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PHARMACOGNOSTIC AND THERAPEUTIC IMPORTANCE OF FENUGREEK (*TRIGONELLA FOENUM-GRAECUM* L.)

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Abstract:

Herbs have high medicinal value in Indian homes. Fenugreek (Trigonella foenum-graecum) is one of the most promising medicinal herbs and having nutritional value found on the continents of Asia, Europe, Africa and Australia. It is traditional remedy for treatment of various diseases. After various studies on its chemical constituents the therapeutic importance of fenugreek are known. Seeds provide the dietary fibres because of high fibre content. Fenugreek contains the gum, fibre, alkaloid, flavonoids, saponin and volatile contents. It has various therapeutic applications like antidiabetic, anticarcinogenic, hypocholesterolemia and antioxidant, antibacterial agent, hypoglycemia, gastric stimulant, and anti-anorexia agent etc. This review article summarizes the therapeutic importance of fenugreek.

Keywords: *Trigonella foenum-graecum; Therapeutic; Hypocholesterolemic; Flavonoids, Fenugreek, bioactive compounds, medicinal and nutraceutical effects*

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INTRODUCTION:

Trigonella foenum - graecum (L.) belonging to the family Fabaceae. It is commonly known as Fenugreek. It is native to an area extending from Iran to northern India. Fenugreek is widely cultivated in China, India, Egypt, Ethiopia, Morocco, Ukraine, Greece, Turkey, etc. [1-2]. Among them, India is the leading producer of fenugreek in the world. It is a flowering annual plant, with autogamous flowers. It is an aromatic, annual herb, cultivated throughout the country [3]. It is 30- 60 cm tall plant, appearance of seed solid- rhomboidal, 3 to 5 cm long, 2 nm thick, hard and pebble like. Colour of seed is yellowish brown to light brown with little spicy and bitter-mucilaginous odour and taste respectively. Fenugreek is as one of the oldest cultivated medicinal plants. Many studies showed that it acquire anti-oxidant properties in seeds and leaves. It is also known as Methi. It is used as an Ayurvedic medicine in the treatment of abscesses, wounds, arthritis, bronchitis, and digestive disorders. Fenugreek as a chemurgic crop has a wide use for industrial purposes. Its seeds are source of a steroid diosgenin, which is used in pharmaceutical industry.

Figure 1: Leaves and seeds of Fenugreek plant

Trigonella foenum-graecum (Fenugreek) plant contains a variety of components i.e. alkaloids, glycoside, polyphenols, steroids, amino acids and volatile components. In various medicinal applications, it works as antidiabetic, anticarcinogenic, remedy for hypoglycemia and hypocholesterolemia, antioxidant, antibacterial agent, gastric stimulant, and anti-anorexia agent.The seeds are hot, with a sharp bitter taste; tonic, antipyretic, anthelmentic, increase the apetite, astringent to the bowels, cure leprosy, "vata", vomiting, bronchitis, piles; remove bad taste from the mouth, useful in heart disease [4] 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. This plant is used as supplement in maize and wheat flour for bread making in Yemen and Persia, it is used as daily meal preparation and as a medicinal plant in various parts of the world [5-6]. It is also used in traditional Chinese medicine for treating weakness and edema of legs. Trigonelline compound can be used for the manufacture of maple syrup and as an artificial flavor for vanilla, rum, and butterscotch [7-9].

Table 1: Classification of Fenugreek

Domain	Eukarya
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Fabales(orLeguminales)
Family	Fabaceae
Sub-family	Trifoliae
Genus	Trigonella
Sub-genus	Foenumgraecum
Species	*Trigonella foenum-graecum*

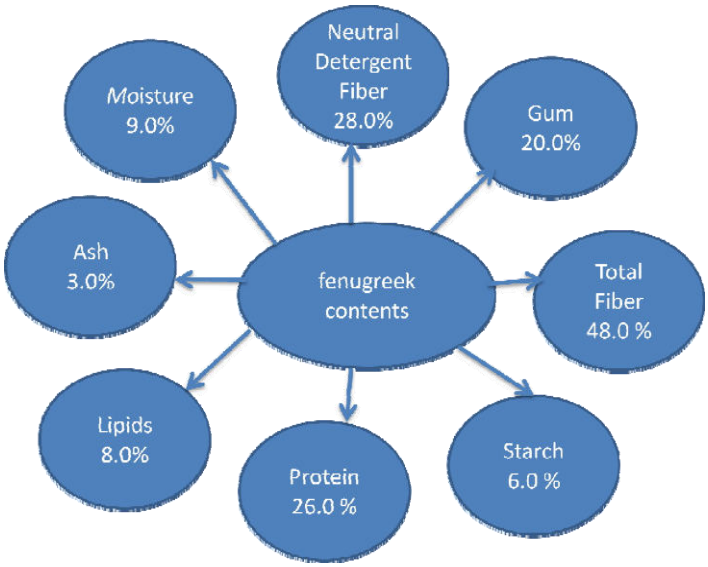


Figure 2: Chemical constituents of Fenugreek

Table 2: Chemical constituents of Fenugreek and their pharmacological effects

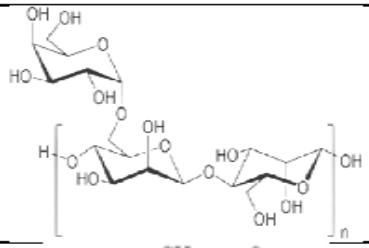
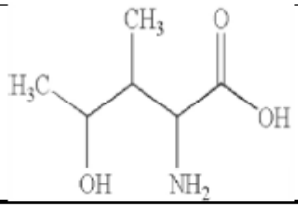
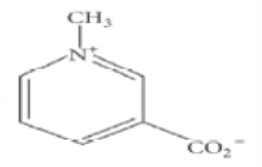
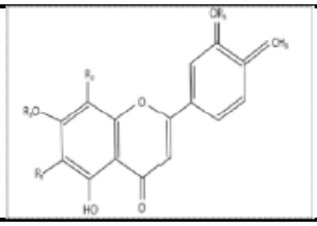
Galactomannan		The potential to modifying glycemic and lipidemic status as well as body weight in rats. A It is also inhibiting the pro-inflammatory cytokines [46]. It is suggested to be acting by extrapancreatic pathway rather than insulin stimulating effects
4-hydroxyisoleucine		It is a natural nonproteinogenic 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 transfered 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 3: 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.

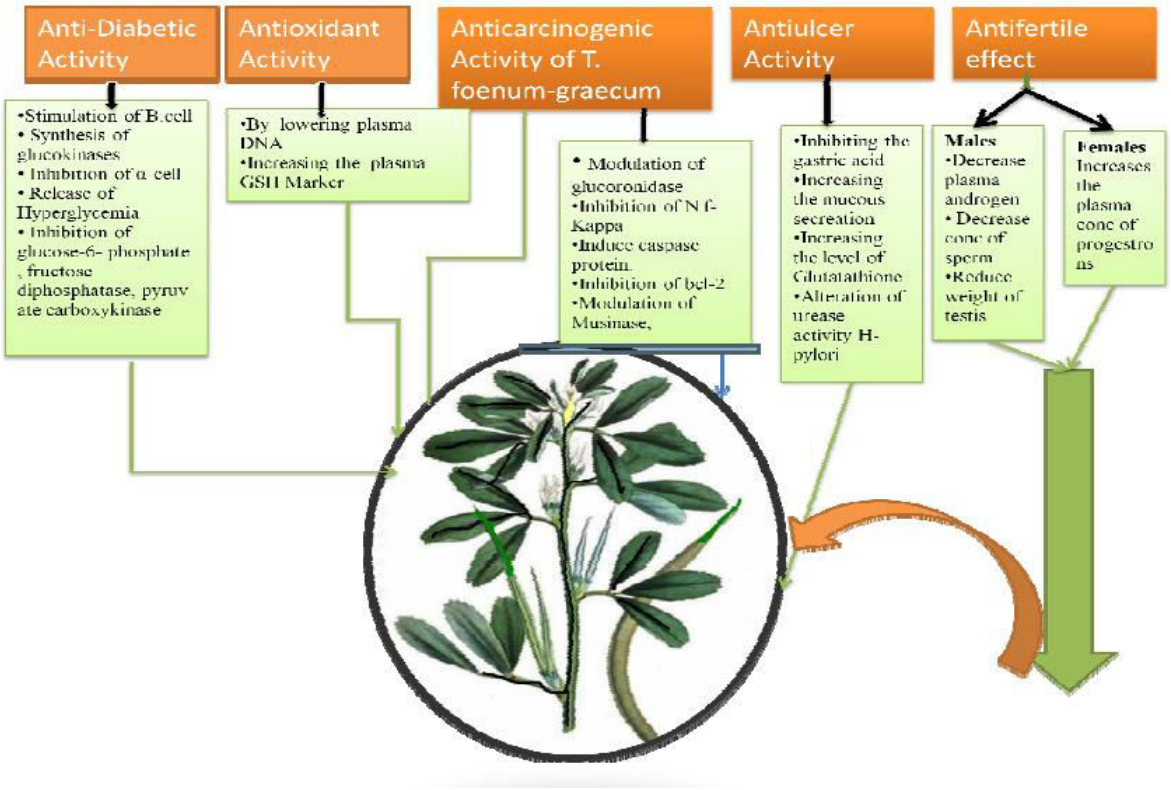


Figure 3: Pharmacological activities of Fenugreek seed and their mechanisms

Applications of different parts of Fenugreek and Fenugreek oil

The oil which is extracted from fenugreek represents 6-8% of seed weight and has a bitter taste and fetid order [10-13]. 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 perfumes [14-15].

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 cattles. 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 basis [16-18].

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. Dietry 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 bread [19-20]. Galactomannan act as a thickener in certain foods like soups and ice-creams [21]. 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 [22].

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, galactogogue 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 zinc [22].

Bioactive compounds of Fenugreek and their medicinal properties

Steroid saponins

Fenugreek contains steroids, sapogenins & diosgenin being major constituents. Sapogenins 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 sapogenins 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. [19-22]

Poly Phenol

Recent reports concluded that fenugreek seeds have five different types of flavonoids namely, vitexin, tricin, naringenin, quercetin, and tricin -7-O-β-d-glucopyranoside [23]. Iso-flavanoid phytoalexins are also reported to occur in the fenugreek in the form of the pterocarpans, medicarpin and maackiaian [24]. A current report showed the common phenolic compounds extracted from fenugreek to be coumarin, scopoletin, chlorogenic, caffeic p-coumaric acids and quercetin [25]. 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* conditions [28]. 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, inhibit11-β- hydroxysteriod dehydrogenate type 1 enzyme, increase glucokinase activity, prevention degeneration of β-cells, increase glucosidase inhibition, reduction in insulin resistance, and enhancement in adiponectin expression [29]. Recent studies indicate that quercetin effectively ameriolates 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 rats [30].

Alkaloids

In fenugreek seeds trigonelline is a methyl betaine derivative of necotinic 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. [31]

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 & fungi [31].

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 effect [32].

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 agent [33].

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. 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 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 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). fasting serum glucose (Table 4). The experiment showed that a small randomized controlled of fenugreek seeds effect in hypoglycemic regulation or control [35]. 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 sapogenins, which increase biliary cholesterol excretion and lower serum cholesterol levels (Table 5).

Health benefits of fenugreek

Fenugreek seeds are used as a preservative as they are rich in vitamin E which is an antioxidant. Vitamin E protects body tissue from damage caused by substances called free radicals which can harm cells, tissue and organs. For treatment of indigestion, flatulence leaves used for flavour and for recurrent mouth ulcers the infusion of leaves are used as a gargle. For hair therapy, the fresh leaves paste is used by applying it over the scalp. It helps to hair grow, keeps natural color, makes hair silky and remove dandruff. Fenugreek seeds made in gruel and given to nursing mothers. It helps to increase the flow of milk. For skin treatment, the gelatinous texture of fenugreek seed is used to soothing the skin which is irritated by eczema in this the skin patches become rough and inflames with blisters which cause bleeding and itching. In kidney stones problem, the seeds reduce the amount of calcium oxalate. To relieve muscle aches and gout pain warm poultice/cataplasm of fenugreek is used. Fenugreek seeds help in reducing the amount of calcium oxalate in the kidneys which causes kidney stones. Now a day's fenugreek is used as source of the steroid diosgenin, one of its active constituents from which other steroids can be synthesized.

Therapeutic importance of fenugreek

Fenugreek in the Treatment of Diabetes

In animal and human trials, fenugreek seeds have been found to lower fasting serum glucose levels. Fenugreek also to be used as antidiabetic remedy for both type I and II diabetes. Saponins and diosgenin present in fenugreek are responsible for hypolipidemic and anti-diabetic action [5-7]. Fenugreek is described as an antihyperglycemic herb in humans and laboratory animal [8, 9].

Fenugreek in cancer therapy

Fenugreek is a medicinal herb for therapy in cancer patients under chemotherapeutic interventions. Fenugreek extract shows a protective effect by modifying the cyclophosphamide induced apoptosis and free radical-mediated lipid peroxidation in the urinary bladder of mice.It has been found to be potentially important in cancer treatment [5]. Flavonoids and catechins were first shown to be apoptotic in human carcinoma cells. Diosgenin present in fenugreek prevents cell growth and induced apoptosis in the H-29 human colon cancer cell line [10]. Fenugreek seed was found to have hepatoprotective properties. Polyphenolic extract of fenugreek seed acts as a protective agent against ethanol induced abnormalities in the liver [11].

Fenugreek as antioxidant

Fenugreek has a property as an antioxidant because of the presence of Flavenoids and polyphenols [12, 13]. Fenugreek seeds rich in polyphenol which showed protective effects against hydrogen peroxide-induced oxidation by protecting the erythrocytes from haemolysis and lipid peroxidation [14]. A recent *in vitro* study has reported that the fenugreek extract has shown and by inhibiting the γ-radiation induced strand break formation in plasmid pBR322 DNA [11].

Fenugreek effect in cholesterol lowering

The abnormal deficiency of cholesterol level in the blood is known as hypocholesterolemic problem. Fenugreek increased the fecal bile acid and cholesterol excretion. It may be secondary to a reaction between the bile acids and saponins causing the formation of micelles too large for the digestive tract to absorb. Another effect is that, the fiber-rich gum portion of the seed that reduces the rate of hepatic synthesis of cholesterol. Both this mechanism contributes to cholesterol lowering. Fenugreek seeds have hypocholesterolemic effects [15]. Hence fenugreek seeds have lowered serum cholesterol, triglyceride [16, 17].

Fenugreek in anthelmintic activity

Seeds of fenugreek showed mark and potent anthelmintic activity. In this the alcoholic extracts showed promising results as anthelmintic activity. Besides it water extract show lesser activity [18].

Fenugreek in antibacterial activity

The seed extracts are effective against Escherichia coli, Salmonella typhi and Staphylococus aureus. To make this aqueous extract seeds are boiled in water [18]. Fenugreek has antibacterial activity that, these plants kill bacteria according to reports [19, 20]. The synthetic α-glucosidases inhibitors such as acarbose can cause adverse side effects on abdomen such as abdominal distention because of excessive inhibition of pancreatic enzymes which results in the abnormal bacterial fermentation undigested carbohydrates in the colon. Therefore research on the development and utilization of anti-diabetic plants with mild inhibition of pancreatic enzymes is beneficial [21, 22]. The glycolytic activity of α-amylase may occur through the direct blockage of the active center at several subsites of the enzyme as also suggested for other inhibitors [21]. The fenugreek extract contains α-amylase inhibitory factors which probably interact with the active sites of the enzyme in a substrate specific manner. To inhibit the growth of Pseudomonas spp., E. coli, Shigella dysentiriae, and Salmonella typhi, fenugreek is effective [23, 24].

Fenugreek in obesity

Obesity is one of the major risk factor for morbidity and mortality. It may be defined as abnormal growth of adipose tissue [25]. In some research's it's indicated that fenugreek seed extract supplementation reduces the body and adipose tissue weight [26]. The probable mechanism of fenugreek decreasing the total body and adipose tissue weight may be that fenugreek flushes out the carbohydrates from the body before they enter the blood stream resulting in weight loss and fenugreek seeds contain a high proportion (40%) of soluble fiber. These fibers forms a gelatinous structure which may have effects on slowing the digestion and absorption of food from the intestine and create a sense of fullness in the abdomen, thus suppresses appetite and promotes weight loss [25]. Hence fenugreek is effective on blood lipids and sugar and on some bacterial strains, antioxidant activity of fenugreek causing protective of organs and inhibition of entrance diseases to body, too decreases body fats and is effective on obesity.

Fenugreek in Gastro protection

The fenugreek seeds are effective on gastric ulcer. The aqueous extract and a gel fraction isolated from the seeds of fenugreek showed significant ulcer protective effects. The cytoprotective effect of the seeds is due to the anti-secretory action and effects on mucosal glycoproteins. The rise in lipid peroxidation induced by ethanol is also prevented by fenugreek seeds. The mechanism besides it that it enhances the antioxidant potential of the gastric mucosa hence it can lowers mucosal injury. By various researches it can revealed that the soluble gel fraction derived from the seeds was more effective than omeprazole in preventing lesion formation. These observations show that fenugreek seeds possess antiulcer potential [22, 27].

Fenugreek influence in Digestion

Spices consumed in diet influenced the pancreatic digestive enzymes.Fenugreek prominently enhanced pancreatic lipase activity with the help of feeding rats with spicy diets for eight weeks [28]. High fibre of fenugreek helps in relieving constipation ailments.

Fenugreek in Inflammation

The 100 and 200 mg/kg dose of fenugreek reduced carragenean-induced paw edema in rats [29]. Fenugreek extract contains the alkaloid and it has been reported that to produce anti-inflammatory property by reducing formalin-induced edema in rat and antipyretic property by significantly reducing hyperthermia induced by Brewer's Yeast this alkaloids are essential [30]. The anti-inflammatory property of fenugreek is probably due to the presence of saponins and flavonoid. Flavonoids act as antioxidant and potential inhibitors of cyclooxygenase, lipoxygenase, and nitric oxide synthase [26, 31-33].

Fenugreek in Hypertension

Endothelial dysfunction is a devastating condition which is associated to induce various disorders such as atherosclerosis, hypertension, diabetes mellitus etc. [34]. The essential oil obtained from fenugreek in combination with other essential oils has been employed to reduce systolic blood pressure in spontaneously hypertensive rat [35]. The aqueous and benzene extract of fenugreek has been found to show diuretic activity in a dose dependent manner by increasing the volume of urine and naliuretic activity by increasing the levels of Na+/K+ ions ratio in Wistar rats; which can be employed to treat hypertension [36,37].

CONCLUSION:

The Present review shows the different therapeutic applications of fenugreek. The major health beneficial properties of fenugreek, which can give promising therapeutic application has been discussed in this review article. Antidiabetic, antioxidant, anticarcinogenic, anthelmintic, hypocholesterolemic, antibacterial activities are the major medicinal properties of the fenugreek demonstrated in various studies. High fibre content, gummy nature and chemical constituents present in it make it a naturally health promoting herb. By studying these observations fenugreek is recommended as a safe and can be used in daily diet. . 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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