Review Article

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Trigonella foenum-graecum: A review on its traditional uses, phytochemistry and pharmacology

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Abstract

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

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

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1. Introduction

Plant *Trigonella foenum-graecum* belongs to the family **Fabacea** and it is popularly known as Fenugreek [1]. It has been in use as a food and flavouring since time immemorial. It is native to the area from the Eastern Mediterranean to Central Asia and Ethiopia, and much cultivated in India and China [2]. Plant seeds and leaves are used not only as food but also as an ingredient in traditional medicines [3]. It has been mentioned in Ayurveda and Siddha that these plants are used to treat fever, dysentery and heart diseases, while in Unani system, this plant is used as an aphrodisiac, diuretic, emmenagogue and tonic [4].

Due to its strong flavor and aroma fenugreek in one of such plants whose leaves and seed are widely

consumed in Indo-Pak subcontinent as well as in other oriental countries as a spice in food preparations, and as an ingredient in traditional medicine.[5]

A robust, erect, aromatic annual herb reaching up to 60 cm in height. The leaves are compound, up to 5 cm in length, with long pedicel. Leaflets are lanceolate or obovate, about 2.5 cm long, with slight toothed margins. The flowers are axillary, occurring singly or in pairs, sessile, yellow in colour. The fruits are typically leguminous pods 5-8 cm long, narrow and with a persistent 'bark', enclosing 10-20 golden yellow seeds, which possess a characteristic savoury aroma.[6]

1.1 Use in traditional medicine

Fenugreek (*Trigonella foenum-graecum* L. *Leguminosae*) is one of the oldest medicinal plants, originating in India and Northern Africa. More recent ethno pharmacological studies show and aromatic leaves are often eaten as a vegetable and the seeds are widely used as condiment in curries. A poultice made of the herb can be applied locally to relieve swelling and the leaves are also made into paste and applied over burns or to the scalp to prevent premature graying of the hair. [6]

Applications of fenugreek were documented in ancient Egypt, where it was used in incense and to embalm mummies. In modern Egypt, fenugreek is still used as a supplement in wheat and maize flour for bread-making [7]. 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].

Trigonella foenum-graecum is used in many parts of the world for the treatment of a number of diseases, e.g. urotoxicity, immunomodulatory, antiradical and antioxidant, chemopreventive, anticancer, antidiabetic, gastro protective, anti-inflammatory and antipyretic, regulation of hyperthyroidism, anthelmintic, antigenotoxic, anti-plasmodial, hepatotoxicity and nephrotoxicity, wound healing, hypocholesterolemic, nutritive, anti-plasmodial, allergenicity and antigenicity, antiseptic, aphrodisiac, astringent, bitter, demulcent, emollient, expectorant.

Place, country	Part (s) used	Ethno medical uses	Preparation(s)	Reference(s)
Pakistan	Seeds	Antioxidant	Methanol, ethanol, dichloromethane, acetone, hexane and ethyl acetate extra	Syeda Birjees Bukhari et al. [10]
China	Seeds	Blood glucose, blood lipid, hemorheology	Decoction or thick paste	Xue <i>et al</i> [11]
Iran	Leaves	Anti-inflammatory, and antipyretic		Ahmadian <i>et al</i> [12]
India	Seeds	Antidiabetic	Ethanolic extract	Renuka C. <i>et al.</i> [13]
India	Seeds	Anthelmintic	Alcoholic extract	Khadse et al[14]
India	Seeds	Antifertility	Chloroform extract	Sharma et al. [15]
Spain	Seeds	Antigenotoxic	Infusion	Mezzoug et al. [16]
India	Leaves	Anti-plasmodial	Ethanol extract	Palaniswamy, M et al[17]
India	Seeds	Antioxident	Methanol extract	Kaviarasan et al. [18]
India	Seeds	Anticancer	Methanol extract	Verma <i>et al.</i> [19]
India	Leaves	Urotoxicity	Aqueous extract	Bhatia, K. <i>et al.</i> [20]
India	Leaves	Immunomodulater	Chloroform extract	Bin-Hafeez B et al [21]
India	Seeds	Analgesic and anti-inflammatory	Extract	Vyas Savita et al[22]
India	Seeds	Anti-inflammatory	Aqueous extract	Malviya et al [23]
India	Seeds	Antimicrobial activity	Ethanolic extract	Khanra. R <i>et al</i> [24]
India	Seeds	Antifungal and antibacterial	Oil	Wagh <i>et al</i> [25]
India	Seeds	Diuretic	Various extract	Rohini et al. [26]
India	Seeds	Antidiabetic	Methanol extract	Abou El-Soud <i>et al.</i> [27]
India	Seeds	Anti-inflammatory	Alcoholic extract	Datta Debranjan et al [28]
India	Seeds	Antiradical and antioxidant activities	Methanol extract	Kaviarasan <i>et al</i> [29]
India	Seeds	Estrogenic	Chloroform extract	Sreeja et al. [30]
India	Seeds	Gastric ulcer	Chloroform extract	Pandian <i>et al</i> [31]
India	Seeds	Anti-hyperglycemic	Aqueous extract	Moodrthy et al. [32]
India	Seeds	Antifertility	Ethanol : water (70:30) extract	Aaswer et al [33]
China	Seeds	Hypoglycaemic and hypercolesterolamic effect	Extract	Xue et al. [34]
Iran	Leaves	Anti-inflammatory and antipyretic	Extract	Ahmadiani et al. [35]
Arab	Seeds	Chemopreventiv activity against breast cancer	Extract	Amin <i>et al.</i> [36]

Table 1: Ethnomedical uses of Trigonella foenum-graecum

2. Phytochemistry

2.1. Seeds:

The endosperm of the seed is rich in galactomannan, young seeds mainly contain carbohydrates and sugar. Mature seeds content amino acid, fatty acid, vitamins, and saponins. The seeds of fenugreek contain a large quantity of folic acid (84mg/100g). It also contents disogenin, gitogenin, neogitogenin, homorientin saponaretin, neogigogenin, and trigogenin. The main chemical constituents of *T.foenum-graecum* are fibers, flavonoids, polysaccharides, saponins, flavonoids and polysaccharides fixed oils and some identified alkaloids viz., trigonelline and choline. (The Wealth of India &Compendium of Indian Medicinal Plants)

Neutral and polar lipids of fenugreek were investigated. Triacylglycerol and phosphatidylethanolamine were the major molecular species identified in the neutral and polar lipid fractions, respectively. The seeds raised from treated plants showed increased level of kaempferol, luteolin, quercetin, and vitexin.

2.2. Leaves:

Young fenugreek leaves yield: total lipids (dry wt), 1.50%; neutral lipids, 0.98; glycolipids, 0.38; and phospholipids, 0.14%. The leaf lipid is a rich source of essential fatty acids, viz. linolenic and linolenic acid. The leaves also contain: α -tocopherol, 0.87; and β -tocopherol, 0.37 mg/g (dry weight)

3. Biological activity

3.1 Medicinal and Pharmacological activities 3.1.1 Antidiabetic activity:

The aqueous and alcoholic extracts of *Trigonella foenum-graecum* leaf were tested for hypoglycaemic activity in normal and alloxan-diabetic rats. The results suggest that the aqueous extract of *Trigonella foenum-graecum* leaves given both orally and intraperitoneally possesses a hypoglycaemic effect in normoglycaemic and alloxan induced hyperglycaemic rats [37].

The hyperglycemic activity of the seeds and various extracts was studied in experimental rabbits and the glucose tolerance test showed a significant hypoglycemic activity in the alkaloid-rich fraction [38]. *Trigonella foenum-graecum* (fenugreek) seeds have previously been shown to have hypoglycemic and hypocholesterolemic effects on type 1 and type 2 diabetes mellitus patients and experimental diabetic animals [39]. In a controlled clinical trial, the effect of three preparations of the seeds (raw, boiled and germinated) was seen in six healty and six diabetic patients taking raw and germinated seeds. Raw and germinated seeds significantly reduced postprandial glucose levels in all subjects; however, boiled seeds did not produce any such effects [40]. Administrations of the ethanolic

extract of *Trigonella foenum-graecum* seed powder decreased blood glucose, serum cholesterol, serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) levels [41]. The aqueous extract of *Trigonella foenum- graecum* leaves given both orally and intraperitoneally possesses a hypoglycaemic effect in normoglycaemic and alloxan induced hyperglycaemic rats [42]

3.1. Immunomodulatory effect:

Trigonella foenum graecum L.showed a stimulatory effect on immune functions in mice. Immunomodulatory activity of aqueous extract of *Trigonella foenum graecum* L. was evaluated in male mice [43].

3.1.3 Antioxidant

A freeze- dried extract of fenugreek was reported to be antioxidant in a carotene and linoleic acid emulsion, with an activity comparable to standard commercial antioxidents. The fenugreek extracts (methanol, ethanol, dichloromethane, acetone, hexane and ethyl acetate) act as potent source of antioxidants [44]. Flavonoids of fenugreek extract have been observed to possess anti-oxidant activity [45]. Fenugreek seeds have been reported to raise the antioxidant levels and lower the lipid peroxidation in liver of ethanol intoxicated and diabetic rats [46]. The free radical scavenging potential of the seeds of (*Trigonella foenumgraecum*) ethanolic extract at 500μ g/ml showed maximum scavenging of the radical cation. An aqueous methanolic extract of fenugreek seeds having antiradical and *in vitro* antioxidant activity [47].

3.1.4 Chemopreventive activity

Trigonella foenum-graecum (Fenugreek) seeds showed potential protective effect against 7, 12dimethylbenz (a) anthracene (DMBA)-induced breast cancer in rats at 200 mg/kg body wt [36]. The methanolic extract of *Trigonella foenum graecum* L was proved to have maximum growth inhibition against 502713 and HT-29 human cancer cell lines [48].

3.1.5 Antimicrobial activity:

The fatty oil and unsaponifiable matter of fenugreek seeds were evaluated against six bacterial and six fungal strains and the study concluded that the unsaponifiable matter was more active than the oil. Trigonella foenum-graecum was screened against 26 common pathogens and demonstrated a broad-spectrum antibacterial activity. The ethanolic extract of seeds of Trigonella foenum-graecum was evaluated for antimicrobial activity against eight bacterial stains the result revealed that the ethanolic extract is potent in inhibiting bacteria growth of both gram-negative and gram-positive bacteria [24].

3.1.6 Anticancer activity:

Apoptosis is a type of cell death, and agents with the ability to induce apoptosis in tumors have the potential to be used for antitumor therapy. Flavonoids produce several biological effects, and the apoptosis inducing activities of flavonoids have been identified in several previous studies [49]. Flavonoids and catechins were first shown to be apoptotic in human carcinoma cells [50]. Similar observation has since been extended to lung tumor cell lines [51], *Trigonella foenum graecum* has also been shown to have stimulatory effects on macrophages. Phagocytosis and killing of invading microorganisms by macrophages constitute body's primary line of defense against infections [52]. On the bases of published studies, flavonoids seem to be most likely candidates eliciting antitumorigenic effect.

3.1.7 Gastroprotective effect

The aqueous extract and a gel fraction isolated from the seeds showed significant ulcer protective effects [31].

3.1.8 Anti-inflammatory

The anti-inflammatory activity was exhibited by all three (ether, alcohol and aqueous) extracts but the ether extract was the most potent and comparable to sodium salicylate. The methanolic extract obtained from *Trigonella foenum-graecum* seeds produced marked acute antiinflammatory activity in rats [22]. Anti– inflammatory effects of the *Trigonella foenum-graecum* leaves significantly reduced formalin-induced edema in single dose [23]. The alcoholic extract of *Trigonella-foneumgraecum* exhibited anti-inflammatory effect on carrageenan induced paw oedema in rats at dosage of both at 100mg & 200mg/kg b. wt. This low dose of fenugreek was more significant than Indomethacin. The alcoholic and petroleum ether extracts of fenugreek seeds can be used safely as anti inflammatory agent [28].

3.1.9 Antipyretic activity

The *Trigonella foenum-graecum* leaves extract (1000 mg/kg) significantly reduced hyperthermia induced by brewer's yeast in 1 and 2 hours after administration. The antipyretic effects in this extract suggest a NSAID-like mechanism [35].

3.1.10 Analgesic activity:

The aqueous and ethanol extracts of *Trigonella* foenum – graecum (TFG) seeds having analgesic potential in rats [23]. The methanolic extract obtained from *Trigonella foenum-graecum* seeds was found to be a potent analgesic activity [22].

3.1.11 Neuropharmacological Activity

The *Trigonella foenum-graecum* seeds of total alcoholic extract, total aqueous extract, total alkaloidal extract, petroleum ether extract, total glycosidal extract,

fenugreek oil, diosgenin and trigonelline were assessed for their neuropharmacological activity. All the extracts and active principles except total aqueous extract showed significant central nervous system (CNS) stimulant activity, while total aqueous extract alone showed significant CNS depressant activity [53]

3.1.12 Anthelmintic activity:

The alcoholic extracts of seeds of *Trigonella Foenum-graecum* has shown a potent anthelmintic activity, which was compared with albendazole as reference drug [54].

3.1.13 Anti-plasmodial activity:

The *Trigonella foenum-graecum* leaves extracts (ethanol, butanol, chloroform, ethyl acetate, chloroform and ethyl acetate and water extract) are shown the most interesting anti-plasmodial activity. The ethanol and butanol extracts having significant anti-plasmodial activity, chloroform and ethyl acetate shows moderate activity, and the other two extracts, hexane and water appeared to be inactive against *Plasmodium falciparum* [55].

3.1.14 Hepatoprotective and nephroprotective activity:

The protective effect of aqueous extract of germinated fenugreek seeds against Cypermethrin induced hepatic and renal toxicity [56].

3.1.15 Wound healing activity:

The aqueous suspension and extract of the seed of *Trigonella foenum graecum* was investigated for wound healing properties in excision, incision and dead space wound models in rats. Results indicated that the suspension and extract promoted significant wound Healing activity [57]. Traditionally the crushed seeds are in use for application on the wound [58].

3.1.16 Hypocholesterolemic activity:

Fenugreek seeds have been shown to prevent the elevation of cholesterol in rat when given with a hypocholesterolemic diet. Steroidal saponins isolated from fenugreek seeds administered to rats with food significantly reduced plasma cholesterol in both normal and diabetic rats⁻ Fenugreek seeds showed some hypocholesterolemic activity. Fenugreek seeds contain both the galactomannans and the saponins. Galactomannans decrease the uptake of bile acids, lower blood and liver concentration of cholesterol and decrease hepatic cholesterol synthesis; Saponins were also shown to interact with bile salts in the GIT [59].

3.1.17 Nutritive activity

In one presently preferred embodiment of the present invention, the bio-active compounds are extracted from fenugreek seeds. A method for extracting a composition of bio-active compounds from fenugreek seeds is also disclosed, wherein the method comprises the steps of: (1) providing a plurality of fenugreek seeds; (2) preparing the fenugreek seeds; and (3) extracting a composition of bio-active compounds from the fenugreek seeds, wherein the bio-active compounds comprise 4-hydroxyisoleucine and one or more amino acids selected from the group consisting of arginine, aspartate, threonine, serine, glutamate, proline, glycine, alanine, cysteine, valine, methionine, isoleucine, leucine, tryptophan, phenylalanine, ornithine, lysine, histidine and gamma-amino butyrate. The composition of bio-active compounds and methods for extraction of same preferably include between about 10% and 70% of 4-hydroxyisoleucine and between about 20% and 40% of the amino acids.

3.1.18 Antifertility Activity:

The *Trigonella foenum graecum* seeds extract exerts antiestrogenic and antifertility activity in female rats [15].

3.1.19 Urotoxicity activity:

Cyclophosphamide is a commonly used anticancer drug which causes toxicity. Pre-treatment of *Trigonella foenum-graecum* L. extract restored activities of all the enzymes and thus showed an overall protective effect in urinary bladder [22].

3.1.20 Diuretic activity:

The *Trigonella foenum-graecum* Linn. (fenugreek) seeds extract at 150 and 350 mg/kg body weight showed a dose dependent increase in volume of urine [26].

3.1.21 Effect on enzyme activity:

Fenugreek seeds powder reduces the activities of glucose-6-phosphatase and fructose-1, 6-biphosphatase in liver and kidneys of diabetic rats [50].

3.1.22 Effect on ovaries and liver tissues:

Fenugreek oil has stimulating effect on the ovarian activity of mice. Administration of fenugreek oil showed that the total number and quality of cumulus-oocyte complexes increased and the oil stimulated the oocytes to progress in meiosis, but the levels of nucleic acid contents were unaffected [60].

3.1.23 Nematicidal activity:

The aqueous, methanol and chloroform extract of fenugreek seeds cause significant mortality of *Melodogyne javanica* larvae [61]. Aqueous leaf extract of fenugreek leaves shows nematicidal activity against J2 of *M. incognita.*

3.2 Miscellaneous effects

3.2.1 Regulation of Hyperthyroidism:

The combined effects of *T. foenum graecum* and *Allium sativum* extracts were evaluated for their ameliorative potential in the L-thyroxine-induced hyperthyroidic rat model to contribute to an understanding of interaction between the two extracts. The investigation was carried out using two different doses. A comparison was made with the response of individual plant extracts at

the previously studied effective dose in adult Wistar rats rendered hyperthyroidic by daily injections of L-thyroxine (300 µg/kg body wt., s.c.). Propylthiouracil, an antithyroid drug, was used as a reference compound. Alterations in serum triiodothyronine, thyroxine, glucose, hepatic glucose-6-phosphatase and oxygen consumption were studied as end parameters. Superoxide dismutase, catalase activities, lipid peroxidation and reduced glutathione were examined to reveal any toxic effects of the drugs. The combined effects of Trigonella and Allium at 200 and 500 mg/kg body wt. respectively, were equipotent as compared to the individual extracts in lowering the serum concentrations of triiodothyronine and thyroxine hyperthyroidic rats. Our findings reveal that some plant extracts in combination may not always prove to be synergistic. It is therefore suggested that T. foenum-graecum and Allium sativum extracts may be used individually and not together in the regulation of hyperthyroidism.

3.2.2 Larvicidal effect:

The combined effects of extracts of *Trigonella* foenum and Nerium oleander against mosquito were evaluated for their larvicidal potential and to test their activity in combination with each other. Mosquito, the primary vector for malaria, dengue and other severe infectious diseases are the major problem in Vellore city. The larvicidal activity of *Trigonella foenum* and *Nerium oleander* leaf extracts on the different mosquito larvae were studied. The results showed that, there are four genera of mosquitoes present in Vellore city and the leaf extract of both the above plants contains larvicidal activity, and the combination of the extracts, increased the activity considerably to a high percent. From the obtained data the *Nerium oleander* has a less larvicidal activity than the nutritional plant, fenugreek. **[62]**

3.2.3 Toxicology:

This toxicologic study was conducted using dry leaves and seeds of Trigonella foenum-graecum L. An acute intraperitoneal and oral toxicity study of the glycosidic extract of fenugreek leaves concluded that the extract was considered to be safe and have a minimal adverse effect. The interperitoneal study was aimed at four target organ, e.g. liver, kidney, stomach, small and large intestine, and found that the liver was the only organs affected, where early degenration with infiltration of mononuclear and mild hepatitis was found in some animals treated with toxic doses of the glycosidic extract administrated twice a week for 4 weeks, at dosages of 1.0, 1.5 and 2.0g/kg of body weight, exhibited a necrotic effect on liver and kidney tissues of male albino wister rats. Spermatogenesis was observed in the testes at dosage levels of 1.5g/kg and 2.0g/kg of extract. Fenugreek powder does not produce any significant acute and cumulative toxicity in

mice and rats up to 10% level [53]. Fenugreek seeds are used to treat dysentery, diarrhea, dyspepsia, cough, enlargement of liver and spleen, rickets and gout. No renal or hepatic toxicity was observed in patients ingesting an experimental diet containing fenugreek seeds powder (25g/day), even after 24 weeks [15].

4. Clinical trials:

4.1 Hypoglycaemic activity:

A study on cyclists showed that a fenugreek extracts increases insulin concentration and glycogen resynthesis after exercise. Various clinical trials of fenugreek showed improvement in glucose tolerance in healthy volunteers as well as in type 2 and type 1 diabetic patient [26]. However, all these studies were considered as methodologically weak and classified as preliminary. 4.2 Hypocholesterolemic activity:

A clinical trial on hyperlipidemic non-diabetic patients whom diet was supplemented in defatted fenugreek showed significant reduction of serum total cholesterol, LDL and VLDL cholesterol and triglyceride levels, while HDL cholesterol levels were unchanged. In another trial, fenugreek seed powder did not affect the blood profile in healthy subjects, but significantly reduced the total cholesterol and triglyceride without affecting the HDLcholesterol in patients with coronary artery disease [63]. Similar results were obtained with germinated seeds, which are less bitter. Long lasting hypo-cholesterolemic activity was also demonstrated in diabetic subjects. Altogether, the methodology of these studies was considered as poor [64]. 4.3 Galactogogue activity:

One study involving ten women indicated that fenugreek seeds would increase milk production. However a stronger methodology would be required before this claim could be endorsed.

5. Interactions

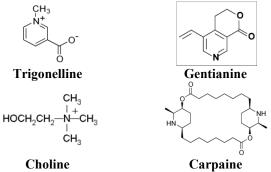
5.1 Interaction with drugs

- Potential interaction with antiplatelet/anticoagulant drugs (incl. NSAIDs): the presence of coumarin in fenugreek may theoretically increase the risk of haemorrhage (speculative) (65, 66)
- Potential interaction with exogenous insulin in diabetic patients who do not adjust insulin dosage: could lead to hypoglycaemia (speculative).
- Potential interaction with oral hypoglycaemic drugs sulfonylurea, biguanides, or both: could lead to hypoglycaemia (speculative).
- Potential enhancement of the activity of cholesterollowering agents due to additive effects (speculative).

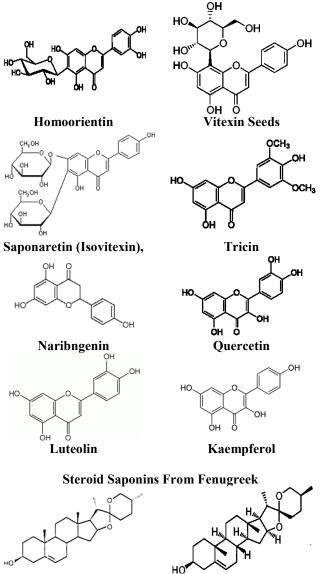
5.2 Interactions with Other Herbs / Herbal Constituents

Fenugreek seeds extract and garlic extract are less effective in the regulation of hyperthyroidism in rats than administrated independently.

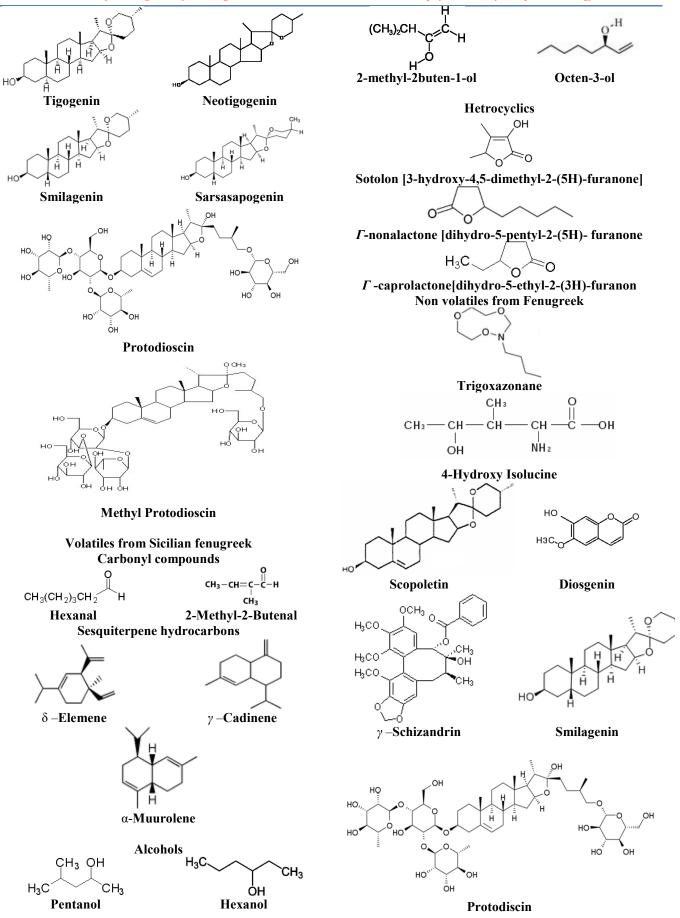


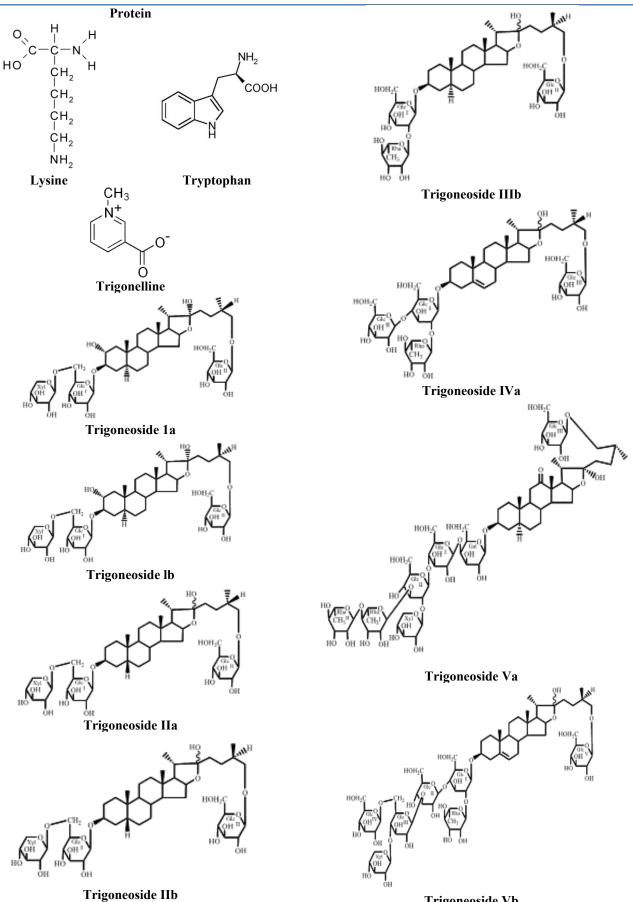




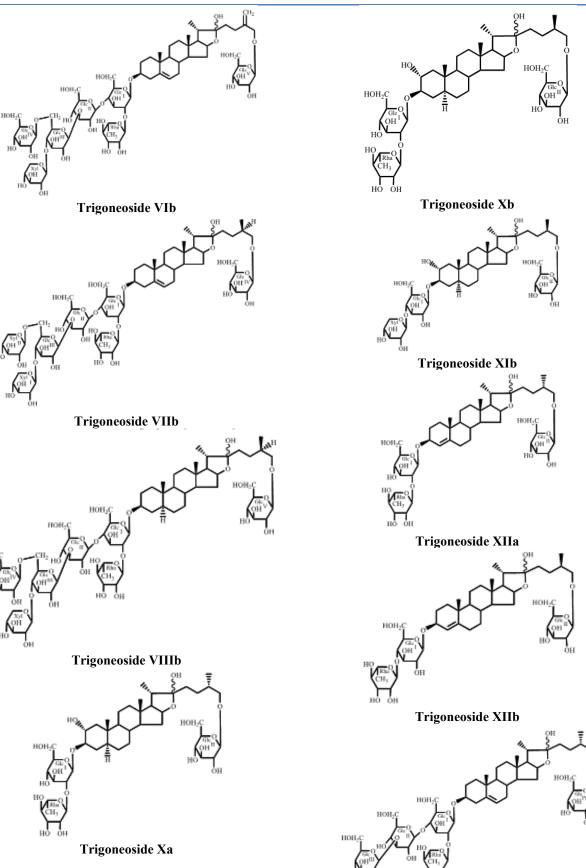


Yamogenin





Trigoneoside Vb



Trigoneoside XIIIa

HOH/

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