

Therapeutic Uses of Fenugreek (*Trigonella foenum-graecum* L.)

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Abstract

Herbs are used medicinally in different countries by around 80 % of people around the world, mostly in the developing countries. They are a source of many potent and powerful drugs, principally due to the common belief that they are without any side effects along with being economical and locally accessible. Fenugreek (*Trigonella foenum-graecum* L.) is an herb that grows anywhere around the world. Fenugreek is one of the oldest medicinal plants, originating in India and Northern Africa. Its dried seeds have a wide application as a flavoring additive and are good source of protein, fat, crude fiber, minerals and vitamins. In addition It has a broad spectrum of therapeutic properties. It has been used for numerous indications, including labor induction, aiding digestion, and as a general tonic to improve metabolism and health. Human and animal trials suggest possible hypoglycemic and antihyperlipidemic properties of oral fenugreek seed powder. Mucilaginous fiber present in fenugreek seeds may bind bile acids to reduce cholesterol and fat absorption. The plant protein in fenugreek might exert a lipid lowering effect. Steroidal saponins, alkaloids and 4-hydroxy-isoleucine may promote glucose metabolism and inhibit absorption of cholesterol. Furthermore some chemical constituents of fenugreek may directly stimulate insulin secretion from B-cells resulting in blood sugar reduction. Its cardioprotective effects are attributed to its modulating effect on blood lipid levels and anti-oxidant properties. In a number of studies, extracts of fenugreek seeds and some of their constituents have shown anticarcinogenic potency. In addition, fenugreek was reported to have gastroprotective effect, antimicrobial activities, anticancer effect, used in treatment of arthritis, reducing weight, increasing milk production and may regulate hyperthyroidism. The aim of this chapter is to review the literatures that investigate the various therapeutic uses of fenugreek.

Keywords: Fenugreek, *Trigonella foenum-graecum* L., therapeutic uses, pharmacological, hypoglycemic, diabetes

Abbreviations: **AlCl₃**: Aluminum Chloride; **CRP**: C- Reactive Protein; **DMBA**: 7,12-Dimethylbenz [a] Anthracene; **DNA**: Deoxyribonucleic Acid; **EAC**: Ehrlich Ascites Carcinoma; **ER**: Estrogen Receptor; **ERK**: Extracellular Signal Regulating Kinase; **ESR**: Erythrocyte Sedimentation Rate; **HDL**: High Density Lipoprotein; **HL**: Human Leukemia; **JNK**: c-Jun N-terminal Kinase; **L-Dopa**: L-3,4-dihydroxyphenylalanine; **LDL-C**: Low Density Lipoprotein Cholesterol; **NSAIDs**: Non-Steroidal Anti-Inflammatory Drugs; **PD**: Protodioscin; **SH**: Sulfhydryl; **TG**: Triglycerides; **Th**: T-helper; **WBC**: White Blood Cells

INTRODUCTION

Herbs have been used in all parts of the world not only as food but also as potent drugs for thousands of years. They do not work like chemical drugs and they are not substitute of them [1, 2]. Medicinal plants are used by 80 % of the world population especially in developing countries to cure and improve the general health, principally due to the common belief that plant-derived drugs are without any side effects along with being economical and locally accessible [3]. Fenugreek, *Trigonella foenum-graecum* L., is an annual herb grown in various countries around the world. It was thought to be indigenous to the countries bordering on the eastern shores of the Mediterranean [4], but now is widely cultivated in India, China, northern and eastern Africa, and parts of Europe and Argentina [5]. The health-promoting property of fenugreek has been long documented when it is taken as vegetables, food supplements or medicinal remedies. It has been used in many different cultures, but especially in Asia and the Mediterranean region [6].

Historical uses of fenugreek

Fenugreek has a long history as both a culinary and medicinal herb in the ancient world. Applications of fenugreek were documented in ancient Egypt, where it was used in incense and to embalm mummies [7]. The Greeks and Romans used it for cattle fodder (hence the Latin *foenum graecum* meaning Greek hay). In ancient Rome, fenugreek was purportedly used to aid labor and delivery. In traditional Chinese medicine, fenugreek seeds are used as a tonic, as well as a treatment for weakness and edema of the legs [8]. In India, fenugreek is commonly consumed as a condiment and used medicinally as a lactation stimulant [9].

Active constituents

Fenugreek seed contains 45-60 % carbohydrates, mainly mucilaginous fiber (galactomannans); 20-30 % proteins high in lysine and tryptophan; 5-10 % fixed oils (lipids); pyridine-type alkaloids, mainly trigonelline (0.2-0.3 %), choline (0.5 %), gentianine, and carpaine; the flavonoids apigenin, luteolin, orientin, quercetin, vitexin, and isovitexin; free amino acids, such as 4-hydroxyisoleucine (0.09 %); arginine, histidine, and lysine; calcium and iron; saponins (0.6-1.7 %); glycosides yielding steroidal saponins on hydrolysis (diosgenin, yamogenin, tigogenin, neotigogenin); cholesterol and sitosterol; vitamins A, B₁, C, and nicotinic acid; and 0.015 % volatile oils (n-alkanes and sesquiterpenes), which are thought to account for many of its presumed therapeutic effects [10-12].

Pharmacological effects and mechanisms of action

Fenugreek is known to have several pharmacological effects such as: hypoglycemic [13], and antilipidemic or hypocholesterolemic [14]. However, the exact mechanism of action is still unclear. The antidiabetic effect of Fenugreek was thought to be due to formation of a colloidal-type suspension in the stomach and intestines when the mucilaginous fiber of the seeds is hydrated, therefore affecting gastrointestinal transit, slowing glucose absorption. The antilipidemic effects of Fenugreek was thought to be due to inhibition of intestinal cholesterol absorption due to saponin-cholesterol complex formation, increased loss of bile through fecal excretion due to saponin-bile complexes, thus increasing conversion of cholesterol to bile by the liver, and effects of amino acid pattern of fenugreek on serum cholesterol [15]. Furthermore, this plant has an antioxidant action [16], gastroprotective

activity [17], appetite stimulation [18], and antirheumatism [19]. Histopathological examination of liver and brain has revealed that, aqueous extract of fenugreek seeds offer a significant protection against ethanol toxicity [20].

THERAPEUTIC USES OF FENUGREEK

Diabetes mellitus

Diabetes mellitus is a chronic metabolic disorder characterized by derangements in the metabolism of carbohydrate, protein and lipids caused by complete or relative insufficiency of insulin secretion or/and action [21]. Diabetes is a major health concern and its burden is increasing globally. Herbal medicine plays an important role in treatment of diabetes [22, 23]. Fenugreek seeds, leaves and extracts had been used as an anti-diabetic in many model systems [24-26]. In Arab countries, in Saudi Arabia [27] and Iraq [28], fenugreek was found to be among the most common herbs used among people with diabetes. Animal studies suggest hypoglycemic effects of fenugreek [29, 30]. Human studies also showed possible hypoglycemic properties of fenugreek. Sharma et al (1990) [31] conducted a randomized, controlled, crossover trial in 10 patients with type 1 diabetes. Over a 10-day period, the subjects were served meals that contained 100 g fenugreek seed powder in two divided doses each day (lunch and dinner) or meals without fenugreek. At the study's end, significant improvement was noted in the fenugreek group in several parameters, including a 54 % reduction in 24-hour urine glucose levels and mean reductions in glucose tolerance test values and fasting serum-glucose levels (from 15.1 ± 2.4 mMol/L to 10.9 ± 2.75 mMol/L; $P < 0.01$).

Gupta et al reported the results of a double blind placebo controlled study to evaluate

the effects of fenugreek seeds on glycemic control [32]. Twenty five newly diagnosed patients with type 2 diabetes (fasting glucose < 200 mg/dl) were randomly divided into two groups. Group I ($n = 12$) received 1 gm/day hydroalcoholic extract of fenugreek seeds and Group II ($n = 13$) received usual care (dietary control, exercise) and placebo capsules for two months. There were no significant differences between groups in mean glucose tolerance test values at the study's end, but there was an increase in percent insulin sensitivity. The authors concluded that adjunct use of fenugreek seeds improves glycemic control and decreases insulin resistance in mild type-2 diabetic patients. In a study done in Iran, on 24 Type 2 diabetics showed 10 g a day of fenugreek for 8 weeks decreased fasting blood glucose from 182 mg/dl to 136 mg/dl, but did not change the HbA1C [33]. A study on 166 type 2 diabetics in Jordan showed a dose dependent improvement in 2 hour post prandial sugars in the group receiving 5 g fenugreek compared to those on 2.5 g fenugreek and the control group [24]. In another study on healthy subjects, Shakib et al found those who consumed bread with fenugreek had an improvement in the postprandial glucose response compared to those who ate bread without fenugreek [34]. Apart from biochemical improvements, fenugreek seeds have been reported to markedly suppress the clinical symptoms of diabetes such as polyuria, polydipsia, weakness and weight losses [35]. The hypoglycaemic effect of fenugreek is thought to be largely due to its high content of soluble fiber which acts to decrease the rate of gastric emptying, thereby delaying absorption of glucose from the small intestine [36]. 4-hydroxyleucine, a novel amino acid from fenugreek seeds increased glucose stimulated insulin release by islet cells in both rats and humans [37]. Owing to its particular insulinotropic action, 4-

hydroxyisoleucine might be considered as a novel secretagogue with potential role in treatment of diabetes [38]. Saponin compounds diosgenin, alkaloids and trigonelline were shown to be associated with inhibition of intestinal glucose uptake *in vitro* [39]. Fenugreek has been shown to increase erythrocyte insulin receptors and improve peripheral glucose utilization, thus showing potential pancreatic as well as extrapancreatic effects [40].

Effect of fenugreek on serum lipids

There is some evidence from randomized clinical trials that fenugreek reduces serum cholesterol. In a single-blind study of 20 healthy male volunteers, Abdel-Barry et al found a non significant decrease of 9.2 % in total serum cholesterol after a single dose of an aqueous extract made from fenugreek leaves (40 mg/kg) compared with a reduction of 2.8 % after dilute coffee extract (placebo)[26]. Sharma et al investigated 15 non-obese, asymptomatic, hyperlipidemic adults. After ingestion of 100 gm defatted fenugreek powder per day for three weeks, the subjects showed a decrease in their triglyceride (TG) and low density lipoprotein cholesterol (LDL-C) levels as compared with baseline values. Slight decreases in high density lipoprotein (HDL) levels were also noted [41].The triglyceride lowering effect may be due to the pectin component that absorbs bile acids [42]. Sowmya and Rajyalakshmi observed significant reductions in total cholesterol and low density lipoprotein cholesterol (LDL-C) levels in 20 adults with hypercholesterolemia who received 12.5-18.0 gm powdered, germinated fenugreek seeds for one month [43]. To evaluate the effect of combination of *Nigella sativa* L. and *Trigonella foenum-graecum* L. seeds with Glibenclamide on serum triglyceride, and high density lipoprotein (HDL) levels in type-2 diabetes mellitus patients, Memon et

al conducted a study on 100 diabetic patients. Those patients were randomly divided into two groups. Fifty patients as a control group were maintained on routine dose of Glibenclamide, while the other 50 patients as an intervention group were given capsules containing equal amount of combined powder of *N-sativa* and *T. foenum-graecum* seeds, in addition to their routine dose of Glibenclamide. Serum triglyceride, and HDL levels were measured for every patient at the start and after 3 months of therapy. Comparison of the mean values of parameters measured in both groups showed that serum HDL levels were significantly ($P < 0.05$) raised in intervention group as against the control, whereas the levels for serum triglycerides was comparable in both the groups [44]. The fiber constituents of fenugreek delay the digestion and absorption of carbohydrates [45]. The soluble fiber from fenugreek appears to decrease reabsorption of bile acids in the small intestine increasing the excretion of cholesterol and bile acids into the feces. Consequently, the need of cholesterol for bile acid biosynthesis is enhanced and blood cholesterol concentrations are reduced [46].

Diosgenin, the primary furostanol saponin in fenugreek has been proven to have various effects on cholesterol metabolism, the most important being its capacity to lower plasma cholesterol concentration. This hypocholesterolemic effect appears to be dependent upon the capacity of diosgenin to inhibit cholesterol absorption, to decrease liver cholesterol concentration and to increase biliary cholesterol secretion and the fecal excretion of neutral sterols. The lipid-lowering effect of fenugreek might also be attributed to its estrogenic constituent, indirectly increasing thyroid hormone [47]. The quality and quantity of protein in the diets have a direct effect on the levels of

cholesterol. Generally plant protein appears to lower cholesterol level [48].

Cardioprotective effects

An animal study revealed that administration of fenugreek proved to be effective in reducing the extent of myocardial damage and significantly counteracted the oxidative stress during isoproterenol-induced myocardial infarction in rats [49]. Fenugreek has a strong modulating effect on blood lipid levels. It has demonstrated a remarkable ability to lower cholesterol, triglycerides and LDL levels while raising HDL levels [50], so can substantially reduce the risk of atherosclerosis. Another property of fenugreek is the reduction of platelet aggregation due to its coumarin and other constituents which, in turn, dramatically reduces the risk of abnormal blood clotting associated with heart attacks and strokes [15]. Fenugreek also contains many important antioxidants and has the added benefit of protecting other dietary and internally produced antioxidants from free-radical damage. This has important cardioprotective benefits, as well as helping to fortify the body against a range of other chronic conditions [49].

Gastroprotective effect

One of the historical uses of fenugreek is treatment of gastric ulcer. The ulcer protective effect of fenugreek seeds compared to omeprazole was studied on ethanol-induced gastric ulcer in rats. The aqueous extract and a gel fraction derived from the seeds showed significant ulcer protective effects compared to those on omeprazole. The researchers found that the cytoprotective effect of the seeds seemed to be due to the anti-secretory action and to the effects on mucosal glycoproteins. The fenugreek seeds also prevented the rise in lipid peroxidation induced by ethanol

presumably by enhancing antioxidant potential of the gastric mucosa thereby lowering mucosal injury [51]. In another study done on rats also, aqueous extracts of barley grains (*Hordeum vulgare* L.) and fenugreek seeds (*Trigonella foenum - graecum* L.) were administered to a group of Albino rats previously subjected to aspirin at 400mg/kg b.w., for gastric ulcer induction. The results revealed that rats treated with barley and fenugreek aqueous extracts showed significant decline in ulceration severity as determined by ulcer index as well as curative ratios. Also, there was a significant increase in gastric mucus (carbohydrate/ protein ratio in mucosa). The anti-ulcer effect was further confirmed histopathologically [52]. Another study investigated the effect of fenugreek seeds on Aspegic induced gastric mucosal ulcer in rats. The results showed that fenugreek seeds possess antiulcer potential [53]. The antiulcer activity of fenugreek may be attributed to its flavanoids contents since they were reported to protect the mucosa by preventing the formation of ulcerative lesions by various necrotic agents [54, 55]. It was reported that the polysaccharide fraction of fenugreek seeds forms a mucin like gel layer of galactomannan on the surface of the mucosa, or forms a protecting complexes between gel and mucus as a barrier against the agents introduced into the stomach or against endogenously formed acid and pepsin in the stomach [56]. Increase in gastric mucosa content of sulfhydryl may contribute to the anti-ulcer activity of the fenugreek seeds. Gastric mucosal sulfhydryl compounds (SHs) act as antioxidants and are important for maintenance of mucosal integrity in the stomach [57, 58].

Anticancer effect

In a number of studies, extracts of fenugreek seeds and some of their constituents have shown anticarcinogenic potency.

Consumption of fenugreek was accompanied with decreased polyamines (spermine, spermidine, putrescine) content in tumor tissue [59]. Srinivasan et al [60] investigated the effect of diosgenin, a biologically active constituent of fenugreek seeds on breast cancer cell lines. Diosgenin caused G1 cell cycle arrest by down regulating cyclin D1, cdk-2 and cdk-4 expression in both estrogen receptor positive ER (+) and estrogen receptor negative ER (-) breast cancer cells resulting in the inhibition of cell proliferation and induction of apoptosis. Furthermore, diosgenin was found to inhibit migration and invasion of prostate cancer PC-3 cells by reducing matrix metalloproteinases expression. It also inhibited extracellular signal regulating kinase (ERK), c-Jun N-terminal kinase (JNK) and phosphatidylinositide-3 kinase (PI3K/Akt) signaling pathways as well as nuclear factor kappa B (NF- κ B) activity [61]. Das et al also showed that diosgenin alone or in combination with Thymoquinone obtained from black cumin (*Nigella sativa* L.) inhibit cell proliferation and induce apoptosis in squamous cell carcinoma [62]. The antineoplastic effect of *Trigonella foenum graecum* seed extract has been also evaluated in the Ehrlich ascites carcinoma (EAC) model in Balb-C mice. Intra-peritoneal administration of the alcohol extract of the seed both before and after inoculation of EAC cell in mice produced more than 70 % inhibition of tumour cell growth with respect to the control. Treatment with the extract was found to enhance both the peritoneal exudate cell and macrophage cell counts. The extract also produced a significant anti-inflammatory effect [63].

The effects of Protodioscin (PD) which was purified from fenugreek on cell viability in human leukemia HL-60 and human stomach cancer KATO III cells were investigated.

PD displayed strong growth inhibitory effect against HL-60 cells, but weak growth inhibitory effect on KATO III cells. The fragmentation by PD of DNA to oligonucleosomal-sized fragments, that is a characteristic of apoptosis, was observed to be both concentration and time-dependent in the HL-60 cells. These findings suggest that growth inhibition by PD of HL-60 cells results from the induction of apoptosis by this compound in HL-60 cells [64]. In 1,2-dimethylhydrazine (DMH) [which is a colon carcinogen] treated rats, inclusion of fenugreek seed powder in their DMH treated diet reduced the colon tumor incidence to 16.6 % through modulation of DMH-induced oxidative stress [65]. Chatterjee et al reported a chemopreventive activity of the methanolic extract of fenugreek seeds on 7,12-dimethylbenz [a] anthracene (DMBA) induced skin papilloma genesis in Swiss albino mice. They supposed that the inhibition of tumorigenesis by the seed extract might have been executed either by preventing the formation of active carcinogens from their precursors or by augmenting detoxification process, preventing promotional events in the mouse skin through free radical scavenging mechanism. The chemopreventive activity of the methanolic extract of fenugreek seeds may be due to the rich chemical constituents (such as, saponins, flavonoids, alkaloids, galactomannans) that are present in the seed working synergistically at various stages of angiogenesis [66]. Fenugreek tea was reported to have an ability to inhibit further growth of cancer cells without harming the healthy cells of the body. Shabbeer et al demonstrated that fenugreek extract were cytotoxic *in vitro* to a panel of cancers but not normal cells. Treatment with 10-15 μ g/mL of fenugreek extract for 72h was growth inhibitory to breast, pancreatic and prostate cancer cell lines [67].

Use of fenugreek in arthritis

Rheumatoid arthritis is an autoimmune disease and estrogen-like compounds have been known to inhibit inflammation of tissue by activating pathways that counteract the effects of autoimmunity disorders through binding of estrogen metabolites to DNA [68]. Fenugreek has been shown to stall auto-immune disorders by acting as a mimic of estrogen. Sreeja et al found that fenugreek bound to estrogen receptors and acted as estrogen by influencing genetic activities and inducing the expression of estrogen-responsive proteins [69]. In another study, Ethanol extract of fenugreek was tested against Freund's complete adjuvant-induced arthritis in rats. It was found that the activities of cyclooxygenase-2 and myeloperoxidase and concentration of thiobarbituric acid reactive substance were decreased and the activities of antioxidant enzymes, vitamins C and reduced glutathione level were increased on treatment with fenugreek mucilage. The increment in erythrocytation rate (ESR) and total white blood cells (WBC), reduction in red blood cells (RBC) count and hemoglobin and aberrant changes to the C-reactive protein (CRP) levels observed in the arthritic animals were also found to be significantly restored in fenugreek mucilage treated rats. Histo-pathological examination also revealed decreased edema formation and cellular infiltration on supplementation with fenugreek mucilage [70]. Vyas et al reported that combination of *fenugreek*, *Boswellia* and *Acacia* shows restoration of vascular and endothelial dysfunction caused by chronic arthritis in rats [71]. It was hypothesized that the anti-inflammatory and antioxidant activities of *T. foenum graecum* L. may be the possible reason behind the observed anti-arthritic activity [72].

Antimicrobial effects of fenugreek

Herbal extracts are fast becoming popular as natural antimicrobial preservatives or

additives [73, 74]. The antimicrobial activities of plant extracts may reside in a variety of different components, including aldehyde and phenolic compounds. Many studies had reported the antibacterial activity of fenugreek. Omolosa and Vagi reported strong activity of *T. foenum-graecum* against 26 bacterial pathogens [75]. Randhir et al observed a high antimicrobial activity against peptic ulcer-linked *Helicobacter pylori* in the fenugreek sprout extract. They hypothesized that in fenugreek sprouts, simple free phenolics that are less polymerized have more antimicrobial function [76]. Phenolic-type antimicrobial agents have long been used for their antiseptic, disinfectant, or preservative properties [77]. Methanol extract of fenugreek (*Trigonella foenum-graecum* L.) and coriander (*Coriandrum sativum* L.) revealed an elevated antimicrobial activity against *Pseudomonas* spp., *Escherichia coli*, *Shigella dysenteriae* and *Salmonella typhi* [78]. Also it was reported that fatty oil of fenugreek seeds showed very significant antimycotic activity against *Aspergillus niger* and *A. fumigates* [79].

Effect of fenugreek on body weight

Fenugreek seeds have long been used as a herbal medicine for treating metabolic and nutritive dysfunctions. Some studies indicated that fenugreek seed extract supplementation may reduce the body and adipose tissue weight [80, 81]. A 6-week double-blind randomized placebo-controlled parallel trial of a fixed dose of a fenugreek seed extract on 39 healthy overweight male volunteers revealed that repeated administration of a fenugreek seed extract slightly but significantly decreased dietary fat consumption in those healthy overweight subjects [82]. 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. Also, fenugreek seeds contain a high proportion (40 %) of soluble fiber. This fiber forms a gelatinous structure (similar to gaur gum) which may have effects on slowing the digestion and absorption of food from the intestine and creates a sense of fullness in the abdomen, thus suppresses appetite and promotes weight loss [81]. The 4-hydroxyisoleucine component of fenugreek extract may also decrease plasma triglyceride gain consequently leading to prevent the obesity induced by a high-fat diet [80].

Other uses of fenugreek

Both leaves and seeds of fenugreek were advised because of their haematinic value. It was reported that the seeds contain high amounts of iron and germination of the fenugreek improves its vitamins A, B and C content. They are rich in proteins with essential amino acids, Ascorbate and Folate content, have restorative and nutritive properties and were found to raise blood haemoglobin [83]. *T. foenum-graecum* extract indicated a stimulatory influence on immune functions in mice through increasing the phagocytic index and phagocytic capacity of macrophages [84]. Fenugreek may correlate with increased milk production [85]. Fenugreek has also been used to protect liver from ethanol-induced hepatotoxicity [86], aluminum chloride (AlCl₃) induced hepatotoxicity [87], and regulate hyperthyroidism [88]. It was found to be useful therapeutic agent in allergic inflammatory diseases. In animal study, fenugreek extract cures T-helper 2 (Th2)-induced allergic skin inflammation by enhancing T-helper 1 (Th1) differentiation [89]. An emulsion containing fenugreek seeds extract using liquid paraffin oil was applied to the cheeks of human volunteers for six weeks. A significant decrease in skin melanin and erythma was produced by that

formulation [90]. Fenugreek was also reported to be a useful adjuvant treatment with L-Dopa in management of Parkinson's disease patients [91]. Reduction in cataract incidence has been demonstrated in diabetic rats receiving an extract of fenugreek seeds and leaves [92]. Another study showed a significant delay in the onset and progression of galactose-induced cataracts in rats fed on 2.5 % fenugreek diet [93]. Fenugreek leaves extract can exert analgesic effects. *Trigonella foenum-graecum* extract may have analgesic activity similar to non-steroidal anti-inflammatory drugs (NSAIDs) [94]. Analgesic effects of fenugreek seed extract were shown in other studies, perhaps by decreasing inflammation [95], or the blocking of spinal purinoceptors may contribute to the analgesic effect of *Trigonella foenum-graecum* leaves extract [96]. Wound healing properties of fenugreek seeds have also been demonstrated in excision, incision and dead-space wound models in rats [97].

Adverse effects

Although fenugreek has traditionally been considered safe and well tolerated, some side effects have been associated with its use. Caution in using fenugreek is warranted in patients known to be allergic to it or who are allergic to chickpeas because of possible cross-reactivity [9]. Hypersensitivity reactions that have been reported including rhinorrhea, wheezing and fainting after inhalation of the fenugreek- seed powder [98] and facial angioedema after application of a topical fenugreek paste for dandruff [9]. Hypoglycemia is an expected effect; therefore, monitoring of blood glucose levels should be taken once starting supplementation [31]. Fenugreek may increase the risk of bleeding due to its coumarin content [99]. The effects of fenugreek on haematopoietic stem cell of bone marrow were reported. Fenugreek in

teratogenic dosages can decrease the severity of bone marrow cell proliferation and increase fetal mortality rate [100]. A potential antifertility activity of fenugreek had been reported in rabbits fed diets containing 30 % fenugreek [101]. Dyspepsia and mild abdominal distention have been reported in studies using large doses of the seeds [32]. Mild central nervous stimulation, rapid respiration and tremors were observed following high doses of the aqueous extract of fenugreek [102, 103].

Interactions with other drugs

Caution in using fenugreek with some drugs should be warranted. Because of its coumarin constituents, it may potentially enhance the effect of anticoagulant drugs [104]. Also, due to its high content of fiber which is mucilaginous and has high viscosity in the gut, fenugreek may decrease or delay absorption of concomitant oral medications [105]. Since fenugreek was reported to reduce potassium level in some healthy subjects [26], it may precipitate hypokalemia when used with some diuretics, laxatives or other hypokalemic agents. Because of its hypoglycemic effects, fenugreek may have additive hypoglycemic activity when used with other anti-diabetic medication [106]. Although, some herbalists advocate its use during prolonged labor, use of fenugreek during pregnancy should be avoided because it has documented uterine stimulant effects. In addition, Maple syrup urine disease, a disorder of branched-chain amino acid catabolism that results in abnormal accumulations of the amino acids and their metabolites, was suspected in a healthy infant born to a mother who ingested a paste prepared from fenugreek seeds early *in labo* [107].

CONCLUSION

Natural products have been a major source of new drugs. Herbs have gained more

attention in medicine due to the rising popular concern about their safety. However, the long-term safety for use as herbal medicinal products has not been established; fenugreek an herb that may hold promise in this regard. Depending on human and animal studies, fenugreek had been considered by many researchers as a potential medicinal herb particularly as an anti-diabetic, hypolipidemic and an anti-oxidant agent. It has an influence on immune functions, anticancer properties, antimicrobial, gastro and cardioprotective effects, anti-arthritis and vascular protective effect. However, many of its effects are subjected to lack of clinical trials confirmation. Furthermore, fenugreek can cause undesired effects and it is also reported to interact with many drugs. Therefore, detailed clinical studies are needed to strengthen these findings and to evaluate the pharmacological properties and effects of fenugreek.

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