



Mini Review

The use of fenugreek supplementation in diabetes

Aamir Jalal Al Mosawi*

Advisor Doctor, Baghdad Medical City and the Iraqi Ministry of Health, Baghdad, Iraq

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***Corresponding author:** Aamir Jalal Al Mosawi, Advisor Doctor, Baghdad Medical City and the Iraqi Ministry of Health, Baghdad, Iraq, E-mail: almosawiAJ@yahoo.com

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Abstract

Dietary health supplements have increasingly used in the prevention and treatment of chronic disorders. During the previous decades, fenugreek (*Trigonella foenum-graecum*) seeds have been reported to have hypoglycemic and cholesterol lowering effects when used in type 1 and type 2 diabetes mellitus patients, and in experimental diabetic animals. The aim of this paper is to review fenugreek research findings relevant to its use in diabetes.

There is convincing research evidence suggesting that fenugreek can improve hyperglycemia and has a protective effect against diabetic complications through immunomodulatory, insulin stimulation, and antioxidant effects, enhancing adipocyte differentiation, inhibition of inflammation in adipose tissues, and preventing or lessening pancreatic and renal damage. Many of the beneficial effects of fenugreek in diabetes have been attributed to four bioactive components including diosgenin, 4-hydroxyisoleucine, furostanolic saponins, and the fiber in fenugreek.

During the 1970s and 1980s, several experimental researches on rats and dogs suggested that fenugreek (*Trigonella foenum-graecum* seeds) has a hypoglycemic effect [1-4].

The work of Madar, et al. (1988) suggested that fenugreek has the potential to be used in the treatment of non-insulin dependent diabetics, as they reported that the use of powdered fenugreek seed in a dose of 15 g soaked in water was associated with a marked decrease in the postprandial glucose levels [5].

Sharma and colleagues (1990) reported that the use of defatted fenugreek seed powder in the treatment of type I diabetes, in a dose of 100 g divided in two doses for ten days, was associated with a considerable lowering of fasting blood sugar and resulted in an improvement in the glucose tolerance test. They also found a 54% lowering of 24-hour urinary glucose excretion. Treatment also had an important lowering effect on serum total cholesterol, LDL and VLDL cholesterol and triglycerides were also significantly reduced [6].

Khosla and colleagues (1995) reported an experimental study on rats which showed that oral fenugreek (2 and 8 g/kg dose) was associated with a considerable lowering ($P < 0.05$) in blood glucose in normal and diabetic rats, and the hypoglycemic effect in this study was dose related [7].

Sauvaire, et al. (1998) reported that 4-hydroxyisoleucine which is an amino acid extracted and purified from fenugreek

seeds has an insulinotropic effect. 4-Hydroxyisoleucine augments glucose-induced insulin secretion from islets of Langerhans from rats and humans [8].

The experimental work of Broca, et al. (1998) on rats suggested that the antidiabetic effects of 4-hydroxyisoleucine on rats with non-insulin dependent diabetes result is partly attributed to a direct stimulation of the pancreatic B cell. They found that in non-insulin-dependent diabetic rats, a single intravenous administration of 4-hydroxyisoleucine in a dose of 50 mg/kg restored to some extent glucose-induced insulin response without affecting glucose tolerance. They also found that the subchronic intake of 4-hydroxyisoleucine, 50 mg/kg, daily lowered basal hyperglycemia, reduced basal insulinemia, and improved glucose tolerance [9].

The experimental work of Raju, et al. (2001) on alloxan diabetic rats showed that fenugreek seed powder improves glucose homeostasis in tissues by reversing the abnormal glycolytic, gluconeogenic and lipogenic enzymes [10].

The experimental work of Anuradha and Ravikumar (2001) on rats showed that diabetic rats experience an increased lipid peroxidation and a higher susceptibility to oxidative stress associated with depletion of antioxidants in liver, kidney and pancreas. They reported that treatment with fenugreek seed powder normalized the antioxidant status [11].

Gupta, et al. (2001) reported a study which included 25 new cases of type 2 diabetes who had fasting glucose less 200 mg/dl. They treated twelve patients with hydro-alcoholic extract of fenugreek seeds 1 gm daily, and thirteen patients were treated with dietary control, exercise and placebo capsules for two months. The study showed that the addition of fenugreek seeds was associated with improved glycemic control and reduced insulin resistance in mild type-2 diabetic patients, and had a favorable effect on hypertriglyceridemia [12].

Puri and colleagues (2002) reported an experimental study on sub-diabetic and mild diabetic rabbits treated with fenugreek seeds in a dose of 50 mg/kg body weight for 15 days. Treatment was associated with a considerable lessening of the glucose tolerance curve and improvement in the glucose induced insulin response.

Puri and colleagues attributed the hypoglycemic effect to stimulation of insulin synthesis and/or secretion from the beta pancreatic cells of Langerhans.

Puri and colleagues also reported that treatment of five severely diabetic rabbits markedly reduced fasting blood glucose, but the reduction was not much correlated with the elevation of fasting serum insulin level, suggesting an extra-pancreatic effect [13].

The experimental work of Thakran, et al. (2004) alloxan diabetic rats suggested that treatment with fenugreek seed powder can reverse the diabetic state at the cellular level, help with the metabolic normalization, has a protective effect against the development of liver degenerative and nephropathic changes in diabetic rats [14].

Xue, et al. (2007) reported an experimental study on streptozotocin-induced diabetic rats which showed that fenugreek can reduce blood glucose, kidney/body weight ratio, blood lipids, and improve hemorheological properties when treatment repeated for six weeks [15].

Lu, et al. (2007) reported a clinical study which included sixty-nine patients with type 2 diabetes mellitus whose blood glucose levels were not adequately controlled by oral sulfonylureas hypoglycemic treatment. Forty six patients received fenugreek and 23 patients received placebo for 12 weeks. The addition of fenugreek to sulfonylureas hypoglycemic treatment was associated with reduction of blood glucose level and improved symptoms [16].

Kassaian, et al. (2009) reported the treatment of eighteen diabetic patients with fenugreek seeds powder 10 grams daily. Eleven patients took fenugreek mixed in hot water and seven took it mixed with yoghurt for eight weeks. Fasting blood sugar, triglycerides, and VLDL-C were considerably (25 %, 30 % and 30.6 % respectively) only in patients who took fenugreek seed soaked in hot water [17].

Mowla, et al. (2009) reported an experimental study on alloxan-induced diabetic rats showed that treatment with fenugreek seed extract 1g/kg/body weight has an effective hypoglycemic effect, and a high dose of 3g/kg/body weight was not associated with any toxicity [18].

Hamden, et al. (2010) reported an experimental study on rats with alloxan-induced diabetes who had pancreatic islet and beta-cells damage, low activities of superoxide dismutase, glutathione peroxidase, catalase, and reduced glutathione content in kidney.

Treatment with fenugreek oil was associated with marked improvement in blood glucose levels, glucose intolerance, and insulin sensitivity occurring in association with improvement in pancreatic and renal damage, and reduction of raised levels of lipid peroxidation, creatinine, albumin, and urea. The beneficial effects of fenugreek in this study were attributed to immunomodulatory, insulin stimulation and antioxidant effects [19].

Uemura T, et al (2010) reported an experimental study on diabetic obese KK-Ay mice which showed that fenugreek can improve diabetes by enhancing adipocyte differentiation and inhibiting inflammation in adipose tissues through the effects of diosgenin which is an aglycone [20].

Xue, et al. (2011) reported an experimental study on rats with streptozotocin induced diabetic nephropathy who had reduced activities of superoxide dismutase and catalase, elevated levels of malondialdehyde in the serum and kidney, and elevated levels of 8-hydroxy-2-deoxyguanosine in renal cortex DNA and urine. Treatment with fenugreek restored these abnormalities in a dose-dependent manner. Treatment considerably improved all of the ultrastructural renal changes, including the uneven thickening of the glomerular base membrane. This experimental study showed that fenugreek has a protective effect against functional and morphological renal damage in diabetic rats mediated through enhancing antioxidants and inhibition of buildup of oxidized DNA in the kidney [21].

Puri and colleagues (2012) reported an experimental study on rabbits with alloxan-induced diabetes which showed that a compound GII purified from the water extract of fenugreek had an antidiabetic property [22].

Hamza, et al. (2012) reported an experimental study on mice which showed that fenugreek had a preventive and curative effect in type 2 diabetes induced by high-fat diet [23].

Gupta, et al. (2014) reported an experimental study on streptozotocin-induced diabetic rats that had marked increase in the expressions of retinal inflammatory tumor necrosis factor- α and interleukin- 1β and angiogenic vascular endothelial growth factor and protein kinase C - β molecular biomarkers. The study showed that treatment with fenugreek 100 and 200 mg/kg body weight for 24 weeks was associated with significant inhibition in the expression of the elevated inflammatory and angiogenic molecular biomarkers. Fenugreek also had a positive modulatory effect on retinal oxidative stress, and prevented the development of retinal vascular leakage. This study suggested that fenugreek supplementation can help in preventing diabetes-induced retinal degeneration [24].

Neelakantan, et al. (2014) conducted a meta-analysis which included ten clinical trials and showed that fenugreek seeds had beneficial effects on glycemic control in diabetic patients [25].



Smith, et al. (2014.) reviewed the research findings relevant to the use of dietary supplements lowering blood glucose, and found that the strongest research evidence was associated with alpha-lipoic acid and fenugreek [26].

Rawat, et al. (2014) reported an experimental study on high-fructose diet fed streptozotocin-induced diabetic rats which showed that 4-Hydroxyisoleucine isolated from fenugreek seeds improved insulin resistance by promoting mitochondrial biogenesis and acting through AMPK and Akt dependent pathway [27].

Gaddam, et al. (2015) reported a 3-year randomized, controlled, parallel clinical study which included pre-diabetic individuals. Sixty-six individuals were treated with fenugreek powder, 5 g twice a day before meals, and seventy-four individuals served as controls. Treatment was associated with considerable lowering of fasting plasma glucose, postprandial plasma glucose, and low density lipoprotein cholesterol, and marked increase in serum insulin. Controls had 4.2 times higher chance of developing diabetes compared to treated individuals. Treatment was not associated with adverse effects and the beneficial effect was attributed to reduction of insulin resistance [28].

Verma, et al. (2016) reported a placebo-controlled clinical study which included 154 patients with type 2 diabetes. 90-day treatment with Fenugreek extract, furostanolic saponins (Fenfuro) 500 mg **twice daily was associated with marked lowering of** fasting plasma and post-prandial blood sugar levels. More than 80% of the treated patients experienced reductions in fasting plasma sugar levels compared to 62% of patients who received placebo. 89% of the treated patients experienced a decrease in post-prandial plasma sugar levels compared to 72% of patients who received placebo. 48.8% of the treated patients reported lowering of anti-diabetic therapy dosage, while 18.05% of the patients who received placebo reported lowering of anti-diabetic therapy dosage. Treatment was not associated with adverse effects [29].

Geberemeskel, et al. (2019) reported a study which included 114 newly diagnosed uncomplicated type II diabetic patients. 57 patients received 25 g fenugreek seed powder solution orally twice a day for one month, and 57 patients received metformin. The study showed that fenugreek had marked effects in improving lipid metabolism in type II diabetes without the occurrence of adverse effects [30].

Hadi, et al. (2020) reported an 8-week controlled clinical study which included 50 patients with type 2 diabetes whom were treated with anti-diabetic drugs. The patients received either 5 g fenugreek seed powder, three times daily or served as control patients. Compared to the control patients, treated patients experienced a considerable lowering of fasting plasma glucose ($p = 0.024$) [31].

Conclusion

There is convincing research evidence suggesting that fenugreek can improve hyperglycemia and has a protective effective against diabetic complications through

immunomodulatory, insulin stimulation, and antioxidant effects, enhancing adipocyte differentiation, inhibition of inflammation in adipose tissues, and preventing or lessening pancreatic and renal damage. Many of the beneficial effects of fenugreek in diabetes have been attributed to four bioactive components including diosgenin, 4-hydroxyisoleucine, furostanolic saponins, and the fiber in fenugreek.

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