Chapter

Assessment of Secondary Metabolites with Different Uses of Fenugreek

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Abstract

Fenugreek (*Trigonella foenum-graecum*) is an annual medicinal plant with trifoliate leaves, a branched stem, white flowers, rooted tubers, and golden yellow seed belonging to Fabaceae family. Fenugreek is used in different industries such as pharmaceutical, nutraceutical and food industries as an ancient crop plant. Fenugreek is grown as a medicinal herb in many countries and has antioxidant, hypoglycemic, hypercholesterolemia, stomach protective, chemopreventive, laxative and appetite stimulating properties. In recent years, many important studies have been conducted on the biological activities and therapeutic properties of fenugreek mainly secondary metabolites such as alkaloids, flavonoids, steroids and saponins. These compounds are used for multipurpose uses in different industries and also appreciated by scientists. Based on these several health usefulness as discussed in review, fenugreek might be a good candidate for a herbal drug and used for preparation of new drugs. In this review, secondary metabolites used in different industries of fenugreek will be discussed and general benefits of them will be expressed within the all significant aspect of fenugreek as clearly. This review also highlights the traditional uses and nutraceutical properties (antioxidant activity, antibacterial, antifungal, anticancer hypoglemic effects and anti-inflammatory and immunological activity) of fenugreek. These uses and effect properties of fenugreek have been discussed and researchable areas were implied to depending on the previous studies. In the future, studies on fenugreek are needed some important applications to increasing the popularity of fenugreek. In this context, researchers should be focused on secondary and primary metabolite studies in fenugreek seeds and leaves. In addition to these, fenugreek germplasm should be collected and subjected to intensive selection via modern breeding programs and new fenugreek genotypes with desired properties should be obtained.

Keywords: Fenugreek, *Trigonella foenum-graecum* L., ancestor plant, multipurpose uses, secondary metabolite

1. Introduction

Fenugreek (*Trigonella foenum-graecum* L.) is commonly grown in many parts of the world for both culinary purposes and health benefits. Fenugreek is rich in minerals, protein, vitamin A and C, and contains several bioactive compounds including proteins, protease inhibitors. Its seeds contain 23–43% protein, up to 58% carbohydrate, nearly 10–13% moisture, 5–6% lipid and less than 1% minerals.

In particular, the plant is rich in soluble fiber, mucilage and galactomannan which decrease the uptake of bile salts and starch absorption [1].

The main secondary metabolites and seed contents of fenugreek were given in **Figure 1** [2–4].

Polyphenol compounds *viz.* rhaponticin and isovitexin were noted as major bioactive compounds in seeds of fenugreek [5]. In addition, fenugreek seed extracts have a number of phenolic constituents similar to beta-D-glucopyranoside, methyl, alpha-d-mannopyranoside, methyl, and diethyl phthalate. Fenugreek also represents a significant source of antioxidants [6].

A wide range of beneficial effects of fenugreek seeds has been reported by a number of researchers. In addition to antidiabetic effects, seeds have significant anti-atherosclerotic [7], anti-inflammatory [8], antinociceptive [9], and antiulcerogenic activities [10] which are essential for cure of diabetes and cancer disease. Antioxidant property helps in anti-aging. The phenolic antioxidants present in the extract of fenugreek show free radical scavenging activity which reduce oxidative stress in the body. This reduced oxidative stress reduces frequency of age-related disorders [11].

It was reported that fenugreek seeds had low amount essential oil and fatty oil [12]. According to the essential oil compounds findings; olfactometry diacetyl, 1-Octen-3-one, sotolone, acetic acid; 3-Isobutyl-2-methoxypyrazine, butanoic acid, isovaleric acid, 3-isopropyl2-methoxypyrazine, caproic acid, eugenol, 3-Amino-4,5-dimethyl-3, linalool, (Z)-1,5-Octadiene-3-one, 4-dihydro-2(5H)-furanone were determined as the main components [13]. It has been noted that sotolone is mostly found in fenugreek (5 s)-enantiomeric form (95%) among these essential oil components.

A study on human sweat was conducted by Meghwal and Goswami [3] and regarding essential oil components; pinene,3-octen-2-one, 2,5-dimethylpyrazine, b-camphor; terpinen-4-ol, 4-isopropylbenzaldehyde were found as the odor in sweat, while neryl acetate and b-caryophylene, 2,5-dimethylpyrazine has been observed to be the main component responsible for the compound contributing to sweat odor.

Many studies have been conducted on the therapeutic applications of various plant species on different diseases such as fungal, viral and bacterial contamination. Therefore, approximately one third of the world's population uses traditional/therapeutic plants and their extracts in their treatments [14]. A drug with both antidiabetic and antioxidant activity is much more beneficial in the treatment of diabetes. In addition, herbal medicines are more preferred due to the undesirable side effects of the existing antidiabetic medicine. As can be seen from the above explanations, fenugreek has the potential to be a versatile herbal medicine. Therefore, further studies are needed to provide detailed information

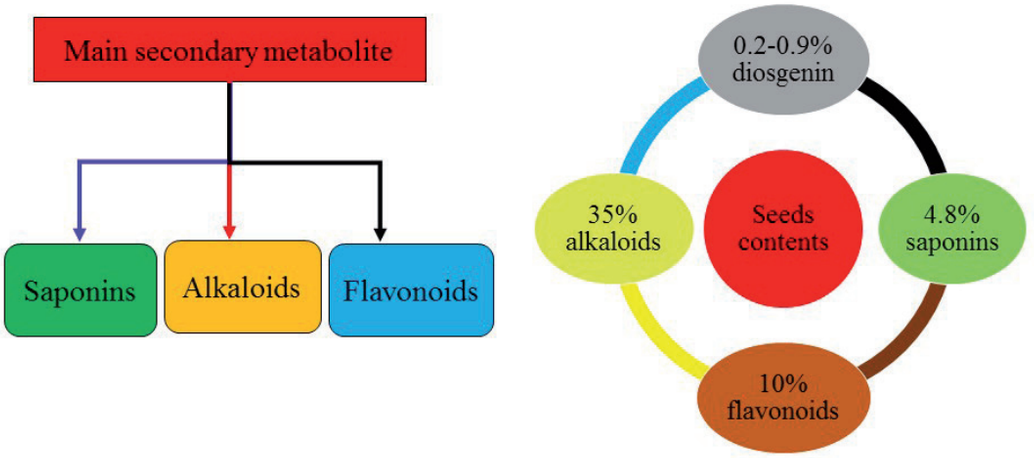

Figure 1.
Main secondary metabolites and seed context of fenugreek.

about the effects of fenugreek. So, in this review, it was aimed to inform about the studies conducted with the effects of fenugreek.

Generally, this study revealed the importance of focusing on the antioxidant, hypoglycemic, hypercholesterolemia, anticancer, antibacterial and antifungal properties, as well as on its medicinal properties, phytochemical and nutrient contents. In case, fenugreek is grown for bioactive secondary metabolites, concentrating on different activities such as polyphenol compounds, anti-inflammatory, antimicrobial properties.

2. Traditional uses of fenugreek

Fenugreek has been used in traditional cure treatments dates back to the 15th century. Different parts of fenugreek such as seeds and leaves were used to treatment of symptoms and ailments. For instance, a paste prepared with ground fenugreek seeds was used to treat eczema, local inflammations of the skin-as locally administered poultice or added to a hot bath [15].

Fenugreek is easily grown all over the world because of its wide adaptation and its usage varies significantly between countries.

Many studies were conducted to determine and confirm the traditional uses of fenugreek as herbal cure using different plant part (seeds and leaves) or pure phytochemicals (saponins, steroids, alkaloids). Fenugreek seeds have been reported to have an aphrodisiac effect in ancient times, but modern vaidyas have used it more for digestive and respiratory problems caused by phlegm and wind. In ancient Egypt, it was recorded that methi (fenugreek) was used to facilitate childbirth and increase milk flow, and modern Egyptian women still use fenugreek to make hilba tea to relieve menstrual cramps and relieve other abdominal pains. The Chinese call it hu lu ba and also use it to treat abdominal pain. While the fresh stems and leaves are mostly used as a winter vegetable, seeds are used as a flavor agent in different foods in India [16].

The seeds are also eaten raw as sprouts and used medicinally. While fenugreek is used in baking bread by Egyptian and Ethiopian, Switzerland uses it to flavor cheese. In the USA, it is mostly used in spice mixes for soups and stews [16]. Fenugreek has been used as a spice in cooking for centuries in European countries and remains a popular ingredient in curry powders, pickles, and spice mixes in India, Pakistan, Bangladesh, and other Asian countries. Fenugreek has been used in folk remedies to treat cellulite, boils and tuberculosis. Fenugreek remained a key ingredient in a 19th century patented drug for dysmenorrheal and post-menopausal symptoms [17].

Fenugreek was also used for ethnoveterinary applications such as the decrease of serum cholesterol in animals [18] and the increase of milk production in animals [19].

In the Ayurvedic and Unani systems of medicine, fenugreek is used to cure epilepsy, paralysis, gout, dropsy, chronic cough and piles. This crop has also known as potential of oleoresin and steroid production for oral contraceptives. In addition, ground seeds use as a control mechanism for the blood sugar and thereby checks the diabetes in human beings [20].

Fenugreek leaves are widely used for treatment of eye diseases in Iran [21] and gynecological disorders [22]. In traditional medicine, it is used to prepare infusions, water and alcohol extracts, tinctures, honeys, tonics with antidepressant and psychotonic properties, and muscle growth supplements. It is also used in the treatment of seborrhea, acne and dermatitis. The plant is widely used in cosmetology [23]. It was reported that fenugreek seeds have been used as an oral insulin substitute to decreasing blood sugar [17].

The aroma and taste of fenugreek has led to its use in imitation maple syrup [24]. Furthermore, fresh and dried leaves are used as vegetables in the diets. It was found that these leaves included calcium; zinc iron, phosphorous, riboflavin, carotene,

thiamine, niacin and vitamin C. The leaves of fenugreek, which are stored in either in refrigeration conditions or dried in oven, are used to prepare in pressure cooker [25].

Aqueous solutions and softened fenugreek oils exert protective effects on mucous membranes in ulcer disease [26] and prevent colon cancer [27]. It is being utilized in the folk medicines for the treatment of cellulitis, tuberculosis and boils [28].

In Turkey, it has been found to be beneficial in healing internal wounds when taken with butter and sugar. It is used in healing hemorrhoids and it can be also used as a supplementary food supplement in the treatment of hyperthyroidism.

3. Nutraceutical properties of fenugreek

Pharmacological activities have been studied by Mehrafarin et al. [29] to explain the medicinal properties of fenugreek and its main metabolites. Many studies were conducted to increase the secondary metabolites of fenugreek by different applications (**Table 1**).

Part of fenugreek	Application	Secondary metabolites	References
Leaves	UV Radiation	Total phenols, Flavonoids, Alkaloids, Tannins, saponins, Anthocyanin content	El-Shora et al. [30]
Hypocotyls of the sprouts for callus initiation	Mannitol and Sodium Chloride	Total phenolics, Total flavonoids, Tannins,	Hussein and Aqlan, [31]
Seedling	Methyl Jasmonate	Diosgenin	Chaudhary et al. [32]
Fenugreek plant	Trichoderma strains	Trigonellin	Hosseini et al. [33]
Seeds and Callus	Cultured on MS medium	Trigonellin, Diosgenin	Altabtabaai et al. [34]
Leaf and stem	Collected from the local market Surat, Gujarat	Phenol content, Flavonoids content,	Varsha and Jain, [35]
Seeds	Collected from 50 regions of Iran	4-hydroxy isoleucine, Trigonellin	Rajabihashjin et al. [36]
Leaf	Water deficit, exogenous ethylene application and root symbioses	Trigonellin	Irankhah et al. [37]
Growth stages (Vegetative, full flowering and well-developed pods)	Rainfeed conditions	Proximate composition, total phenols, tannins, flavonoids and saponins	Abdouli et al. [38]
Fenugreek plants	Mycorrhizal fungal inoculum and exogenous methyl jasmonate; Water deficit	ABA, IAA, trigonelline, diosgenin	Irankhah et al. [39]
Seeds	Charcoal and drought stress	Trigonellin, diosgenin	Bitarafan et al. [40]
Plant tissues	Copper stress	Total phenols, Total flavanoids	Elleuch et al. [41]
Seeds	Gamma irradiation	Trigonelline, nicotinic acid, Diosgenin, Mucilage content	Parchin et al. [42]

Table 1.
Variation of fenugreek secondary metabolites in different cultural applications.

Fenugreek seeds contain the neuroprotective alkaloid trigonelline, which is one among the foremost alkaloids found in fenugreek seeds. Trigonelline consists of a methyl betaine derivative of nicotinic acid, aids in curing diabetes and treatment of neurodegenerative diseases. In addition, alkaloids like trimethylamine, neurin, choline, gentianine, carpine and betain are found in fenugreek. These alkaloids exhibit antibacterial, antiviral and memory improving activities [43].

Fenugreek also represents an important source of diosgenin, a saponin used as a precursor for the synthesis of steroid hormones. Diosgenin is a very valuable phytochemical due to its biological activities and pharmaceutical applications. In fact, this phytochemical has anticancer, anti-aging, cardioprotective and contraceptive properties [44–49] and antiviral, antimicrobial, antifungal and insecticidal activities [50, 51]. Anticancer effect of diosgenin has also been investigated in a number of preclinical studies, including growth inhibition and apoptosis induction in human colon cancer cells [27] and cell cycle in different cancer cell lines [52] has been documented.

So, fenugreek seeds have anti-inflammatory, hypoglycemic effects, anti-diabetes, cardioprotective, anticancer, antimicrobial properties, antipyretic and analgesic properties [53, 54]. Therefore, breeding strategies should be re-validated to increase the amounts of important active substances such as diosgenin and trigonellin in fenugreek seeds. Genetic variation in fenugreek should be introduced and a combination of traditional and molecular approaches should be used. In addition, the advantage of applying mutants to tissue cultures should be used in fenugreek.

3.1 Antioxidant activity of fenugreek

The fenugreek seeds contain polyphenolic compounds, which have been correlated to the beneficial health effects of fenugreek [55]. These polyphenolic compounds are known for several beneficial actions, such as antioxidant effect [56], cancer preventive activity [27], anti-diabetic effects [57] and hypocholesterolemic effect [12, 56].

In earlier studies Bors et al. [58] reported that the scavenging activities of phenolic substances are attributed to the active hydrogen donating ability of hydroxyl substituents. As an overall assessment, the presence of various phytochemicals, particularly naringenin and quercetin, may be responsible for the OH radical scavenging activity. Similarly, trigonellin isolated from ethanol extract of fenugreek seeds has been reported to reduce blood sugar and lipid profile in alloxane-diabetic rabbits [59]. This effect can be partially explained by the antioxidant properties of trigonellin due to its structural similarity to nicotinamide, which has an antioxidant effect [60].

Bukhari et al. [61] reported that fenugreek seed extract with methanol, ethanol, dichloromethane, acetone, hexane and ethyl acetate has a radical scavenging activity. In addition, Bhatia et al. [62] reported protective effect of fenugreek, on lipid peroxidation and on enzymatic antioxidants. Naidu et al. [63] reported that extracts of husk, fenugreek seed, and endosperm exhibited 72%, 64%, and 56% antioxidant activity respectively by free-radical scavenging method. Also, it was indicated that separation of fenugreek seeds into husk and endosperm could have advantage of process viability with respect to prior selective fractionation of bioactive components for their effective isolation.

In a similarly study, it was determined that fenugreek has a high phenolic content. Furthermore, antioxidant property was checked by reducing power, nitro blue tetrazolium (NBT) assay and H_2O_2 scavenging reported to show high superoxide and free radical scavenging [64].

Furthermore, Kaviarasan et al. [65] reported that 2,2′-Azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radicals are more reactive than 1,1-diphenyl-2-picrylhydrazyl (DPPH) radicals and unlike the reactions with DPPH radical which involve H atom transfer, the reactions with ABTS radicals involve electron transfer process. In addition, Shang et al. [66] identified five different flavonoids in fenugreek seeds, namely vitexin, tricin, naringenin, quercetin, tricin-7-O-beta-D-glucopyranoside, and fenugreek seed extract was found to have significant antiradical and antioxidant properties depending on the concentration.

In line with above researchers [65], they reported that an aqueous methanolic extract of fenugreek seeds was investigated for antiradical and antioxidant activity in different model systems, and antiradical activity was associated with the polyphenolic contained in the extract. As a result, it was determined that fenugreek seeds provide some important factors responsible for the antioxidant potential and provide evidence for numerous in vivo beneficial effects of seeds reported in the literature.

Similarly, Belguith-Hadriche et al. [67] investigated the hypocholesterolemic and antioxidant activities of various extracts of fenugreek seeds (water, methanol, ethyl acetate, hexane, dichloromethane) in rats fed cholesterol, and ethyl acetate only for rats fed a cholesterol-rich diet (HCD). It has been found that fenugreek extracts reduce triglycerides and low density lipoprotein cholesterol (LDL-C) and increase high density lipoprotein cholesterol (HDL-C). Based on these results, it was reported that ethyl acetate extract of fenugreek seeds had a significant hypocholesterolemic effect and antioxidant activity in cholesterol fed rats.

Furthermore, Liu et al. [68] determined the lipid peroxidation (LPO) and cyclooxygenase enzyme (COX) inhibitory activities of hexane, ethyl acetate, methanolic and water extracts to investigate the functional food use quality of fenugreek. They found that the extracts inhibited LPO by 55–95%, COX-1 by 6–87% and COX-2 by 36–70% at 250 lg/ml, respectively. Also, the isolates, excluding the saccharides, inhibited LPO and COX-1 and COX-2 enzymes between the ranges of 8–89%, 4–51% and 15–70%, respectively, at 25 lg/ml. The fenugreek seeds that were studied afforded 3.9 g of triglycerides and fatty acids, 6 g of polysaccharides and 233 mg of flavone C-glycosides per 100 g of seeds. The strong antioxidant activity in the LPO assays of the aqueous extract of fenugreek seed might be attributed to the flavones C-glycosides [69].

Likewise, the different solvent extracts of fenugreek seeds were used to examine the effects of extraction solvent on total phenolic content (TPC), DPPH and iron reducing antioxidant power (FRAP). It was observed that the extracts obtained using higher polar solvents were more effective than less ones, and the addition of 50% water to methanol, acetone or ethanol can enhance the extracting power and antioxidant activity estimation especially acetone and methanol. As a result, it was determined that the total phenolic content showed a good correlation with antioxidant activity FRAP and DPPH [70].

In similarly, Deshmukh et al. [71] reported that silver and iron oxide nanoparticles were successfully synthesized in a simple way at room temperature using an aqueous extract of fenugreek seeds. Then, all nanoparticles were characterized by various techniques to elucidate the stability and functionality of the nanoparticle. It has been determined that the nanoparticles synthesized with the assistance of ultrasound show higher stability and antibacterial and antioxidant activity due to the combined effect of ultrasound and biomolecules adhering to the surface of the nanoparticles.

Naidu et al. [6] also observed that the husk of fenugreek seeds contained higher total polyphenols (103.8 mg gallic acid equivalent/g and the total dietary fiber

(77.1 g/100 g), insoluble dietary fibers (31.9 g/100 g) and soluble dietary fibers (45.2 g/100 g). The bark, fenugreek seeds and endosperm extracts were reported to exhibit 72%, 64%, and 56% antioxidant activity, respectively, by the free radical scavenging method. As a result, separation of fenugreek seeds into husk and endosperms showed that the process viability advantage.

The antioxidant properties of germinated fenugreek seeds were examined in a study conducted by Dixit et al. [72]. Different fractions of germinated seeds were used at different levels to determine their antioxidant potential. Tests used are ferric reducing antioxidant power, DPPH, feriylmyoglobin / 2,2-azobis-3-ethylbenzthiazoline-6-sulfonic acid, pulse radiolysis, oxygen radical absorbance capacity and lipid peroxidation in rat liver mitochondrial preparations. An aqueous fenugreek fraction showed the highest antioxidant activity. Since the amount of phenolic and flavonoid compounds can be correlated with antioxidant activity, the contents of these extracts were measured and their polyphenols, flavonoids and other components were determined by HPLC analysis. This study reveals significant antioxidant activity in germinated fenugreek seeds, which may be due in part to the presence of flavonoids and polyphenols.

As seen from previous studies, the obtained different results may be attributed to different extraction methods and solvents used, different cultivars, growing conditions, maturity stage at harvest, or the storage conditions and time elapsed before the seeds were analyzed. Synthetic drugs used for the treatment of the diseases like cancer, diabetic and the antioxidants used for some treatment have side effects such as mutagenic and carcinogenic effects [73]. Some patients also have resistance to the synthetic drugs. To overcome this problem there is need to find effective natural drugs from traditional medicine. Therefore, fenugreek, which possesses phenolic compounds and antioxidant activity should have the ability to counteract these situations and might be a good candidate for a herbal drug.

3.2 Antibacterial and antifungal effect of fenugreek

The antibacterial activity of the plant extraction has been extensively investigated in many studies. Microbiological analyses revealed that fenugreek extracts exhibit antimicrobial activity against numerous bacteria [74]. Haouala et al. [75] determined the aqueous extracts obtained from various plant parts of fenugreek, different solvents such as methanol, petroleum ether and ethyl acetate fractions and their effects against fungal strains such as *Fusarium graminearum*, *Botrytis cinerea*, *Alternaria sp*., *Rhizoctonia solani* and *Pythium aphanidermatum*. It was found that all parts of the fenugreek exhibited antifungal potential and the magnitude of the effect varied according to plant parts and fungal species. So, they suggested that fenugreek is an important source of biologically active compounds that are useful for developing better and new antifungal drugs.

Many studies have indicated the effectiveness of fenugreek extracts against *Helicobacter pylori* [76–80]. In a study conducted with honey produced with different plant pollens, the highest antibacterial activity against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli* was found in honey produced with fenugreek pollens [79].

Since cysteine-rich peptides, defensins have strong antifungal activity, the methanol-soluble fraction of fenugreek extract has been studied against nematodes and has been found to show nematicidal activity. It has also been reported to significantly cause the death of *Meloidogyne javanica* larvae [80]. Laroubi et al. [81] studied the prophylaxis effect of fenugreek seeds on renal stone formation in rats. They reported that, the fenugreek can be used in the treatment of patients with calcic urolithiasis.

In addition, Shaheed et al. [82] recorded that the inhibition results for each *Proteus mirabilis* and *E. coli* reached 10.5 and 10.0 mm, 9.0 and 9.5 mm, respectively at 50 mg/ml, and 13.0 and 11.5 mm, 10.5 and 7.5 mm, respectively at 100 mg/ml. Similarly, Hamadii [83] showed the highest percentage of inhibition against *Proteus mirabilis* and *E. coli* at 50 mg/ml from alcoholic fenugreek seed extract.

In another study, the antibacterial effects of fenugreek oil against *Escherichia coli, Samonella, typhimurium, Taphylococcus aureu, Aspergillus niger* microorganisms were investigated. These microorganisms have been chosen as common causes of some human and animal diseases and are contaminants that damage certain foods and are resistant to antibiotics. These results showed that fenugreek oil was stated to be suitable for human consumption and eating [84].

Similarly, it was determined that fenugreek essential oil showed the highest activity against *E. coli*, the inhibition zone reached 21 mm at 100% concentration, and against *Staphylococcus aureus*, it was found to reach 17 mm at 80% concentration [85]. Also, Sulieman et al. [86] found that the inhibition results for *Salmonella* reached 16 mm at 100% concentration. Thereby, these results are promising and may contribute to the future development of natural bio pesticides for the control of fenugreek for the microorganisms. Likewise, antibacterial effect was determined against *Escherichia coli* with an inhibition value of 20 mm at 100% concentration of fenugreek seed oil, while the antimicrobial activity was not detected at 50% and 90% concentrations [86]. As a result, fenugreek extracts show antibacterial activity against many gram positive and gram negative bacterial isolates. In addition, fenugreek seeds are potential sources of new antibacterial compounds as emphasized by the antibacterial activity of their different extracts. So, identification of different effective bacteria from crude plant extracts will assist in the development of drugs against pathogenic microorganism.

3.3 Anticancer effect of fenugreek

Cancer remains one of the leading causes of death worldwide. Flavonoids could also significantly contribute to fenugreek's anticarcinogenic properties. Fenugreek constitutes valuable raw material for the pharmaceutical industry that has long searched for effective cures for cancer.

Previous studies reported that fenugreek seeds have a preventive effect on cancer as in experimental models of cancer using cell lines or experimental animals.

Earlier studies revealed that seed extract of fenugreek importantly inhibits 7,12-dimethyl benz(a)anthracene-induced mammary hyperplasia and decreases its ratio in rats. It was also advised that anti-breast cancer preventive effect of fenugreek could be depending on the increasing apoptosis [87]. Furthermore, alcoholic whole plant extracts of fenugreek effected in vitro cytotoxicity against different human cancer cell lines such as IMR-32, a neuroblastoma cell line, and HT29, a cancer cell line [88].

A selective cytotoxic effect of fenugreek extract in vitro to a panel of cancer cell lines has been observed, including T-cell lymphoma by Alsemari et al. [89]. In addition, Sebastian and Thampan [90] and Prabhu and Krishnamoorthy [91] examined the growth of MCF-7 cells, which is an estrogen receptor positive breast cancer cell line, with ethanol extracts of fenugreek, and reported that the ethanol extract of fenugreek decreased cell viability and induced early apoptotic changes such as inversion of phosphatidyl serine and decreased mitochondrial membrane potential.

In a study conducted by Shabbeer et al. [92] treatment with fenugreek extract showed growth inhibitory effects on breast, pancreatic and prostate cancer cell lines but primary prostate or immortalized prostate cells remained unaffected.

In addition, in a dietary study involving fenugreek seed powder, it reduced colon tumor incidence and hepatic lipid peroxidation in rats treated with 1,2-dimethylhydrazine and also increased catalase, superoxide dismutase, glutathione S-transferase and glutathione peroxidase activities in the liver [93].

Li et al. [94] recorded that diosgenin modulates the STAT3 signaling pathway in hepatocellular carcinoma by suppressing the activation of c-Src, JAK1 and JAK2. They also noted that diosgenin reduced the expression of various STAT3-regulated genes, inhibited proliferation, and potentiated the apoptotic effects of paclitaxel and doxorubicin, which could be a new and potential treatment option for hepatocellular carcinoma and other cancers. Also many researchers reported that diosgenin exhibited anticancer and antiaging activities, as well as cardioprotective and contraceptive properties [44–49].

In addition, in different studies with diosgenin, it has antiproliferative activity such as prostate cancer (PC-3 and DU-145 cells) [95], colon cancer (HCT-116 and HT-29 cells) [96], erythroleukemia (HEL cells) [97], carcinoma (A431, Hep2 and RPMI 2650 cells) [98], stomach cancer (BGC-823 cells) [99], lung cancer (A549 [100], breast cancer (MCF-7) [101], hepatocellulacarcinoma (HepG2 and HCC cells) [102] and human chronic myeloid leukemia (CML) (K562 cells) [103].

As a result of the studies mentioned above, the role of fenugreek seeds and its main active ingredients as new supplements in diet-based preventive / therapeutic strategies to potentially alleviate human diseases remains an important area of study for future research [104].

3.4 Hypoglycemic effect, anti-inflammatory and immunological activity of fenugreek

Immunological changes include altered levels of cytokines and chemokines, changes in the numbers and activation states of various leukocyte populations, apoptosis, and fibrosis during diabetes. Therefore, treatment of diabetes and its complications may include pharmacological strategies to reduce inflammation [105]. Laroubi et al. [81] studied the prophylaxis effect of fenugreek seeds on renal stone formation in rats. And they said that the fenugreek can be used in the treatment of patients with calcic urolithiasis. Chauhan et al. [106] reported an antiinflammatory potential of fenugreek. Jung et al. [107] observed a reduction in the production of several inflammatory mediators, including NO and interleukins 1 and 6, in murine macrophages which had been pretreated with diosgenin and stimulated with lipopolysaccharide/interferon-γ.

In addition, Roberts [108] said that the gum, composed of galactose and mannose, is associated with reduced glycemic effect. Also, the hypoglycemic effect of fenugreek has been especially documented in humans and animals with type 1 and type 2 diabetes mellitus.

Xue et al. [109] reported that the fenugreek extract can lower kidney/body weight ratio and blood glucose and also improves hemorheological properties in experimental diabetic rats following repeated treatment for 6 weeks. A study on animals evaluated the hypoglycemic effects of the fenugreek seeds on dogs. The seeds lowered blood glucose levels, plasma glucagons and somatostatin levels; carbohydrate-induced hyperglycemia also was found to be reduced [110]. Most of the studies with polar fractions of fenugreek seeds point toward a strong anti-inflammatory and anti-arthritic activities mediated through anti-oxidant mechanisms [68, 111, 112].

In addition, Sharma et al. [113] recorded that guar gum of fenugreek prevents the rapid uptake of glucose in the small intestine, aids in blood sugar retention in diabetic patients and may also be effective in the treatment of hypercholesterolemia.

4. Conclusions

Especially recently, many of the beneficial properties of fenugreek have been experimentally proven and the potential of fenugreek's therapeutic applications has been demonstrated. It has high economic values because of including a lot of bioactive compounds. The important compounds can be listed steroidal sapogenins such as diosgenin, alkaloids as trigonelline, flavonoids, tannins, amino acids, steroidal glycosides, protein and others.

As can be seen from this review, the phenolic acids, dietary fiber, saponins and proteins contained in fenugreek are valuable additives to improve human nutrition. Additionally, in neurological studies conducted with fenugreek, the antidiabetic, antifertility, anticancer, antimicrobial, antiparasitic, lactation stimulating and hypocholesterolemic effects of fenugreek have been proven by many researchers. So, it has been also universally used as a spice in a conventional food or it has been interfered to prepare for some functional foods.

In the future, studies on fenugreek are needed some important applications to increasing the popularity of fenugreek. In this context, researchers should be focused quality criteria as primer or secondary metabolite, different cultural and molecular application, different techniques from sown to harvest times of fenugreek. Further research will be required to determine to know the molecules responsible the antioxidant properties in these extracts. Also, fenugreek germplasm can be collected and subjected to intensive selection via modern breeding programs. In addition to these, by selecting genotypes with superior characteristics, gene transfer can be made by determining suitable genes among these genotypes and new fenugreek genotypes with desired properties can be obtained. In addition, studies on fenugreek leaves are limited and generally focused on fenugreek seeds. In this context, researchers should be focused the quality criteria as primer or secondary metabolite in fenugreek leaves.

This study will help the researchers to obtained optimal fenugreek production, optimum biochemical components and adapt to difference environmental, other and specific farming conditions. In the future, when fenugreek is evaluated with all these aspects, its economic, industrial and medicinal value may increase and add value to the relevant sector.

Conflict of interest

The authors declare no conflict of interest.

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