-GRACUM

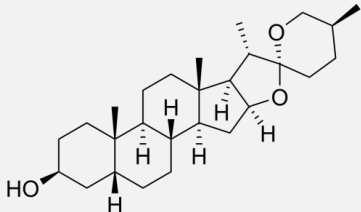
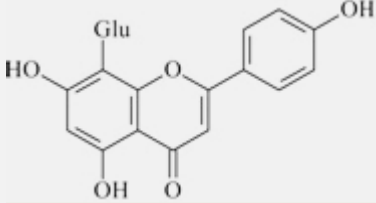
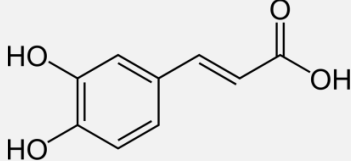
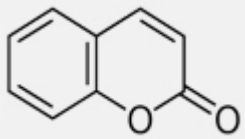
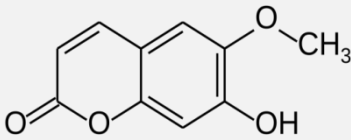
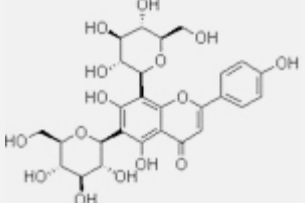
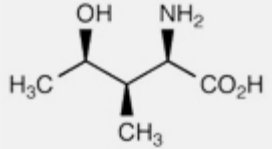
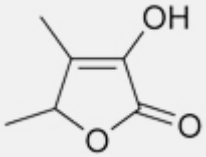
TABLE 1: IMPORTANT CHEMICAL CONSTITUENTS OF TRIGONELLA FEONUM-GRAECUM

Alkaloids	Amino acids	Saponins	Steroidal saponogens	Flavonoids	Fibers	Other
Trimethylamine	Isoleucine	Graecunins	Yamogenin	Quercetin	Gum	Coumarin
Trigonelline	4-Hydroxyisoleucine	Fenugrin B	Diosgenin	Rutin,	Neutral detergent	Lipid
Neurin	Histidine	Fenugreekine	Smilagenin	Vetixin	Fiber	Vitamins
Gentianine	Leucine	Trigofoenosides	Sarasapog-enin	Isovetixin		Minerals
Carpaine	lysine		Tigogenin			28% mucilage
Choline	L-tryptophan		Neotigogenin			22% proteins
Betain	Argenine		Gitogenin			5% of stronger swelling
			Neogitogenin			Bitter fixed oil
			Yuccagenin			
			aponaretin			

TABLE 2: PHYTOCHEMICAL CONSTITUENTS OF TRIGONELLA-FEONUM-GRAECUM^{38 - 43}

S. no.	Name	Structure
1	Carpaine	
2	Gentianine	
3	Trigonelline	
4	Trigofoenoside E1	

5	Yamogenin	
6	Trigofoenoside A1: R= -Glu-Rha Trigofoenoside D1: R= -Glu-Rha-Glu Trigofoenoside F1: R= -Glu-Glu-Rha Trigofoenoside G1: R= -Glu-Glu-Rha-Xyl60	
7	Trigofoenoside B1: R= -Glu-Rha R1= α - Me Trigofoenoside C1: R= -Glu-Rha-Rha R1= β - Me	
8	Diosgenin	
9	Trigocoumarin	
10	Tigogenin	
11	Smilagenin	
12	Yuccagenin	

13	Sarsasapogenin	
14	Vitexin	
15	Caffeic acid	
16	Coumarin	
17	Scopoletin	
18	Vicenin-2	
19	4- Hydroxyisoleucine	
20	Sotolone	

Reported Pharmacological Properties of *Trigonella Foenum-Graecum* Linn:

Anti-diabetic Activity: Many medicinal agents have been used to treat diabetes among them fenugreek is one of the oldest plants documented in some traditional and folk system of medicine⁴⁴. Major alkaloid trigonellin from fenugreek seeds produced hypoglycemic activity⁴⁵. Lethal doses (LD₅₀) of aqueous leaf extract were 1.9 g/kg at intra-peritoneal and 10g/kg at oral administration⁴⁶. From fenugreek seeds, the soluble dietary fibre

(SDF) fraction (0.5g/kg, orally administered twice daily, for 28 days) inhibited platelets aggregation in type 2 diabetic rats and produced beneficial effect in dyslipidemia⁴⁷. 4-hydroxyisoleucine: 5, an amino acid, isolated from seeds, produced anti-hyperglycemic effect and decreased the 33% plasma triglyceride, 22% total cholesterol (22%) and 14% free fatty acids⁴⁸⁻⁴⁹. Three weeks medicine of the diabetic assembly for insulin, and TSP independently brought about a stamped decrease done hyperglycemia in the diabetic animals⁵⁰⁻⁵².

Na^+ K^+ ATPase and Ca^{2+} ATPase assume a part in the fine tuning for neuron works which would diminished diabetes because of oxidative anxiety furthermore film harms⁵³⁻⁵⁴. TSP and insulin response medicine restored the modified Ca^{2+} ATPase movement should control levels. Moreover, it diminish the oxidative stress what's more lipid peroxidation⁵⁵. Fenugreek seed water extract (FSE) ameliorates hyperglycemia through 6-phosphofructo-1-kinase activity in streptozotocin induced diabetic rats. Treated with 0.5g/500ml and 1.0g/500ml of FSE, have been shown lower plasma glucose concentration by 18 and 43% respectively⁵⁶. In another study, ethanolic extract of *T. foenum graecum* leaves was shown to be effective against higher glucose concentration in alloxan induced diabetic animals⁵⁷. Fenugreek seeds elevate blood glucose level at concentration of 2.5 and 5g for 4 weeks in dose dependent manner⁵⁸.

Analgesic and Anti-Inflammatory Activities:

Analgesic and anti-inflammatory effects were examined in a partially purified fraction (MTH) of the *Trigonella foenum-graecum* seed extract. MTH at the dose of 40 mg/kg has shown significant analgesic activity ($p < 0.001$) as compared to diclofenac sodium and pentazocine at the doses employed.

In comparison to control, MTH at the employed doses produced marked acute anti-inflammatory activity in rats which suggests that the water soluble fraction (MTH) of herbal origin has significant analgesic and anti-inflammatory potential as reflected by the parameters investigated⁵⁹. Additionally, fenugreek seed exerts anti-inflammatory effect against bleomycin induced lung fibrosis model in rat⁶⁰. It has been reported that alkaloids, saponins and flavanoids are mainly responsible for anti-inflammatory activity. Besides seed, also leaves of this plant exert anti-inflammatory effects as well⁶¹. In another study, ethanol extract of trigonella has been found to be effective against paw edema in adjuvant-induced arthritis in albino rats and in carrageenan-induced rat paw edema⁶²⁻⁶³.

Effect on Blood Glucose and Lipid Profiles in Type 2 Diabetic Patients: Recently use of herbal medicines, have been considered as an alternative for therapeutic usage. In a clinical trial study, it had

been shown that fenugreek seeds can be used as an adjuvant in the control of type 2 diabetes mellitus in the form of soaked in hot water⁶⁴. Fenugreek seeds supplements which would nontoxic have been demonstrated to smother high-fat diet-induced expand about plasma lipids and diminished fat affidavit over mice⁶⁵. In the available study, TEFS over a dose-dependent way repressed the amassing of TG on differentiating alternately separated units. This property for TEFS may be imperative on account of restraint about TG union may be a medication method to dyslipidemia, also stoutness⁷⁰.

Additionally, TEFS diminished cellular TG and cholesterol in HepG2 cells which proposes that it manages lipid digestion system on liver as well⁶⁶. Triton induced hyperlipidemic rats can be cured with ethanolic extract of *T. foenum-graecum* leaves⁶⁷. Synergistic effect of *Lagenariasi ceraria* and *Trigonella foenum-graecum* can control triglyceride, LDL and HDL levels significantly at the concentration of 200 mg kg^{-1} . Thus, the combination can be used as therapeutic agents in treating coronary artery diseases⁶⁸. If 5g of fenugreek seeds is taken, the reduction of cholesterol level and triglycerides are significant in type 2 diabetic patients⁵⁸. Fenugreek seed therapy along with diet and medication give better result in type 2 diabetes mellitus other than combination therapy with neem⁶⁹.

Cytotoxic Activity: Cancer is one of the leading causes of death worldwide. Conventional therapies cause serious side effects and thus, there is an increasing demand to utilize alternative concepts or approaches to the prevention of cancer. An extract of fenugreek (*Trigonella foenum-graecum*) seeds was isolated and evaluated for cytotoxic activity and in this report we show a potential protective effect of fenugreek seeds against 7, 12-dimethylbenz (α) anthracene (DMBA)-induced breast cancer in rats. At 200 mg/kg (Body weight) dose, Fenugreek seeds' extract significantly inhibited the DMBA-induced mammary hyperplasia and decreased its incidence.

Epidemiological studies also implicate apoptosis as a mechanism that might mediate the Fenugreek's anti-breast cancer protective effects⁷⁰. According to Chauhan, fenugreek seeds showed protective activity against 7, 12-dimethylbenz (α) anthracene

(DMBA) - induced breast cancer in rats at 200 mg/kg body weight⁷¹. The ethanolic extract of fenugreek seeds was also observed to possess anti-tumor activity in A - 549 male lung carcinoma, MCF-7 female breast cancer and HT - 29 colon adenocarcinoma cell lines and the result establishes the anti- cancer activity of fenugreek.

Antiradical and Antioxidant Activities: An extract of *Trigonella foenum-graecum* seeds was isolated and the antioxidant activity of the isolated seeds was evaluated by using various *in-vitro* assay systems. The ethanol extract of seeds showed scavenging of hydroxyl radicals (OH⁻) and inhibition of hydrogen peroxide-induced lipid peroxidation in rat liver mitochondria. The anti-mutagenic activity of the extract was recorded by following the inhibition of c-radiation induced strand break formation in plasmid pBR322 DNA. The extract at high concentrations acted as a scavenger of 2, 20-azinobis 3-ethylbenzothiazoline-6-sulfonate (ABTS) and 2, 20-diphenyl-1-picrylhydrazyl hydrate (DPPH) radicals. By determining the phenolic content it was estimated that the extract of fenugreek seeds contains antioxidants and protects cellular structures from oxidative damage⁷².

According to Naidu, at 200 µg conc., extracts of fenugreek seeds exhibited 64% antioxidant activity by free radical scavenging method⁷³. Sravanthi used extract of leaves to determine the antioxidant potential in *Trigonella foenum-graecum* and it showed highest phenolic content 38.3 ± 0.5mg/g dry wt. and FRAP free radical scavenging was 10 ± 0.05 % recorded maximum than the other assays⁷⁴. Mashkor studied antioxidant activity by using 3 types of solvent extract of fenugreek seeds where Acetone 50 % and methanol 50 % solvent showed the greatest capability in extracting antioxidants and inhibiting the free radicals produced⁷⁵. Though all extracts of ground fenugreek seeds exhibited antioxidant activities, highest phenolic (156.3 mg GAE/g) and flavonoid (38.5 mg CE/g) content were found in whilst water extract of germinated fenugreek seeds⁷⁶.

Prophylaxis Effect: There is no satisfactory drug to treat kidney stones, though considerable progress in medical therapy. Therefore, Laroubiper formed a study to look for an alternative by using *Trigonella*

foenum-graecum on nephrolithiasic rats as a preventive agent against the development of kidney stones⁷⁷. The results showed that the amount of calcification in the kidneys and the total calcium amount of the renal tissue in rats which were treated with *Trigonella foenum-graecum* was significantly reduced compared with the untreated group.

Micro Determination of Diosgenin: *Trigonella* has received considerable attention as a source of diosgenin⁷⁸. Diosgenin is the most widely used precursor in the preparation of many steroid drugs, sex hormones and oral contraceptives pills⁷⁹. Dwivedi investigated the fenugreek (*Trigonella foenum-graecum* L.) germplasm lines for diosgenin potential and found higher diosgenin content in the plant⁸⁰. Kaid demonstrated that around 1 g of fenugreek seeds aqueous extract (FSA) contains approximately 29.65 µg/ml diosgenin (13.81% w/w)⁸¹. In the micro-determination of diosgenin from fenugreek (*Trigonella foenum-graecum*) seeds showed diosgenin levels of 0.55, 0.42, and 0.75%, respectively⁸². Laila showed that dried fenugreek seed samples contain diosgenin in the range of 0.113-0.135% (w/w)⁸³.

Diuretic Activity: Fenugreek seeds have a wide range of pharmacological activities like hypoglycemic, hypolipidemic, galactagogue and diuretic activities⁸⁴. *Trigonella foenum-graecum* Linn is commonly known as fenugreek and it has a history of traditional use in Ayurveda. The diuretic activity of the extract of fenugreek seeds was inspected in wistar rat and it showed aqueous and benzene extract as an effective diuretic component⁸⁵. Rohini established that the extract of *Trigonella foenum-graecum*-seed at 150 and 350 mg/kg body weight showed a dose dependent increase in volume of urine, which supports the traditional claim about the fenugreek seeds being used as diuretic⁸⁶. However, diuretic property of the fenugreek reduces pelvic hyperemia and this property may describe the effectiveness of fenugreek in dysmenorrhea and reduction of mastalgia⁸⁷. El-Nawasany have found high diuretic effect of fenugreek (*Trigonella foenum-graecum* Linn.) in cirrhotic ascitic patients⁸⁸.

Genetic and Histopathology Studies: There is a rising interest in understanding the biological effect

of medicinal plants. The effects of fenugreek oil administration on the liver and ovarian activity genetically and histopathologically were observed in mice and ovaries of mice treated with 0.1 or 0.15 ml/mouse of fenugreek oil showed improvement in several tissues⁸⁹. Histopathological analysis of fenugreek extraction of pancreas showed normal acini and reduced dimensions of islets in alloxan induced diabetes⁹⁰⁻⁹¹.

Antifungal Activity: Montagner demonstrated that coumarin, a constituent of *T.foenum- graecum*, has antifungal activity⁹². Again, in another in vivo study Yang proved the antifungal activity of saponin⁹³. Dharajiya showed that methanol extraction of *T. foenum- graecum* leaves powder had been shown to provide maximum antifungal activity against *trichoderma viridae* (ZOI = 14.5 ± 0.5mm) at the dose of 100 mg/ml⁹⁴. Again, *T.foenum- graecum* seeds had been proved to possess the antifungal activity against *Aspergillus niger* (ZOI = 20 ± 0.88 mm) and *Candida albicans* (ZOI = 17 ± 0.57mm) while treated with petroleum ether extract and here the concentration was 250 mg/ml⁹⁵. Again, Haouala proved that methanol extraction of not ground seeds of *T. foenum- graecum* showed the strongest antifungal inhibition (71.44%) at the dose of 3g/100 ml⁹⁶.

Antibacterial Activity: A study by Priya shows that *Trigonella foenum-graceum* have many essential phytochemicals such as Aziridine, 1, 2,3-trimethyl-, trans-, that may show antimicrobial activity⁹⁷. Again, some alkaloid components like jentianine and scopoletin are isolated from *T. foenum-graceum* seeds which have antibacterial activity. Patil demonstrated that scopoletin has bacteriostatic activity against *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus sp.*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*⁹⁸.

However, *T.foenum- graecum* seeds had been shown to decrease the activity against *E.coli* (ZOI = 17 ± 0.33 mm) and *Staphylococcus aureus* (ZOI = 15 ± 0.57 mm) while treated with petroleum ether extract and here the concentration was 250 mg/ml⁹⁵. Again, at the dose of 100 mg/ml the aqueous extraction of *T. foenum- graecum* leaves showed antibacterial activity against *Serratiam arcscens* (ZOI = 12.33 ± 0.57 mm) and *Bacillus cereus* (ZOI = 11.50 ± 0.50 mm)⁹⁴.

Further, Sharma used different part of *T. foenum- graecum* like stem, leave and seed extract to determine the antibacterial activity of *E. coli* and *Staphylococcus*. Methanol extraction of these parts showed maximum zone of inhibition against *E. coli* (20 mm) and *Staphylococcus* (19 mm) while for acetone extraction the maximum inhibition zone was 16 mm for both organisms⁹⁹.

Anti-tumor and Anti-cancer Activity: Phyto-estrogen and saponin is the chemical constituent present in *T. Foenum-graecum* that possess anticancer activity. Saponin blocks the cell division and initiates the apoptotic program¹⁰⁰. *T. foenum- graecum* also contain some other bioactive compounds which have anticancer and antitumor activity. Coumarin is a polyphenolic compound of *T. foenum-graecum* that possess anti-tumor activity⁹⁸. Trigonelline, quercetin, caffeic acid, scopoletin and vicenin-2 are the alkaloids derived from *T. foenum graecum* which contain anti-cancer property¹⁰¹⁻¹⁰³.

Furthermore, Chauhan demonstrated that oral administration of 200 mg/kg of *T. foenum-graecum* seeds extract proved protective activity in rats against breast cancer⁷¹. Raju showed that 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 Cells¹⁰⁴. However, a study by Ahmed showed that oral administration of methanol extract of *T. foenum-graecum* at doses ranging from 100 to 250 µg/µL exhibited significant cytotoxicity against Hep2 and breast cancer cells with IC₅₀ ranging from 2.85-3.14 µg/µL¹⁰⁵.

CONCLUSION: Natural products show a valuable and significant role in the health of the human being without or marginally producing any undesirable effects like side effects and adverse effects. They are usually the combination of the primary and secondary plant metabolites like alkaloid, flavonoids, glycoside, saponine etc., and deliver the health protective and disease curing action. *T. foenum-graecum* is one of the natural gifts for us due to their phytochemical constituents which take part in different health related activities. It contains some significant alkaloids like

trigonelline, gentianine; amino acids like 4-OH Ile; saponins like diosgenin, fenugreekine; and flavonoids like quercetin, vitexin, luteolin, homoerietin, isovitexin, saponaretin, vicenin-1 and vicenin-2. *T. foenum-graecum* is used for the treatment of diabetes, oxidative stress, cancer, ulcer, allergy, bacterial, viral infection, fungal, malaria and inflammation etc. It is also used as antioxidant, hypolipaedemic agent, breast enlarging agent, immunomodulator, anti-fertility agent, hepato-protective agent, anti-inflammatory, analgesic and antipyretic agent.

In the delivery and lactating mother, the uterus relaxing effect and galactagogue activity is valuable. Clinical application of fenugreek is useful for present in addition to for future but because of loss of focusing on research and clinical trial, all of actions are not reported for human complications. Research is going to give an explanation of its use in different types of cancer and other disease/ disorder. This review declares that the plant possesses the potential for its use in diseases and as immune-modulatory, galactagogue and also as skin smoothening agent. Therefore more and more research, models and experimental trials are required for accomplishing the highest benefits, and understanding the mode of action of it in human being.

ACKNOWLEDGEMENT: Nil

CONFLICTS OF INTEREST: Nil

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How to cite this article:

Mahbub J, Mou RA, Sikta SA, Rahman A and Dash PR: Biological and medicinal significance of *Trigonella foenum-graecum*: A review. Int J Life Sci Rev. 2018; 4(2): 15-26. doi:10.13040/IJPSR.0975-8232.IJLSR.4(2).15-26.

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