



Review Article

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THE MEDICINAL SIGNIFICANCE OF THE BIOACTIVE COMPOUNDS OF *TRIGONELLA FOENUM-GRÆCUM*: A REVIEW

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Received on: 03/05/16 Revised on: 10/06/16 Accepted on: 25/06/16

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DOI: 10.7897/2277-4343.074139

ABSTRACT

Fenugreek (*Trigonella foenum-græcum*) commonly known as Methi is an annual herb belonging to family Fabaceae. It is cultivated worldwide as a semiarid crop, and its seeds are a common ingredient in dishes from the Indian subcontinent. Its seeds are rich sources of protein dietary fiber, B vitamins, iron and several other dietary minerals. It has many potential medicinal applications in the health industry. It contains compounds which are bioactive such as galactomannan, diosgenin, 4-hydroxyisoleucene, 3-hydroxy-4,5-dimethyl-2(5H) furanone (stolone), etc. Stolone is the flavor compound of fenugreek and it is now a day's commonly used in food industry for various purposes. It shows antidiabetic, hypoglycemic, antiallergic and labor and lactation induction properties. It decreases the cholesterol level reduces the body weight by decreasing plasma triglycerides tri glycerides. Fenugreek is known to have hypocholesterolemic, antioxidant potency, digestive stimulant action, and hepatoprotective effect. It is anticarcinogenic, antioxidant, antibacterial agent, gastric stimulant, and anti-anorexia agent. Recent research revealed that fenugreek is a valuable medicinal plant of multipurpose uses and may be used for preparing various products such as steroidal hormones. 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. In this review, we will summarize nutritional, nutraceutical, antioxidant and medicinal properties of fenugreek.

Keywords: Fenugreek, bioactive compounds, medicinal and nutraceutical effects.

INTRODUCTION

Fenugreek is an annual herb which comes under leguminous crops and its self pollinating. It is mostly found in India, certain regions of Africa, North America & in some parts of Australia. Among them, India is the leading producer of fenugreek in the world. It is best known for presence of pungent aromatic compounds in their seeds that gives color, flavor & aroma to food. It is orally consumed as a leafy vegetable. It has been used as a medicinal plant since more than 4000 years in various parts of world. Due to this reason, it is regarded as oldest medicinal plant in history of mankind. It has wide therapeutic applications including carminative, aphrodisiac, lactation stimulant in women after child birth in traditional Chinese medicines as well as in Indian Ayurvedic medicines. It has many effects e.g. anthelmintic, antinociceptive anticancer, antibacterial, anti-dicer, gastro and hepatoprotective, immunomodulatory, etc. The bioactive compounds of fenugreek include polyphenolic compounds, saponin, flavonoids, alkaloids, steroids and many volatile components anethole & stolone. Fenugreek herb is harvested in central Asia, Europe, Northern Africa, Northern America and parts of Australia & India having largest producer in the world. The plant is most suitable to grow in Canada due to similarity in day length¹. Best known for pungent aromatic compounds in the seed that gives flavor, color & aroma to foods. This plant is used as supplement in maize and wheat flour for bread making in Yemen and Persia, it is used as daily meal² preparation and as a medicinal plant in various parts of the world³. Its ability to treat wounds and sore muscles had made its use wide in science⁴. It has antibacterial effect⁵ and also has anticancer effects⁶. It is also used as an anthelmintic. It has pain reducing properties. It possesses immunomodulatory, hypocholesterolaemic properties⁷. It has hypoglycemic effect. It also has gastro and hepatoprotective properties⁸. It also possesses antioxidative properties^{9,10}. It is

also helpful in diabetes control¹¹. It is also used in cardiovascular health issues¹². It is also used in traditional Chinese medicine for treating weakness and edema of legs¹³. It contains phytochemicals like steroids, flavonoids and alkaloids and they are used as hormonal and therapeutic drugs. Trigonelline compound can be used for the manufacture of maple syrup and as an artificial flavor for vanilla, rum, and butterscotch¹⁴. The unsaponifiable portion of the fenugreek seed oil has lactation stimulating capacity¹⁵. Phenolic compounds offer greater protection against oxidation as compared to other extracts of fenugreek¹⁶. It affects lipid containing tissues selectively. Along with these, it primarily contains protein, lipids, fatty acids, steroidal saponins, carbohydrates and other compounds (Table 2). The composition of fenugreek seed is shown in Figure 2.

Applications of different parts of Fenugreek and its oil

Fenugreek oil

The oil which is extracted from fenugreek represents 6-8% of seed weight and has a bitter taste and fetid odor¹⁷. The fatty acid composition is given below in Table 2. It is reported that unsaponifiable portion of oil has a content of 3.9% and helps in lactation in females after child birth. It has a strong scent and due to this property, it is used as an insect repellent in clothes and grains. It is also used in cosmetics and as well as in perfumes¹⁸.

As a forage crop

Due to the presence of amino acids, proteins and vitamins in fenugreek it has found a high forage value hence it is digestible in cattle. The seeds have diosgenin, which act as a growth and reproduction hormone, they help in growth rate and digestion capability in cattle. The incorporation of fenugreek in cattle dairy diet resulted in good content of fatty acids in the milk and

it has shown an increase in polyunsaturated fatty acids. The fenugreek fed cattle had a 4% reduction in blood cholesterol as compared to control. Due to this reason, it has shown many health benefits in humans also as human used to consume its milk on regular basis¹⁹.

As a food stabilizer, adhesive and emulsifying agent

Only Galactomannan presence in fenugreek seed alone accounts for approximately 15-50% dry weight of seed which is a standard source of dietary fiber in the plant which help in many disease combating symptoms. Dietary fibres in fenugreek seeds have potential effects in reduction of cardiovascular diseases and also have an effect of anticancer by reducing the effect of low density lipoprotein and total cholesterol. It also enhances the bread quality of wheat flour when incorporated in it and it is practiced in Egypt and also has been reported to increase the nutritional quality of bread as well as its organoleptic characteristics, a common practice in Egypt. It was reported that when it was incorporated in bread it has shown the improvement in rheological, nutritional and physiochemical properties of bread²⁰. Galactomannan act as a thickener in certain foods like soups and ice-creams²¹. Due to its low cost it may be used to stabilize the foods in industries as compared to locust bean gum and guar gum which are used as an emulsifiers, thickeners and stabilizers.

Physiochemical properties

Fenugreek leaves supply a huge amount of various minerals and vitamins which is especially rich source of choline compound. Seeds having aromatic, bitter, carminative, galactagogue and antibacterial activity. Fenugreek leaves are one of the most ancient medicinal herbs. Research shows that fresh fenugreek leaves contain ascorbic acid of 220.97 mg per 100 g of leaves and β -carotene 19 mg per 100 g of fenugreek leaves. It constitutes 50% unavailable carbohydrates (fiber) making its highest among all the natural sources of fiber concentration. The insoluble fiber portion consists of 30% and soluble portion consists of 20% fraction which is mostly galactomannan. The fresh leaves are used in the vegetables in the diets. These leaves provide β -carotene, fiber, calcium and zinc²².

Bioactive compounds of Fenugreek and their medicinal properties

Steroid saponins

Fenugreek contains steroids, saponins & diosgenin being major constituents. Saponins are glycone portion of plant steroid derivative saponins. It has 6-C rings with 2 to 3 side chains containing methyl or hydroxyl group. Diosgenin is a 27-C steroidal compound and used as raw material for making oral contractive & sex hormones (Table 3). Fenugreek seeds do not contain free saponins but they occur as complex glycosides. It is a precursor for synthesizing progesterone which was earlier used in combined oral contraceptive pills. It has the property to reduce the level of serum cholesterol.

Poly Phenol

Recent reports concluded that fenugreek seeds have five different types of flavonoids namely, vitexin, tricrin, naringenin, quercetin, and tricrin -7-O- β -d-glucopyranoside²³. Iso-flavonoid phytoalexins are also reported to occur in the fenugreek in the form of the pterocarpan, medicarpin and maackiaian²⁴. A current report showed the common phenolic compounds extracted from fenugreek to be coumarin, scopoletin, chlorogenic, caffeic p-coumaric acids and quercetin²⁵. Strong antioxidant like quercetin has been reported to possess anti-inflammatory, anti-oxidant, anti-tumor, immunomodulatory, anti-ulcer, anti-cancer, antioxidant, anti-diabetic, anti-antigenic,

anti-inflammatory activities and many other properties including the improvement of mental and physical performance^{26, 27}. Recently, quercetin has been reported to possess beneficial antidiabetic effects under *in vitro* as well as under *in vitro* conditions²⁸. The antidiabetic mechanism of quercetin has been reported to involve in reduction of intestinal glucose absorption at the level of glucose transporters (GLUT), increase insulin secretion from pancreatic β -cells blockage of tyrosine kinase activity of β -subunit of insulin receptor, inhibit 11- β -hydroxysteroid dehydrogenase type 1 enzyme, increase glucokinase activity, prevention degeneration of β -cells, increase glucosidase inhibition, reduction in insulin resistance, and enhancement in adiponectin expression²⁹. Recent studies indicate that quercetin effectively ameliorates postprandial hyperglycemia in STZ-induced diabetic rats and these reflection were mediated through α -glucosidase inhibition. Further, it has also been reported to improving its hyperglycemia, hypertriglyceridemia, and antioxidant value of STZ induced diabetic rats³⁰.

Alkaloids

In fenugreek seeds trigonelline is a methyl betaine derivative of nicotinic acid is the major alkaloid. It has mild effective (hypoglycemic & antipellagra) and beneficial in treating diabetes and central nervous system disease. It also shows antibacterial, antiviral & memory improving activities.

Volatile compounds

Anethol which is found in anise, camphor & fennel also occurs in fenugreek and produce lecorece – like aroma. Other compounds in this category include carbonyles and sesquiterpene. Stolone – furanone is the principle volatile compound in fenugreek. All these components together impart burnt sugar; curry or maple syrup flavor. Fenugreek showed antimicrobial properties against bacteria, yeast & fungi³¹.

Galactomannan

Galactomannan is the major polysaccharide found in fenugreek. It is a compound of cell wall & it is also found in concentrated form around the seed coat. It has many health benefits mainly in the reduction of plasma glucose level and has an anti-diabetic effect³².

4-Hydroxyisoleucine

4-Hydroxyisoleucine is the most commonly found free amino acids in fenugreek seeds. It occurs in two isomeric forms. The major isomer has a (2S, 3R, 4S) configuration which gives 90% of it in the seeds. While the minor isomer has a [2R, 3R, 4S] configuration it possess both hypoglycemic & insulin tropic properties *in vitro* or *in vivo*. Due to this reason it has become a potential candidate as an anti-diabetic agent³³.

Nutraceutical properties and utilization in various food products

Fenugreek seeds are the most important and useful part of fenugreek plant. Seeds look like golden-yellow in colour, small in size, hard and have four different faced stone like structure (Figure 1). By the process of roasting raw fenugreek seeds have maple flavour and bitter taste and showed reducing bitterness and flavor can be enhanced. Fenugreek seeds are also important components of many Indian cuisines and used as a condiment and spice. Fenugreek seeds are seen in various forms like gummy, fibrous, and sticky in nature. Biologically, fenugreek seeds are endospermic in nature. Anti-nutritional component like saponins and alkaloids are present in fenugreek. Defatted fenugreek seeds are not bitter in taste but can be easily consumed by those who have problems to consume fenugreek without removing fat, especially by patients.

Fenugreek has a beneficial effect on refining the blood and as a diaphoretic it is able to pass on a sweat and to help detoxify the body. Lymphatic cleansing activity is present in fenugreek though its vital role is to irrigate the cells with nutrients and to remove toxic wastes, dead cells and trapped proteins from the body. Fenugreek maintains mucus conditions of the body, specially the lungs, by helping to relief congestion. It also acts as a throat cleanser and mucus solvent that also eases the urge to cough. Drinking water in which seeds of fenugreek have absorbed helps in softening and dissolving, accumulating and hardening the masses of cellular debris. Fenugreek has been used to relieve colds, bronchial complaints, influenza, asthma, catarrh, constipation, sinusitis, pleurisy, pneumonia, sore throat, laryngitis, hay fever tuberculosis and emphysema (Table 4).

Medicinal properties

In many experiments and trials including human and animals like mice, rat, dog it was reported that fenugreek seed lowers

fasting serum glucose (Table 4). The experiment showed that a small randomized controlled of fenugreek seeds effect in hypoglycemic regulation or control³⁴. The study suggested that the fenugreek doesn't offer many differences in glucose level of people with fenugreek rich diet and people with exercise on daily basis. It was shown that fenugreek and exercise both are equally effective in reducing the blood serum glucose level and it may be an effective strategy to control type 2 diabetes. In a study it was found that the fenugreek treated patients showed a significant improvement and glucose tolerance test scores and serum-clearance rates of glucose. Hypolipidemic effects of fenugreek seed showed lower serum triglycerides, total cholesterol and low-density lipoprotein cholesterol which may be due to saponins, which increase biliary cholesterol excretion and lower serum cholesterol levels (Table 5).

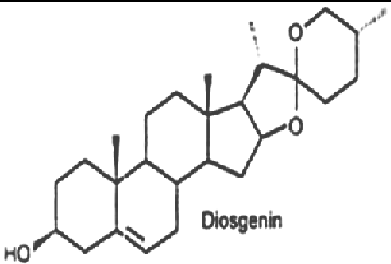
Table 1: Classification of Fenugreek

Domain	Eukarya
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Fabales(orLeguminales)
Family	Fabaceae
Sub-family	Trifoliace
Genus	Trigonella
Sub-genus	Foenumgraecum
Species	<i>Trigonella foenum-graecum</i>

Table 2: Chemical constituents of Fenugreek

Classes of chemical constituents	Chemical constituents	References
Proteins	Globulin, Albumin and Lecithin	35,36
Lipids Fatty Acids	Linoleic Acid, A-Linolenic, Oleic, Stearic Acids, Palmitic and. Sterols: B-Sitosterol Campesterol, Triunsaturated Cycloartenol. And Diunsaturated Triacyl Glycerides.	37
Carbohydrates	Mucilage Or Gum:galactomannan	38
Saponins	Graecunins, Fenugrin B, Fenugreekine, Trigofenosides A-G.	39
Steroidal Saponins	Diosgenin, Yamogenin, Gitogenin, Tigogenin, Neogitogenin, Neogitogenin, Smilagenin, Sarsapogenin, Neogitogenin, Yuccagenin.	40
Flavonoids	Apigenin, Luteolin, Vitexin, Isovitexin, Quercetin, Kaempferol-Dirhamnoside, Kaempferol Rhamnoside. Orientin, Biochanin A, Formononetin, Irlone, Tricine, Daidzein, Calycosin.	41
Alkaloids	Trigonelline (Yields Nicotinic Acid with Roasting), Gentianine, Carpaine, Choline	42
Fibers	Gum, Neutral Detergent Fiber Lipids Triacylglycerols, Diacylglycerols, Monoacylglycerols, Phosphatidylcholine Phosphatidylethanolamine, Phosphatidylinositol, Free Fatty Acids	43
Amino Acids	Isoleucine, 4-Hydroxyisoleucine, Histidine, Leucine, Lysine, L-Tryptophan, Arginine	44

Table 3: Chemical constituents of Fenugreek and their pharmacological effects

Compound	Chemical structure	Effects and mechanism of action
Diosgenin		Used for the treatment of diabetes Hypercholesterolemia It suppressed nf-kappa b activation and antiapoptotic gene products and induce apoptosis in cancer cells ⁴⁵ .

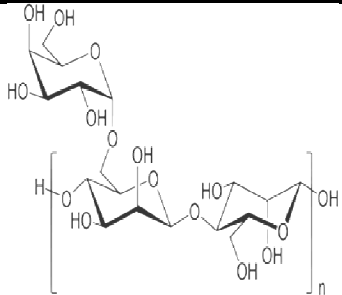
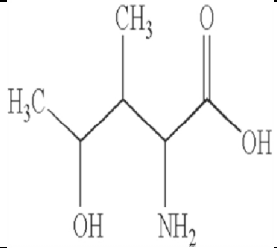
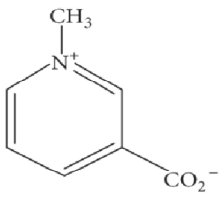
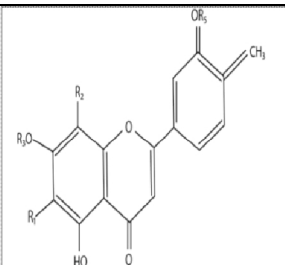
Galactomannan		The potential to modifying glycemic and lipidemic status as well as body weight in rats. A It is also inhibiting the pro-inflammatory cytokines ⁴⁶ . It is suggested to be acting by extrapancreatic pathway rather than insulin stimulating effects
4-hydroxyisoleucine		It is a natural nonproteinogenic amino acid possessing insulinotropic biological activity ⁴⁷ . It allows the evasion of undesirable side-effects, such as hypoglycemia, in the therapy of type ii diabetes.
Trigonelline		It showed that the onset of action and maximum decrease in serum glucose were similar in glyburide, glibenclamide and trigonelline treatment in diabetic animals ⁴⁸ . It has been found to have a function as a hormone that controls plant cell cycle ⁴⁹ . It control the down regulation of two small stress proteins, heat shock protein (hsp27) and αB-crystallin. By interacting with key residues (his6, tyr10, his13 and his14) of β-amyloid (involved in its aggregation
Flavonoids		The aglycones are transferred to the human body through the membranes of the intestinal epithelium, which covers more than 90% of the intestinal surface ⁵⁰ 2-less than 1% of the consumed flavonoids enter the blood ⁵¹ . When portal vein transports these substances to the liver, then they are methylated and sulfated with appropriate transferases ⁵²

Table 4: Nutraceutical effects of Fenugreek

Nutraceutical properties	Description
Lactation Aid	It has been found to stimulate sweat production as it contains hormone precursor to increase milk formation. It can increase a nursing mother's milk supply within 24–72 h after first taking the herb
Immunological Activity	It stimulates immune system.
Hypoglycemic Effect	Hypoglycemic effect may be mediated through stimulating insulin synthesis and/or secretion from the beta pancreatic cells. The hypoglycemic effect of fenugreek has been especially reported in humans and animals with type 1 and type 2 diabetes mellitus. Management of newly diagnosed Type 2 diabetes.
Hypocholesterolemic Effect	It reduces the cholesterolemia, body weight
Antioxidant Activity	Free radical scavenging activity It can be used in the treatment of patients with calcic urolithiasis.
Anticancer Effect	Anti-breast cancer effect. Inhibited 7, 12-dimethyl benz (a)anthracite-induced mammary hyperplasia and ability to induce death of cell, despite simultaneous upregulation of growth stimulatory pathways in normal cells. It was seen that diosgenin could modulate the stat 3 signaling pathway in hepatocellular carcinoma by suppressing the activation of c-src, jak1 and jak2.
Antibacterial And Antifungal Effect	Having potential to develop better and novel antifungal drug. It can be used in the treatment of patients with calcic urolithiasis
Gastroprotective Effect	Lowering mucosal injury having antiulcer potential.
Anti-Inflammatory And Antipyretic Effect	Tfg and ss also significantly reduced hyperthermia induced by brewer's yeast.

Table 5: Mechanism of hypolipidemic effects

Hypolipidemic effects	Mechanisms of lowering blood glucose
1	It stimulates the tyrosine phosphorylation of the insulin receptor and enhances glucose uptake into cells.
2	It has been shown to stop the intestinal disaccharidases in rodents, as well as normalize the deranged levels of Pyruvate Kinase and phosphoenol pyruvate carboxykinase enzymes
3	4HIL compound stimulate glucose-induced insulin release in human and rat pancreatic islet cells.
4	Stimulating glucose-dependent insulin in human's secretion from pancreatic beta cells as well as by inhibiting the activities of alpha amylase and sucrase, two intestinal enzymes involved in carbohydrate metabolism.
5	Decline in somatostatin and high plasma glucagon levels.
6	It is reported in the previous literature it reduces blood glucose level when supplemented to diabetic rats.
7	A study on intestinal and renal disaccharidases activity in STZ-induced diabetic rats proved the beneficial effects of fenugreek seed mucilage by enhancing the reduction in maltase activity during diabetes.
8	Neuroprotective, antimigraine, sedative, memory-improving, antibacterial, antiviral and anti-tumor activities and it has been shown to reduce diabetic auditory neuropathy and platelet aggregation. It effects β cell regeneration, insulin secretion, activities of enzymes related to glucose metabolism, reactive oxygen species, axonal extension and neuron excitability



Figure 1: Leaves and seeds of Fenugreek plant

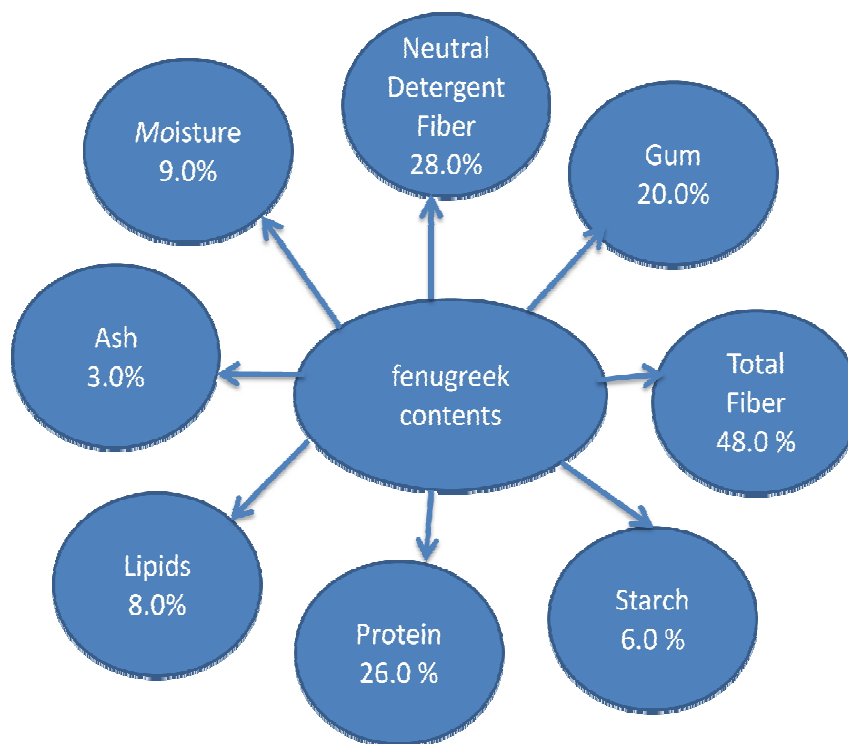


Figure 2: Composition of Fenugreek seed in percentile

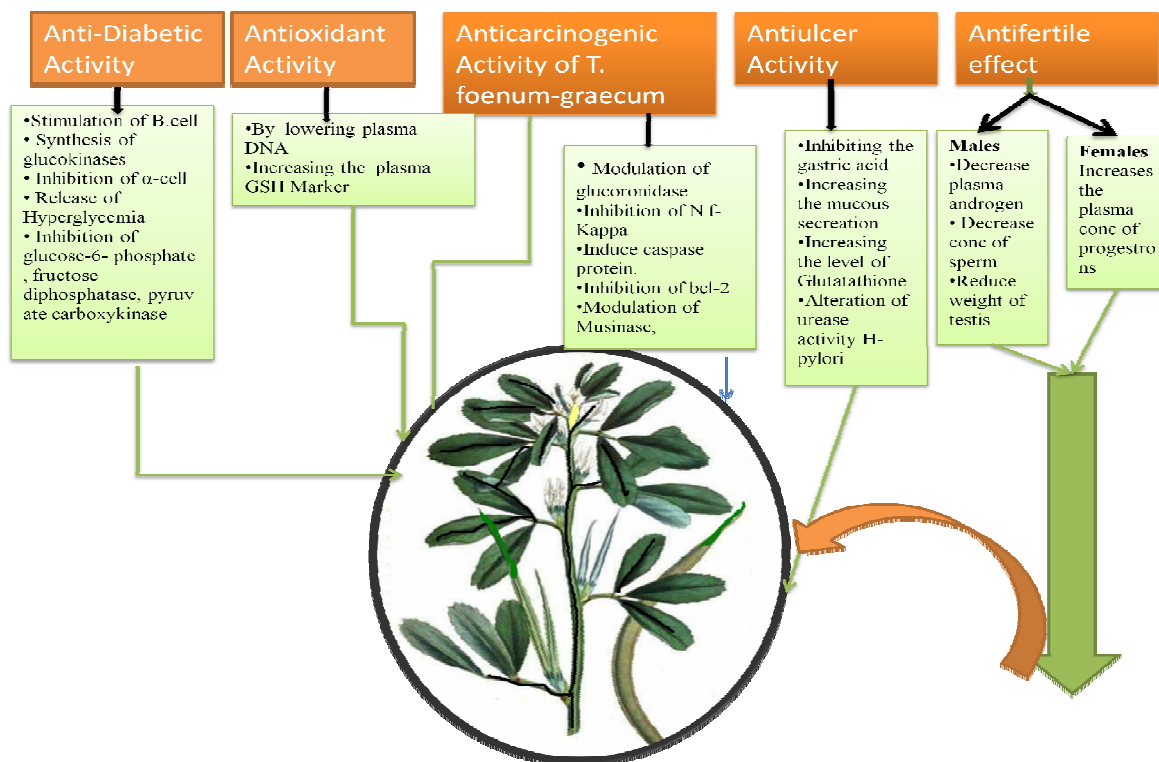


Figure 3: Pharmacological activities of Fenugreek seed and their mechanisms

Fenugreek plant has different medicinal effects which are mediated by different metabolic pathways of the human body.

DISCUSSION

Being annual herb plant it can be grown in any part of the world as it requires moderate day length for its cultivation. It can be used as a therapeutic drug for curing many types of diseases as well as its extracted compounds can be used individually in drug designing and discovery. Polyphenolic compounds have antioxidative properties as compared to other extracts. Fenugreek contains 4-hydroxy isoleucine amino acid in free form that has antidiabetic as well as insulinotropic effects. It has various health benefits which can be enhanced by isolating each and every compound and can be used as a potential candidate for many types of diseases. The consumption of Fenugreek has proved safe and secure for humans and may be simply implemented for health benefit as a dietary component, through its rich full fiber packaged and other bioactive components. Fenugreek seeds not only reduce the low density cholesterol and triacylglycerol but also reduce blood sugar level because of its useful phytochemicals. The various scientific researchers showed that fenugreek which is well known for its hypoglycemic, immunodulatory, inflammatory, antioxidative, nutraceutical effects and induction of labor and lactation during child birth may be a great promising medicinal herbaceous plant. Future research on this plant could lead to the development of drugs which could find potential applications in medicine and pharmaceutical industries due to herbal nature and lower side effects.

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Cite this article as:

Dilkash Bano, Heena Tabassum, Asad Ahmad, Abdul Mabood, Iffat Zareen Ahmad The medicinal significance of the bioactive compounds of *Trigonella foenum-graecum*: A review. *Int. J. Res. Ayurveda Pharm.* Jul - Aug 2016;7(4):84-91
<http://dx.doi.org/10.7897/2277-4343.074139>

Source of support: Nil, Conflict of interest: None Declared

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