IJRAR.ORG E-ISSN: 2348-1269, P-ISSN: 2349-5138

INTERNATIONAL JOURNAL OF RESEARCH AND ANALYTICAL REVIEWS (IJRAR) | IJRAR.ORG

An International Open Access, Peer-reviewed, Refereed Journal

ROLE OF FENUGREEK (TRIGONELLA FOENUM-GRAECUM) IN TYPE 2 DIABETES MELLITUS

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ABSTRACT:

According to International Federation of Diabetes, the data indicates that 537 million adults belonged to the age group of 20–79 years live with diabeties problem worldwide. Commenly patient is seen with the type 2 diabetes, which constitutes more more than 90–95% of cases. Modern medical practices regarding the treatment of diabetes have a strong tendency to be quite dependent on Insulin injection and oral antidiabetic agents. Its effectiveness is counterproductive by the health side effects, drawback of manmade drugs, lack of distribution, unaffordability, are some of the noticable challenges in these approaches.[1]

The volume of those being diagnosed with type 2 diabetes is on the increase across the world. Epidemiology of paediatric type 2 diabetes and childhood obesity prevalence is increasing globally, whereby incidence rate will be highest concerning public health burden. It is associated with several risk factors, some of which are basic and hereditary in nature, others they relate to our way of life. Due to poor treatment of diabetes that eventually results in the onset of relevant comorbidities and the fact that many antidiabetic drugs are associated with adverse side effects, there is a critical demand for identification of new compounds useful in prevention and therapy, aimed at controlling this multifaceted metabolic disorder. Naturally derived compounds are increasingly being used for the therapy and prophylaxis of various complex diseases such as type 2 diabetes.[2]

Keywords: Fenugreek; Type 2 diabetes; 4 hydroxy isoleucine; natural compounds; blood glucose level

INTRODUCTION:

According to IDF International Diabetes Federation, one in ten (10.5%) adults worldwide is now living with diabetes mellitus. This figure is expected to rise to 783 million, or 12.2%, by 2045. Of all people suffering from this condition, over 90% have T2DM type 2 diabetes mellitus. The growth in the population suffering from T2DM is due to the interaction of complex socio-economic, environmental, and genetic factors. The major contributors involve urbanization, an aging population, the less physical activity and increasing rates of over and obesity prevalence. Moreover, there are 10.6% adults who experience IGT around the world also known as prediabetes that is predisposed to T2DM.[3]

Type 2 diabetes mellitus (T2DM) is a complex metabolic disease resulting from the interactions between altered risk factors and essentially unmodifiable genetic and environmental determinants. A factors can not be change include things like age, gender and genetics. Those with modifiable risk factors such as in the area of nutrition exercise and socio-economics. Additional hazards include gestational diabetes, overuse of specific drugs, depression, too much alcohol and tobacco use throughout pregnancy. Type-II diabetes is a complex disease that presents greater challenges to adequately controlling and preventing the disease, necessitating an

expanded understanding of the molecular influences on type 2 diabetes pathogenesis in order to develop and test new, superior treatments.[2]

The main causes of the T2DM are the presence of insulin resistance (IR) and the presence of inadequate insulin secretion [4]. At present, the medicinal therapies aimed at the management of T2DM include metformin, pioglitazone, sulfonylureas and thiazolidinediones. However, these medications are have similar number of side effects when used for long periods such as hypoglycemia, lactic acidosis, gastrointestinal distress from extended use, peripheral swelling due to cut off Any causes of liver disease, and hepatotoxic holding. For that reason, additional investigations and development of new hypoglycemic agents, which are effective in glucose-lowering actions and with fewer side effects, is needed. [4]

Health benefits as an antidiabetic agent are also well documented for Fenugreek (T. foenum-graecum), a member of the Leguminosae family. The various chemical constituents in its seeds and leaves, however, has been used in folk medicine for ages A complex structure20 of macro- And micronutrients along with additional detoxifying bioactive substances (quercetin, diosgenin, trigonelline) and free amino acids (4-hydroxyisoleucine) in fenugreek seeds have been included as factors accounting for its pharmacological and biological potentials. Besides, they have also been reported to lower the occurrence of several types of chronic and degenerative diseases.[5]

FENUGREEK CONTENT :

Fenugreek has vast variety of nutrients and compounds which are useful in improving health and functionality of humans. Fenugreek seeds have 58% of carbohydrates , 23-26% of proteins ,25% of fibres and 0.9% of fats .
Fenugreek leaves have 6% carbohydrates , 4.4% proteins,1.1% fibres
Fenugreek also contain different types of minerals

- Potassium [603mg/100gm]
- Magnesium [42mg/100gm]
- Calcium [75mg/100gm]
- Zinc [2.4mg/100gm]
- Manganese [0.9mg/100gm]
- Copper [0.9mg/100gm]
- Iron [25.8mg/100gm]
- Vitamin c [220mg/100gm]
- Beta-caroteneg/100gm]

have also been considered as the active elements of fenugreek.
Fenugreek is a good source of essential amino acids. This spice further contains trace amounts of sulphur-containing amino acids, namely cysteine and methionine, which have significant physiological functions in the body. The most abundant free amino acids are found in fenugreek is (2S,3R,4S)4-hydroxyisoleusine. 4-Hydroxyisoleusine is the major non-protein amino acid accounting for about 80% of the dry matter amino acid content in the seeds during the seed growth phase that proliferate greatly during this stage.[6]

DIOSGENIN:

Seeds of fenugreek contain about 0.1-0.9% of diosgenin which are extracted commercially. Diosgenin content The seeds of fenugreek contain about 0.1–0.9% of diosgenin and are extracted commercially.

The diosgenin content from the tissue culture of fenugreek seeds from optimal growth conditions can be up to 2%, while smaller amounts are trigogenin and gitongenin. Seeds also contain the saponin (fenugrin B). Several coumarin compounds and many alkaloids (e.g., trigonelline, gentianine, carpaine) are detected. [7]

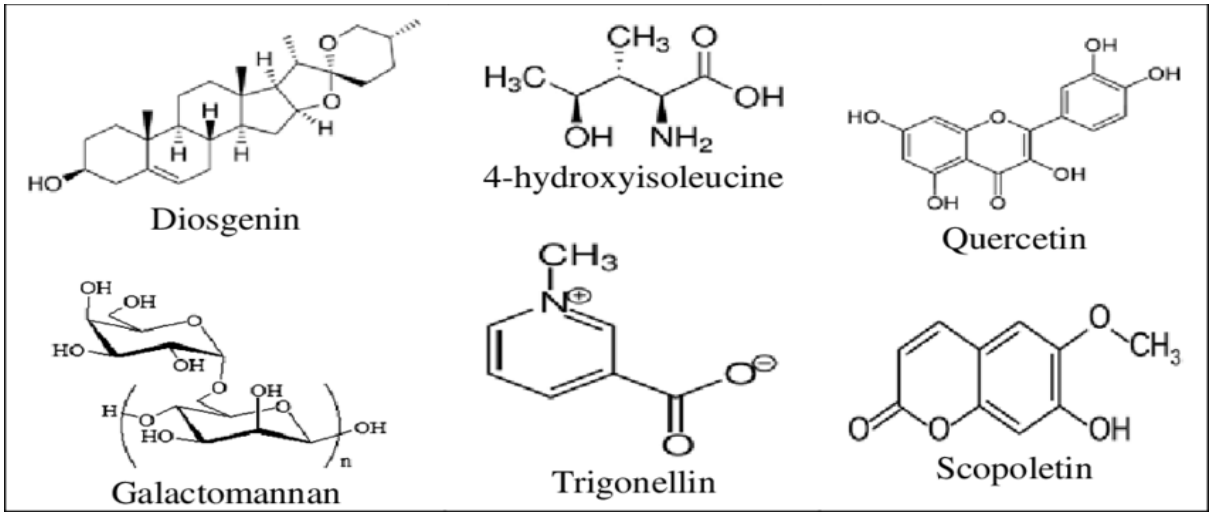

Figure 1 Chemical Structure Of Fenugreek Content[8]

Table 1. The composition of fenugreek shows the percentage present in leaves and seeds.

Constituent Type	Constituent	Fenugreek Seeds (Approximate %)	Fenugreek Leaves (Approximate %)
Macronutrients	Proteins	20–30%	4–6%
	Dietary Fibre	25–30%	3–5%
	Carbohydrates	40–60%	5–10%
	Fats	5–10%	<1%
Vitamins	B Vitamins (e.g., B6, B12)	0.3–0.6%	0.1–0.2%
	Vitamin K	Trace amounts	0.2–0.4%
	Vitamin A	Trace amounts	0.02–0.05%
	Vitamin C	0.1–0.3%	0.3–0.7%
	Folate (Folic Acid)	0.02–0.05%	0.01–0.03%
	Vitamin E	Trace amounts	Trace amounts
Minerals	Iron	1–2%	2–4%
	Calcium	0.2–0.5%	1–3%
	Magnesium	0.1–0.3%	0.2–0.5%
	Phosphorus	0.3–0.6%	0.2–0.4%
	Potassium	0.4–0.8%	0.5–1%
	Sodium	<0.1%	<0.1%
	Zinc	0.01–0.03%	0.01–0.03%
Bioactive Compounds	Saponins	2–6%	<1%
	Alkaloids	<1%	Trace amounts
	4-hydroxyisoleucine	1–2%	Trace amounts
	Flavonoids	0.5–1%	0.2–0.5%
	Phenolic Acids	0.1–0.3%	0.1–0.2%
	Coumarins	Trace amounts	Trace amounts
	Lecithin	0.1–0.3%	Trace amounts
Other Components	Water Content	5–10%	75–85%
	Essential Oils	Trace to 1%	Trace amounts
	Mucilage	1–3%	<1%
	Choline	0.02–0.05%	Trace amounts

4-Hydroxy isoleucine :

4-Hydroxyisoleucine is the most studied fenugreek compound, which was classied as an amino acid representing 1–3% of fenugreek seeds and 0.5–1.5% of the leaves.
It has exerted its antidiabetic action in sucrose-liptic-fed diabetic rat models through the modulation of pancreatic insulin secretion, the enhancement of in vivo insulin release, and increased glucose tolerance. The mechanism of action of 4-HIL has been proposed wherein it positively modulates the production of TNF-alpha to cause insulin sensitivity. Additionally, it causes the translocation of GLUT4 transporter type 4) and p-IRS-1 (insulin receptor substrate 1) in the insulin-signaling pathway . It is assumed to act directly on pancreatic cells and possibly increase the glucose uptake in the peripheral tissues including the skeletal muscle and adipose tissue leading to improved glycemic control.(2)

The endosperm of the seed is rich in fiber content with about 20% and gum contents that are mostly galactomannans (32.4%), GAL is a type of plant seed storage polysaccharides and plays an important role in the germination process of endosperm. GAL consist of a D-galactose branch linked through the α-(1-6) and α– (1-4)-D-mannane backbone with heterogenous polysaccharides. These are separated using the mannose/galactose ratio (M/G). The mannose backbone with side groups of galactose in a 1:1 ratio was said to constitute the fenugreek GAL polysaccharide group. The maximum percentage of galactose (~48%; M/G, 1.02:1) in the fenugreek GAL molecule was found. Almost all the mannose units of the backbone are substituted by a single galactose branch attached at position 1–6 on the linear mannan chain.(9)

Mode of Action :

There are many ways to treat the diabetes for example sulphonylureas, thiazolidine , and , dipeptidyl peptidase-4 inhibitors etc. But patients mostly prefer to the nutraceuticals like fenugreek, berberis and many more, due its efficacy and less number side effects seen in patient. (10)

Diosgenin saponin is the most active compound found in the fenugreek. It has the antioxidative role and effect which plays a vital in reducing the diabetic status by several mechanisms.(11,12) Its MOA include that it act on the pancreas and renews the pancreatic β-cell and which increases the insulin secretion. Also shows the action on adipose tissue enhance PPAR-γ expressions. It also decreases the enzyme involved in gluconeogenesis. Which more importantly decreases the hepatic glucose output.(13)

Similarly like of diosgenin the other compound is present which also helps to reduce the blood sugar level called 4-hydroxyisoleucine. It is a branched chain amino acid (11). Increases the insulin secretion and reduce the plasma triglycerides, and total cholesterol levels. It exerts its inslinotroic and hypoglycemic action by stimulating of insulin secretion. Which determines an increase in the GLUT4 to the plasma membrane and thus a increase in glucose uptake in adipose tissue and skeletal muscle.(13)

Galactomannan a type of carbohydrate which represent the 45 to 60 percent of the fenugreek seed. Also known as soluble fibre. Reduces the alpha amylase and sucrase activity and increases the gastric motility and hence decrease in the gastric emptying time. Which finally results the lowering the postprandial glucose level. (11)

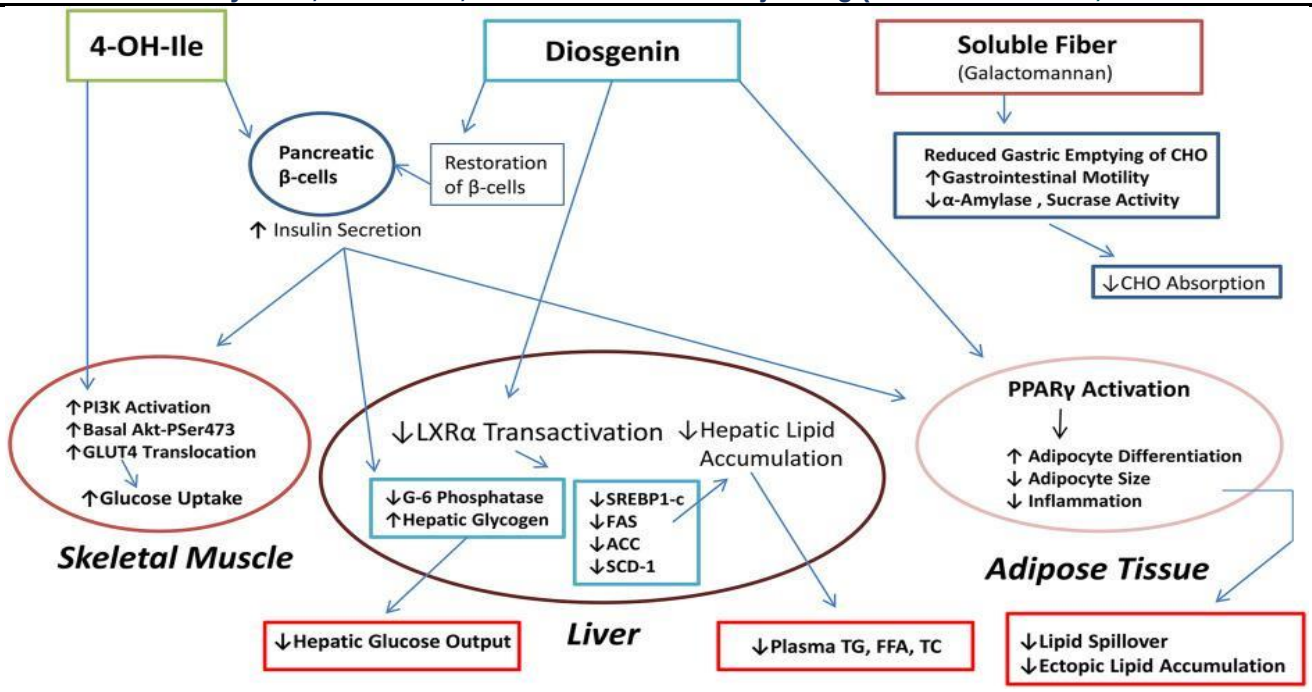

Figure 2 Mechanism of Action (14)

Preclinical studies showed that the primary mechanisms responsible for its hypoglycemic effect were stimulated insulin secretion, preservation of β cells, suppression of glucose-6-phosphatase and fructose-1,6-bisphosphatase activities, inhibition of α-amylase and maltase activities, and increase in glucose transporter type-4 (GLUT4) translocation and increased hexokinase activity. Moreover, only a few have yet provided evidence that it can act as an inhibitor of dipeptidyl peptidase-IV (DPP-IV) or an activator of 5'-AMP-activated kinase (AMPK), and modulates the glucagon-like peptide 1 (GLP-1)(15)

Fenugreek reduces the blood sugar level by :

- Slows carbohydrate absorption
- Increases Insulin Secretion
- Impact of Antioxidants
- Improves Cholesterol Levels

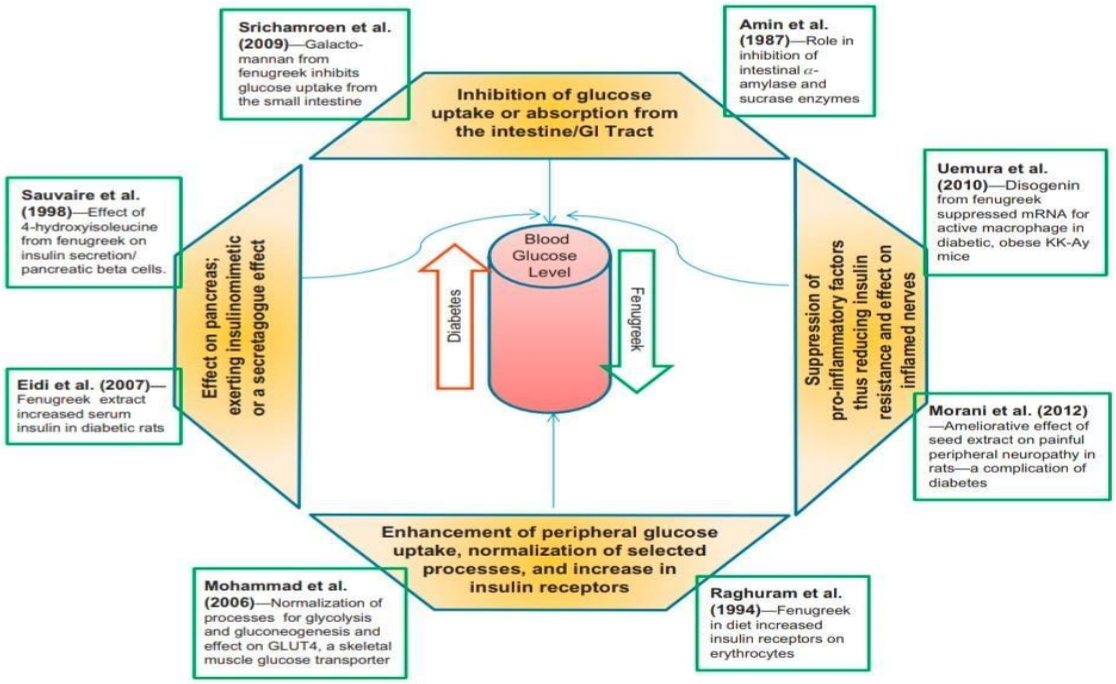

Figure 3 Different Clinical studies for Fenugreek

Specific activities of Intestinal disaccharidases like sucrase, maltase specific activities have been found to be increased many folds during diabetes. The supplementation with the mucilage of fenugreek seeds have reduced the activities of these disaccharidases hence established the beneficial role of fenugreek in diabetes management.(1)

Conclusion:

Fenugreek seeds are now said to be helpful in the natural management of diabetes. This would help reduce blood glucose levels, stimulate and enhance insulin production, and even improve cholesterol profile. It is promising at this point, though clinical research is needed to confirm long-term effects and ideal dosing. During that time, fenugreek is going to be an effective adjunctive therapy to the conventional management of diabetes because it adds more beneficial effects on blood glucose regulation and metabolic health.

Among all the disorders in neuropathy and Diabetic Retinopathy, most of the patients suffer from diabetes mellitus. In one study, it has been found that the supplementation of fenugreek seeds alone or in combination with sodium orthovandate prevents retinopathy. In another study, it has been shown that the powdered seed of fenugreek exhibits neuroprotective properties which might be used to reduce hyperglycemic condition and oxidativestress.

Part Used	Model	Effects demonstrated	References
Fenugreek Seeds and Alkaloids	Normal and diabetic rat	Mild Hypoglycemic effects	(Mishkinsky, Goldschmied, Joseph, Ahronson and Sulman,1974)
Fenugreek and Lupine Seeds	Diabetic Rats	Prevention of diabetic induction	(Riyad et al., 1988)
Fenugreek Powder/ Methanol extract/Water Extract/Soluble Fibre	Normal and streptozotocin induced diabetic Rats	Hypoglycemic effects	(Nahar etal.,1992)
Fenugreek (2%w/w)	Obese KK- AY mice	Helps in improving diabetic condition associated with obesity	(Uemura et al., 2010)
Trigonelline and ethanol extract of Fenugreek seed	Alloxan induced diabetic rabbit	Significant improved in stress induced oxidation Parameter	(Hamadi et al.,2012)
Aquaous extract of Fenugreek Seed	Alloxan diabetic mice	Hypolglycemic effect was Observed which is comparable to Insuline(1.5U/Kg)	(Vijayakumar et al., 2005)
Fenugreek Seed Extract	Streptozocin-induced diabetic Male Sprague-Dawley rats	Reduce Blood Glucose	(Baset et al.,2020)

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