Journal of Pharmacognosy and Phytochemistry
Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8234
JPP 2019; 8(4): 184-187
Received: 04-05-2019
Accepted: 06-06-2019

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Role of fenugreek (*Trigonella foenum graecum*) on in management of diabetes disease

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Abstract
Diabetes mellitus is one of the major metabolic disorders, afflicting a large proportion of the population all over the world. It is recognized for sever complications, which include diabetic nephropathy, neuropathy and retinopathy. Fenugreek (*Trigonella foenum graecum*) is one of the most common medicinal plants used for diabetes, and also it is a key ingredient of curries and other Indian recipes. The plant contains active components such as alkaloids, flavonoids, steroids, saponins etc, and also it is rich in soluble fiber, which helps lower blood sugar by hindering assimilation and retention of carbohydrates. Many trials showed that fenugreek can improve most metabolic symptoms related with both type 1 and type 2 diabetes in humans by bringing down blood glucose levels and improving glucose tolerance.

Keywords: Fenugreek, diabetes

Introduction
Diabetes mellitus is a chronic disease characterized by hyperglycemia, a change in the metabolism of lipids, carbohydrates and proteins (Sajad and Pradyuman 2018) [1]. It is the most common chronic metabolic disease, characterized by elevated glucose levels due to absolute or relative insulin deficiency. The disease is related in the long term with ocular, renal, cardiovascular and neurological complications. It is also associated with symptoms such as weight loss, blurred vision, polyuria, fatigue, delayed wound healing and increased levels of glucose in the urine (Rao *et al*., 2006; Antu *et al*., 2014; Ziamajidi *et al*., 2017) [2, 3, 4].
As per the World Health Organization more than 400 million people live with diabetes in the whole world, yearly 1.6 million deaths are directly attributed to diabetes, it found to be the seventh leading cause of death in 2016 (Anonymous 2018) [5].
Medicinal have been utilized since antiquated occasions for the counteractive action and treatment of diabetes mellitus in customary drug frameworks of numerous societies around the globe (Gurib 2006; Jung *et al*., 2006) [6, 7]. Right now, restorative plants keep on assuming a significant job in the treatment of diabetes, particularly in creating nations, where numerous individuals don't approach regular antidiabetic treatment (Achaya and Shrivastava 2008; Parkash *et al*., 2018) [8, 9]. While in developed countries, the utilization of natural antidiabetic remedies has decreased since the introduction of insulin and synthetic oral hypoglycaemic. However, recently in developed countries there has been a reestablished enthusiasm for therapeutic plants with hypoglycemic properties. The renewed interest in herbal remedies for diabetes in developed countries is because of several factors, including: adverse reactions, high rates of secondary failure and the expense of conventional synthetic antidiabetic drugs. Recently, the World Health Organization (WHO) has recommended the use of medicinal plants for the treatment of diabetes, and has also encouraged the extension of the limits of scientific evaluation of the hypoglycaemic properties of several plant species (Manisha *et al*., 2007) [10].

Common antidiabetic medicinal plants
Several species of medicinal plants used in the management of diabetes worldwide have been evaluated. Some of the plants include: *Allium cepa* (Onion), *Allium sativum* (Garlic), *Gymmema slyvestre* (Gurnar), *Momordica charantia* (Bitter Melon), *Catharanthus roseus* (Madagascar Periwinkle), *Trigonella foemum-graecum* (Fenugreek) and *Pterocarpus marsupium* (Indian Kino) (Bnouham *et al*., 2006; Gondwe *et al*., 2008) [11, 12].

Fenugreek (*Trigonella foenum graecum*)
Fenugreek (*Trigonella foenum graecum*) self-pollinates. An annual plant belongs to the family of *Legumes*. It has been called as "*Trigonella*" of the Latin language which means "small triangle" due to its yellowish-white triangular flower (Awais *et al*., 2015) [13]. And the name of the species "*Foenum-graecum*" means "Greek hay", indicating its use as a forage plant in the

past. Fenugreek is native to the Mediterranean region of Asia and has recently been suggested to originate in Turkey. Fenugreek is known throughout the world (Table 1). About 260 species are currently available in the *Trigonella genus* (Acharya *et al*., 2014) [14].

Table 1: Common names of Fenugreek (*Trigonella foenum graecum*) (Shashikumar *et al*., 2018) [15].

Language	Common Names
Hindi	Methi, Saag methi, Kasuri methi
English	Fenugreek
French	Fenugreec, Trigonelle
Galician	Alforfa
German	Bockshornklee, Griechisch Heu
Georgian	Solinji, Chaman
Japanese	Koruha, Fenu-guriku
Dutch	Fenugriek
Romanian	Molotru, Molotru comun, Schinduf
Assamese	Methi, Mithi
Sanskrit	Methika

Chemical constituents of fenugreek (Trigonella foenumgraecum)

Fenugreek has been described as a medicinal herb in traditional Indian Ayurvedic medicines. It contains several chemical components: proteins, starch, neutral detergent fibers, ash and lipids (Shashikumar *et al*., 2018) [15]. In general, three important chemical components of fenugreek are 1) steroid sapogenins; 2) galactomannans and 3) isoleucine. These components placed fenugreek among the most recognized "nutraceuticals" or dietary products (Srichamroen *et al*., 2008) [16].

Fiber

Fenugreek seeds are rich source of soluble dietary fiber content (Raju *et al*., 2001) [17] revealed that the fiber substance of fenugreek extricate assumes a job in its capacity to direct digestion of glucose in the stomach related tract. Water retention on the external surface makes seeds coat delicate and adhesive. The 100 g of seeds give over 65% of dietary fiber. Non-starch polysaccharides comprise fiber substance of the fenugreek. Fenugreek contains saponins, hemicelluloses, adhesive, tannins and gelatin and these mixes help to diminish the dimension of low thickness lipoprotein-cholesterol (LDL) in blood by hindering bile salts re-ingestion in the colon (Meghwal and Goswami, 2012) [18].

Protein

Fenugreek endosperm is highly rich in protein such as globulin, albumin, histidine and lecithin. Seed of fenugreek has a high proportion of protein ranging from 20 to 30% as well as amino acid, 4-hydroxyisoleucine, which contains high potential for insulin-stimulating activity (Isikli and Karababa, 2005) [19]. Fenugreek proteins are stable enough, and are not affected during booking. Moreover, debitterized fenugreek seeds are rich in protein and lysine contents (Srinivasan, 2006) [20].

Vitamins and Minerals

Fenugreek seed is a rich source of vitamins viz. vitamin A (3 ug/100g), B1 (0.43 mg/100g), B2 (0.36 mg/100g), C (12-43 Mg/100g), nicotinic acid (1.1 Mg/100g) and niacin (6 mg/100g). Its leaves also contain vitamins, but on boiling, steaming or frying, 7–11% of them may be lost. Fenugreek seeds contain of potassium (603.0 mg/100g), magnesium (42.0 mg/100g), calcium (75.0 mg/100g), Zinc (2.4 mg/100g) and iron (25.8 mg/100g) (Al Jasass and Al Jasass, 2012) [21].

Alkaloids, saponin and flavonoids in fenugreek (*Trigonella foenum-graecum*)

Fenugreek contains a fairly high amount of alkaloids, saponins and flavonoids. Alkaloids and volatiles are the two major constituents of fenugreek seed which causes bitter taste. Fenugreek endosperm contains 35% alkaloids, primarily trigonelline. Flavonoid constitutes more than 100 mg/g of fenugreek seed (Naidu *et al*., 2011) [22]. All these compounds are classified as biologically active as these have pharmacological effects on the human body when ingested. Their utilization should, in this manner, be elevated in every day diet to oversee hypercholesterolemia, malignancy and diabetes mellitus as they have hypoglycemic, antilipidemic, anticarcinogenic and cholagogic properties (Meghwal and Goswami, 2012) [18].

Antidiabetic effect of fenugreek with possible mechanisms

Fenugreek seed extracts have been reported to exhibit antidiabetic potential by delaying both gastric emptying time and rate of glucose absorption. It reduced uptake of glucose in the small intestine mainly due to its high fiber content that slows the metabolism of carbohydrates and lowered blood glucose (Patel *et al*., 2012) [23].

It also restores the function of pancreatic tissues, protecting β cells, evaluating serum insulin level possibly through the regeneration of β cells or stimulation of insulin release by the existing β islet cells (Bera *et al*., 2013) [24].

Besides it corrects the insulin-sensitive carbohydrate metabolic enzymes activities, serum lipid profiles, prevents lipid peroxidation, restores glutathione and superoxide dismutase (liver and pancreas), enhances insulin sensitivity, improving insulin action at cellular level, and recovers the level of HbA1c by utilization of glucose in peripheral tissues where by maintain the blood glucose level (Gauttam and Kalia 2013) [25].

Many studies have reported the role of free radicals in the pathogenesis of diabetes, where oxidative stress coexists with a reduced antioxidant status. It has been shown that fenugreek has antioxidant activity (Gauttam and Kalia 2013) [25] that could prevent the pathogenesis of diabetes. In a previous study, solid-state bioconversion of the fenugreek substrate by *Rhizopus oligosporus* has shown to significantly increase the natural α-amylase inhibitors associated with high phenolic antioxidants, which potentially reduces the glycemic index and hence, reported to be useful in the management of carbohydrate metabolism disorders linked to diabetes. 4-Hydroxyleucine, a novel amino acid from fenugreek seed, was reported to increase glucose-stimulated insulin release by isolated islet cells in rats, mice, and humans. A specific amino acid called 4-hydroxyisoleucine, which represents 80% of the free amino acid in fenugreek seeds, was reported to possess insulin-stimulating properties, and enhance insulin sensitivity and glucose uptake in peripheral tissues. In a study, 4-hydroxyisoleucine has reported to suppress the progression of type-2 diabetes in mice model (Randhir and Shetty, 2007) [26].

In another study, it was reported that fenugreek oil produces an antidiabetic effect due to its immunomodulatory action and insulimation in alloxanized rats. Daily oral treatment of fenugreek steroids has shown a significant reduction in blood glucose level and a substantial improvement in the area of insulin-immunoreactive β cells, as well as a considerable reduction in the number of abnormal forms of sperm an

improvement in the number of sperm in diabetic rats (Khan *et al*., 2012) [27].

Role of fenugreek in the pathogenesis and complications of diabetes

Diabetes is associated with a disorder of the metabolism of carbohydrates and lipids. Important carbohydrate metabolic enzymes, such as hexokinase, glucose-6-phosphatase and glucose-6-phosphate dehydrogenase, were altered in Streptozotocin (STZ) induced diabetic rat. However, the seeds of the aqueous extract of *Trigonella foenum-graecum* and *Psoralea corylifolia* in a compound manner (1: 1) showed a significant recovery of the activities of these enzymes in the liver tissue and, therefore, they reported that the extract corrected the abnormal metabolism (Bera *et al*., 2013) [24].

Diabetic retinopathy and neuropathy both are common complications of diabetes. In one study, fenugreek seeds have been shown to be effective in preventing retinopathy and other complications of diabetes when used alone or in combination with sodium orthovate (Khan *et al*., 2012) [27]. In another study, the neuroprotective effects of fenugreek seed powder may have resulted in a decrease in hyperglycemia and oxidative stress, thus improving the control and management of diabetes complications (Kumar *et al*., 2012) [28].

Conclusion

Based on the available literature, this chapter suggests that fenugreek has evidence-based antidiabetic effect, such as stimulating and/or regenerating effect on β cells along with extrapancreatic effects that are effective in reducing blood glucose levels in diabetic patients.

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