IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
February 2018 Vol.:11, Issue:3

The Effect of Fenugreek on Blood Glucose, Lipid Parameters, Insulin and Resistin in Obese Women with Type 2 Diabetes

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Myriam Sfar*[1], Aya Jaouani[2], Kamel Ben-Mahrez[1], Hajer Aounallah Skhiri[3], Chihab Ben Rayana[4], Rachid Chemli[2], Faika Ben Mami[5], Fethi Ben Slama[1,3]

1- Université de Tunis El Manar, Faculté des Sciences de Tunis, LR01ES05 Laboratoire de Biochimie et Biotechnologie, 2092, Tunis, Tunisie
2- Faculty of Pharmacy of Monastir, University of Monastir, Monastir-5000, Tunisia
3- National Institute of Public Health of Tunis, Tunis-1024, Tunisia
4- Laboratory of Clinical Biochemistry, National Institute of Nutrition and Food Technology, Tunis-1029, Tunisia
5- Service "C" of nutrition diseases and diabetology, National Institute of Nutrition and Food Technology, Tunis-1029, Tunisia

Submission: 21 January 2018
Accepted: 27 January 2018
Published: 28 February 2018

HUMAN JOURNALS
www.ijppr.humanjournals.com

Keywords: obesity, diabetes, fenugreek, blood glucose, lipids, resistin

ABSTRACT

Introduction: Fenugreek, scientifically known as *Trigonella foenum-graecum*, is one of the oldest cultivated medicinal plants which belong to the family *Fabaceae*. In fact, several beneficial effects on health, attributed to the consumption of fenugreek, have been demonstrated during tests in both animals and humans. The purpose of our work is to study its effect in a group of obese patients with type 2 diabetes.**Methods:** We followed a population of 56 obese type 2 diabetic women, after a daily consumption of 15g of fenugreek powder in the morning before breakfast during 4 weeks and following regular physical activity. We measured the anthropometric, biochemical and hormonal parameters (insulin and resistin) before and aftercare. Then, we evaluated the variations of these parameters and we studied the correlations between them.**Results:** Improvement of the various parameters monitoring after taking care of patients. Consumption of fenugreek powder show negatively correlated with BMI, waist circumference, HOMA-IR and resistin, whereas it shows positively correlated with HDL-cholesterol. **Discussion:** Fenugreek powder, by its constituents, promotes a better glucose and lipid profile by improving insulin sensitivity and increasing HDL-cholesterol levels. This leads to a regression of the resistin levels, decreasing its effects on insulin sensitivity and its pro-inflammatory role. In addition to its effect in predisposed patients to decrease the prevalence of diabetes.**Conclusion:** This study combined with the literature, allowed us to confirm the role of fenugreek consumption to improve glucose and lipid parameters of obese diabetic patients, thus controlling their complications and leading to a better prognosis.

INTRODUCTION

Type 2 diabetes mellitus and obesity are a major threat to human health due to their increasing prevalence, chronic treatment and disabling complications, in fact the chronic hyperglycemia associated to diabetes and the metabolic disorders of the obesity are associated to microvascular complications in long-term affecting the eyes, kidneys and nerves as well as an increased risk of cardiovascular disease[1]. Clinically, there has been a decline in transmissible diseases, leaving room for no communicable diseases, including diabetes and obesity. These diseases and their associated complications such as atherosclerosis and major cardiovascular diseases become major causes of mortality and their prevalences are continuously growing [2]. In both humanitarian and economic terms, diabetes and obesity are now among the most expensive diseases. The problem becomes more complex because of their multiple manifestations and their complications affecting all body systems [1].

Thus, after years in which allopathy was the only valid treatment, several epidemiological and clinical studies have shown a significant decrease in the morbidity and mortality of these no communicable diseases in subjects following a specific physical activity and diet, indeed, phototherapy is back healing chronic diseases and improving the general health thanks to the scientific progress that has allowed to rationalize its practice and to open new perspectives following galenic innovations in term of more practical forms of use. For this, a dietary treatment at early stages of the disease but with fewer side effects and at lower cost will be an excellent alternative for diabetic patients. Among the medicinal plants, we found the fenugreek, scientifically known as Trigonella foenum-graecum. In fact, several beneficial effects on health have been attributed to the consumption of fenugreek. These effects have been reported in animal's studies as well as human studies. In our work, we propose to study the effect of fenugreek seed powder consumption associated to a regular physical activity in a group of 56 female obese patients with type 2 diabetes.

MATERIALS AND METHODS

Subjects

It involved a group of 56 obese type 2 diabetic female patients, from service C of nutrition diseases and diabetology of the National Institute of Nutrition, Tunis, Tunisia; whose diabetes age was not older than 5 years, these patients are older than 30 years old and they take an oral antidiabetic drugs with unsettled blood glucose and lipids during previous consultations. Type

1 diabetics, patients treated with insulin and who have associated severe conditions such as renal and hepatic deficiency, pregnant and beast-feeding women were excluded from our study. All the patients involved in the study agreed to voluntarily participate by oral consent after an explication of the objectives and the protocol of the study.

Protocol study

During their usual consultation, our participants received a dose of 15g of fenugreek daily in the morning for a period of four weeks. Every week, they come to get the dose of the week. The women consume the fenugreek powder dispersed in a glass of water before breakfast. The fenugreek seeds were cleaned, washed and dried for 10 minutes in the oven on a light fire so that the seeds became easy to grind, and after grinding we measured 15g of fenugreek powder, which was divided in small sanitary bags to be given to each patient. The manner of drinking the powder has been well explained to the patients. The study protocol was approved by the Ethics Committee of the National Institute of Nutrition

Method and tools for Data collection

During this study, every patient benefited for detailed interrogation specifying the general characteristics, family pathological history (type 2 diabetes, arterial hypertension, dyslipidemia, obesity), associated pathology, the duration of evolution of diabetes and any physical activity. The Anthropometric parameters of body Weight, height and waist size were measure during standard techniques in every 56 subjects, the body mass index (BMI) was calculated. The systolic and diastolic blood pressure was taken from each patient.

Assays

The fasting blood levels of glucose and lipids were measured in the clinical biochemistry laboratory of the national institute of nutrition. Cholesterol, triglycerides and blood glucose levels were measured by Beckman enzymatic KIT method on Beckman USA Synchron Cx7, while HDL-C values are measured after selective precipitation (Randox UK Kit).The level of plasma resistin were determined by the "Millipore #" ELISA method EZHR-95K with a sensitivity ranging from 0.16ng / ml to 10ng / ml. Insulin levels were measured by IRMA (Immunoradiometric assay).All these measurements were carried in two phases, at the beginning of the survey and after four weeks of the first intake

Statistical analysis

Data were analyzed using Microsoft Excel 2007 and Statistical Package for Social Sciences "SPSS" in version 19.0. We used the statistical tests related to the matched series the student t test, for the comparison of the mean of the variable measured and assayed on matched series. The concordances between 2 quantitative variables were studied by the Pearson correlation coefficient and in case of non-validity by Spearman's rank correlation coefficient. In all statistical tests, $p<0.05$ considered as statistically significant.

RESULTS

Table 1: Correlations between anthropometric, biochemical and hormonal parameters before fenugreek (N = 56)

		FBS	TC	TG	HDL-C	BMI	Insulin	Resistin
FBS	**Pearson Correlation (r)**	1	,079	,352 (**)	-,291 (*)	,625 (**)	,672 (**)	,355 (**)
	Sig. (bilateral)	,	,562	,008	,030	,000	,000	,007
TC	**Pearson Correlation (r)**	,079	1	,292 (*)	-,423 (**)	,387 (**)	,266 (*)	,280 (*)
	Sig. (bilateral)	,562	,	,029	,001	,003	,048	,036
TG	**Pearson Correlation (r)**	,352 (**)	,292 (*)	1	-,496 (**)	,549 (**)	,263	,097
	Sig. (bilateral)	,008	,029	,	,000	,000	,051	,476
HDL-C	**Pearson Correlation (r)**	-,291 (*)	-,423 (**)	-,496 (**)	1	-,419 (**)	-,339 (*)	-,104
	Sig. (bilateral)	,030	,001	,000	,	,001	,011	,444
BMI	**Pearson Correlation (r)**	,625 (**)	,387 (**)	,549 (**)	-,419 (**)	1	,340 (*)	,484 (**)
	Sig. (bilateral)	,000	,003	,000	,001	,	,010	,000
Insulin	**Pearson Correlation (r)**	,672 (**)	,266 (*)	,263	-,339 (*)	,340 (*)	1	,313 (*)
	Sig. (bilateral)	,000	,048	,051	,011	,010	,	,019
Resistin	**Pearson Correlation (r)**	,355 (**)	,280 (*)	,097	-,104	,484 (**)	,313 (*)	1
	Sig. (bilateral)	,007	,036	,476	,444	,000	,019	,

FBS: fasting blood glucose, TC: total serum cholesterol, TG: triglyceride, HDL-C: hight density lipoprotein cholesterol, BMI: body mass index

* The correlation is significant at the 0,05 level (bilateral).

** The correlation is significant at the 0,01 level (bilateral).

The plasma concentration of insulin is positively correlated with blood glucose, total cholesterol, triglycerides and BMI, in contrast to HDL-C, whose value correlates negatively with that of insulin with r = -0.339 and p = 0.011.

The concentration of resistin is positively correlated with blood glucose, total cholesterol, triglyceride, BMI and insulin with the exception of HDL-C to which it is negatively correlated with r = -0.104 and p = 0.444.

Table 2: Correlations between anthropometric, biochemical and hormonal parameters after fenugreek intake (N = 56)

		FBS	TC	TG	HDL-C	BMI	Insulin	Resistin
FBS	**Pearson Correlation (r)**	1	,332 (*)	,443 (**)	-,464 (*)	,657 (**)	,570 (**)	,443 (**)
	Sig. (bilateral)	,	,012	,001	,000	,000	,000	,001
CT	**Pearson Correlation (r)**	,332 (*)	1	,292 (*)	-,416 (**)	,381 (**)	,338 (*)	,396 (**)
	Sig. (bilateral)	,012	,	,029	,001	,004	,011	,003
TG	**Pearson Correlation (r)**	,443 (**)	,292 (*)	1	-,243	,515 (**)	,208	,198
	Sig. (bilateral)	,001	,029	,	,071	,000	,125	,143
HDL-C	**Pearson Correlation (r)**	-,464 (**)	-,416 (**)	-,243	1	-,471 (**)	-,358 (**)	-,288 (*)
	Sig. (bilateral)	,000	,001	,071	,	,000	,007	,032
BMI	**Pearson Correlation (r)**	,657 (**)	,381 (**)	,515 (**)	-,471 (**)	1	,403 (**)	,476 (**)
	Sig. (bilateral)	,000	,004	,000	,000	,	,002	,000
Insulin	**Pearson Correlation (r)**	,570 (**)	,338 (*)	,208	-,358 (**)	,403 (**)	1	,367 (**)
	Sig. (bilateral)	,000	,011	,125	,007	,002	,	,005
Resistin	**Pearson Correlation (r)**	,443 (**)	,396 (**)	,198	-,288 (*)	,476 (**)	,367 (**)	1
	Sig. (bilateral)	,001	,003	,143	,032	,000	,005	,

FBS: fasting blood glucose, TC: total serum cholesterol, TG: triglyceride, HDL-C: hight density lipoprotein cholesterol, BMI: body mass index

* The correlation is significant at the 0,05 level (bilateral).

** The correlation is significant at the 0,01 level (bilateral).

Insulin remains positively correlated with the same parameters, and we note above all a significant positive correlation with blood glucose (r = 0.570, p = 0.000) and BMI (r = 0.403, p = 0.002) and it remains always negatively correlated with HDL-C with r = -0.358 and p = 0.007.

Resistin remained positively significantly correlated with BMI (r = 0.476, p = 0.000) and blood glucose with r = 0.443 and p = 0.001, contrary to a strong negative correlation with HDL-C (r = 0.288, p = 0.032).

Table 3: Comparison of mean of anthropometric parameters before and after fenugreek intake (N = 56)

		Mean	standard deviation	Mean standard error	Matched differences		P
					Mean	standard deviation	
Pair 1	**BMI** (Kg/m2)	35,1691	4,45957	0,59593	5,5666	1,42241	,000
	BMI after taking fenugreek (Kg/m2)	29,6024	3,66814	0,49018			
Pair 2	**Waist circumference** (cm)	105,71	9,249	1,236	10,46	5,923	,000
	Waist circumference after taking fenugreek (cm)	95,25	8,308	1,236			
Pair 3	**SAP** (mmHg)	142,14	10,568	1,412	24,16	1,797	,000
	SAP after taking Fenugreek (mmHg)	117,98	8,772	1,172			
Pair 4	**DAP** (mmHg)	89,21	4,168	0,557	7,58	0,354	,000
	DAP after taking Fenugreek (mmHg)	81,63	3,814	0,510			

BMI: body mass index, SAP: systolic arterial pressure, DAP: diastolic arterial pressure

After taking fenugreek and applying a regular physical activity that is walking, there is a significant improvement in systolic and diastolic arterial pressure and a decrease in anthropometric parameters with -5.5 ± 1 Kg / m2 for BMI and -10.4 ± 5 cm for waist circumference.

Table 4: Comparison of the means of the biochemical parameters before and after taking fenugreek (N = 56)

		Mean	standard deviation	Mean standard error	Matched differences		P
					Mean	standard deviation	
Pair 1	**FBS** (mg/dL)	7,5139	1,28438	0,17163	1,1605	0,74097	,000
	FBS after taking fenugreek (mg/dL)	6,3534	0,96177	0,12852			
Pair 2	**TC** (mg/dL)	5,3336	1,09265	0,14601	0,6400	0,13112	,000
	TC after taking fenugreek (mg/dL)	4,6935	0,96153	0,12849			
Pair 3	**TG** (mg/dL)	1,8259	0,21112	0,02821	0,2008	0,02322	,000
	TG after taking fenugreek (mg/dL)	1,6250	0,18789	0,02511			
Pair 4	**HDL-C** (mg/dL)	0,7468	0,18332	0,02450	-0,1894	0,17979	,000
	HDL-C after taking fenugreek (mg/dL)	0,9361	0,22923	0,03063			

FBS: fasting blood glucose, TC: total serum cholesterol, TG: triglyceride, HDL-C: hight density lipoprotein cholesterol

We notice that after taking fenugreek and the application of regular physical activity, there is a drop in blood glucose, total cholesterol and triglycerides while there is an increase in HDL-cholesterol.

Table 5: Comparison of the means of hormonal parameters and HOMA-IR values before and after taking fenugreek (N = 56)

		Mean	standard deviation	Mean standard error	Matched differences		P
					Mean	standard deviation	
Pair 1	**Insulin** (µUI/L)	14,6018	4,76297	0,63648	3,2280	2,76684	,000
	Insulin after taking fenugreek (µUI/L)	11,3737	3,43655	0,45923			
Pair 2	**Resistin** (ng/mL)	10,5273	3,11330	0,41603	2,0758	1,04940	,000
	Resistin after taking fenugreek (ng/mL)	8,4515	2,54323	0,33985			
Pair 3	**HOMA-IR**	5,0559	2,33958	0,31264	1,7619	1,41779	,000
	HOMA-IR after taking fenugreek	3,2939	1,39359	0,18623			

After treatment, there was a significant decrease in insulin and resistin levels of -3.22 ± 2µUI / L for insulin and -2.07 ± 1ng / mL for resistin. In addition, a drop in the value of the HOMA-IR of -1.76 ± 1.

DISCUSSION

The objective of our study is to evaluate the effect of fenugreek on the improvement of blood glucose and lipid, anthropometric and hormonal parameters in a group of obese type 2 diabetics. We, therefore, looked for the different correlations between the different parameters needed before and after taking fenugreek and applying a regular physical activity, which is walking. Our population sample consists of 56 female obese and type 2 diabetic patients with the mean of age is 47 years, on oral antidiabetic drugs with unbalanced blood glucose and lipid parameters during previous consultations. Patients received a 15g dose of fenugreek powder daily in the morning for a period of four weeks. The biochemical parameters were compared before and after the management of the study population, with regard to the glycemic balance, there is a good evolution. In fact, there is a decrease in the mean glucose

level of -1.16 ± 0.74 mmol / L and a decrease in the mean of insulin 3.22 ± 2.76 µIU / L and the mean of resistin level of -2.07 ± 1.04 ng / mL and consequently the decrease of the HOMA-IR mean of -1.76 ± 1, 41.These results are consistent with the work of Bawadi H et al. after a study in 166 patients with type 2 diabetes, it was shown that after taking 2.5 or 5g of fenugreek powder, the blood glucose value decreased in a dose-dependent manner by -24, 8 ± 9.3 and 41.1 ± 7.2 mg / dL [3.4].In another study by Kassaian N et al. in 2009 in 24 patients with type 2 diabetes and after daily consumption of 10g of fenugreek powder mixed with yoghurt or after infusion in hot water for 8 weeks, blood glucose decreased by 25% after consumption of the infused in hot water while the decrease was not significant by its consumption mixed with yogurt [5].The study of Madar Z et al. led to the same results after ingestion of 15g of whole fenugreek seeds deceived in water [6]. One study compared the effect of 1g daily intake of the hydroalcoholic extract of fenugreek seeds with the effect of dietary regimen and physical activity on the fasting blood glucose value in 25 patients recently diagnosed with After 2 months, there was a decrease of 148.3 to 119.9 mg/dL and 137.5 to 113.0 mg/dL, respectively [7].The team of Gupta A et al. conducted a study in a group of 25 patients type 2 diabetics, half received capsules of the hydro-alcoholic extract of fenugreek seeds for a daily intake for 2 months of treatment. After this period, she noted a significant decrease in fasting glucose values from 148 ± 44 to 119.9 ± 25 as well as postprandial glucose values from 210.6 ± 79 to 181.1 ± 69 in this group of patients treated with fenugreek capsules. With regard to glycated hemoglobin, also noted a significant decrease from 8.25 ± 1.2 to 7.54 ± 0.9 with p = <0.5. Similarly, for the secreted insulin level, after 2 months of treatment, there is a change in the AUC from 5630 ± 2428 to 2942 ± 1536 with p <0.01 and, consequently, an increase in the sensitivity of the insulin secretion. insulin from 57.14 ± 41.15 to 112.9 ± 67 with p <0.05 [8].Other animal studies have produced similar results, such as the study by Winiarska H et al. in a population of 60 diabetic rats after intraperitoneal treatment with streptozocin, a change in fasting blood glucose from 119.7 ± 7.7 to 84.0 ± 7.9 after 4 weeks' treatment with fenugreek extract due to 1g / kg [9].In the same context Abdel-Barry JA et al. conducted a study in a rat population in which he concluded that intraperitoneal administration of the aqueous extract of fenugreek significantly decreased the glycemic value in both the control and diabetic rats, whereas oral administration of the aqueous extract resulted in a significant decrease only in alloxan-treated rats [10].Annida B et al. by a similar study in a group of 36 rats, 6 of which were normal and 30 treated with streptozocin, showed that supplementation with fenugreek extract significantly decreased the blood glucose value in treated rats by 265.7 ± 21.3 at 195.8 ± 16.7 for a dose of 0.5 g / kg and

118.3 ± 6.3 for a dose of 1 g / kg [11].An Egyptian study led by Ramadan G et al. in 2010 proved the hypoglycemic effect of fenugreek powder as well as other benefits at low and high doses (0.5 and 1g / kg) in a rat population with more modulation of disturbed parameters by increasing the dose of fenugreek [12].On the other hand, a recent study by karimeh Haghani Ph.D. et al. evaluated the effects of swimming training and aqueous extract of fenugreek, alone or in combination, on blood glucose and the activity of cardiac antioxidant enzymes in rats after induction of diabetes by intraperitoneal injection of streptozocin. After 8 weeks of management, there was a marked increase in blood glucose in the group of rats treated with streptozocin compared to the control group, and the blood glucose value in rats treated with fenugreek and after swimming training. has shown a significant decrease and this decrease is more marked after the combination of swimming and taking the aqueous fenugreek extract [13]. The hypoglycemic effect of the soluble fraction of fenugreek dietary fiber was thus evaluated by Hannan JM et al. by administering a dose of 0.5 g / kg to healthy rats, type 1 and type 2 diabetics. A significant decrease was noted with a more marked decrease after simultaneous gavage administration of glucose, this fraction of fenugreek suppressed the peak glucose level after 30 minutes after oral ingestion of sucrose in both healthy rats and streptozocin-treated rats [14].

To conclude, Neelakantan N et al. conducted a meta-analysis of clinical trials investigating the hypoglycemic effect of fenugreek, and as a result, a total of 10 trials were identified that showed that fenugreek was drastically altered fasting blood glucose -0.96mmol / L, postprandial 2H blood glucose -2.19mmol / L, and glycated hemoglobin -0.85% compared to control groups. The heterogeneity of the results in the studies is partly explained by the diabetes status and the dose of fenugreek used, the significant effect is noted only with the studies using a medium or high dose of fenugreek [15].On the other hand, several studies have identified different active principles of fenugreek that have been responsible for the effects mentioned above [16], several authors, such as Basch E, Sauvaire Y, Haber SL and Jasim Naaim were interested in the acid amino-4-hydroxyisoleucine, an amino acid extracted and purified from fenugreek seeds, they have shown that it is the agent responsible for increasing the level of insulin secreted postprandial by pancreatic β cells, the stimulation of the effect of this amino acid is strictly glucose-dependent due to its exclusive secretagogue activity of insulin by pancreatic cells [7,17,18,19], as well as Mohammad Ishraq Zafar in his study focusing on this amino acid as a target of a new diabetes treatment, has shown that in addition to its secretagogue effect of postprandial insulin, 4-amino-hydroxyisoleucine acid has been

shown to inhibit of TNF-α, which increases the sensitivity of insulin, in addition to an increase in TNF-α conversion and a decrease in the expression of TIMP3, hence a decrease in resistance to insulin and better sensitivity. In addition, this study shows that this amino acid accelerates the use of glucose, inhibits hepatic glucose production and possibly a decrease in the plasma glucose value [20,21]. Another potential active ingredient of fenugreek is trigonellin, this is the major alkaloid component of fenugreek responsible for hypoglycemic activity, reduction of diabetic neuropathies and regeneration of pancreatic β cells and secretion of insulin [16].In addition, we find the saponins that are most abundant in the fenugreek composition [22], Yoshikawa discovered six saponins in fenugreek seeds that are generally divided into two major classes: spirostanole and furostanole, of which the furostanole are the majority [22].In his study, Swaroop A et al. cited furan-containing saponins as the active ingredient in fenugreek hypoglycemic activity, which showed strong hypoglycemic activity in type 2 diabetic rats after treatment with streptozocin, compared with the effect of metformin for 30 days of study [23], in addition that Saravanan G et al. considered diosgenin, which is formed secondarily after enzymatic reactions from furostanol saponins [22], as an active ingredient of fenugreek, and evaluated its effect on carbohydrate metabolic modification and glycogen content in carbohydrate. muscles and kidneys made of diabetic rats after treatment with streptozocin, they thus showed a moderation of the parameters disturbed by streptozocin administration such as a significant drop in blood glucose after 45-day treatment with high doses of diosgenin and an increase in plasma insulin concentration [24].While Perla V et al. have established that the biguanide-related compounds may be, in part, the active ingredients since fenugreek seeds contain a good amount (18.98 µg / g) [25].Fenugreek seeds are a source of dietary fiber, they contain 45% dietary fiber, 32% of which is insoluble fiber and 13.3% is soluble, the insoluble fiber is not assimilated by the enzymes present in the human digestive tract, they have an emollient activity for stool and are considered to be hungry [22].Soluble fiber is known by its ability to suppress postprandial glucose elevation in addition to decreased intestinal glucose uptake and decreased gastrointestinal mobility [26], another study of small fenugreek fibers by Hannan JMA showed that soluble fiber significantly improved glucose hemostasis in type 1 and 2 diabetics by delaying digestion and carbohydrate absorption in addition to stimulating the action of insulin [14]. On the other hand, Aditya G showed that the presence of polyphenols and flavonoids, such as vitexin, tricine, naringenin, quercetin and tricine-7-Obeta- D-glucopyranosides, led to an inhibition of α-activity. -amylase and α-glucosidase, two enzymes responsible respectively for the hydrolysis of starch oligosaccharides and oligosaccharides,

trisaccharides and disaccharides in glucose and other monosaccharides, a decrease in blood glucose is the result of this inhibition of metabolism carbohydrates [27].Klim K et al. in a recent study, identified a new compound of fenugreek with potential therapeutic application in the treatment of type 2 diabetes, N-linoloyl-2-amino-γ-butyrolactone (N55), the latter binding to GLP-1R (7-36) -amide, improves the stimulation power of the cAMP pathway. Glucagon-like peptide-1-receptor (GLP-1R) is expressed in several tissues and is involved in many physiological functions, GLP-1R analogs are proven in the treatment of type 2 diabetes subject of different clinical studies of several abnormalities. N55 is known to promote the production of cAMP and stimulate endocytosis of GLP-1 in pancreatic cells [28].Gaddam A et al. studied another property of fenugreek concerning its role in the prevention of type 2 diabetes in predisposed subjects, this is a 3-year investigation of the effect of a twice-daily dose of 5g of fenugreek before meals in subjects predisposed to type 2 diabetes, a control group consisting of 66 and a group of 74 adults treated with fenugreek, at the end of this intervention the prevalence of diabetes was significantly reduced in subjects treated with fenugreek compared to the control group, a reduction in fasting glucose and postprandial blood glucose levels was also noted, as well as a significant increase in plasma insulin levels.

The control group is 4.2 times more likely to develop diabetes compared to fenugreek treated subjects, this is positively correlated with plasma insulin and negatively correlated with insulin resistance (HOMA-IR) [29]. Regarding the lipid balance, our study shows a significant decrease after the fenugreek intake of total cholesterol and triglyceride levels respectively with a difference of -0.6400 ± 0.13 mmol / L (p =, 000) and -0, 2008 ± 0.02mmol / L (p = .000) with an increase in HDL-cholesterol of +0.194 ± 0.17 mmol / L (p = .000).These results are consistent with the work of Sharma et al. who noted a significant reduction in total cholesterol of approximately 1.3mMol / L with p <0.001 and LDL cholesterol of 1.0 mMol / L with p <0.001 but the HDL-cholesterol value remains unchanged [7,30].Another study conducted in 60 subjects with type 2 diabetes with a supplementation with 25g of fenugreek powder daily for 24 weeks, showed a decrease in total cholesterol, LDL-cholesterol and triglycerides by 14-16% during the study period and an increase in HDL-cholesterol by 10% [31].In the same context, Soumaya and Rajyalakshmi also observed a significant reduction in the values of the same parameters in a group of 20 adults with dyslipidemia by consuming 12.5 to 18g of fenugreek powders per day for 1 month [7,32]. In another study, Sharma also reported a reduction in total cholesterol in 5 diabetics treated with 25g of fenugreek seeds for a 21-day period [33].Thus, the study of Bordia et al. investigating the effect of 2.5g fenugreek

powder taken orally twice daily in 40 subjects with coronary heart disease, a reduction in total cholesterol and triglycerides was observed while there was no change in HDL-cholesterol value [34].Annida B et al. in their study in the six groups of rats, showed a rise in total cholesterol and triglyceride values in the group of rats treated with streptozocin compared to the control group, respectively 208.1 ± 12.8 compared to 72, 3 ± 2.1 mg / dL and 25.6 ± 1.8 vs 12.4 ± 0.4 mg / dL. Taking 0.5 and 1 g / kg of fenugreek seeds led the total cholesterol value respectively to 186.0 ± 10.6 mg / dL and 129.2 ± 9.5 mg / dL and the triglyceride value to 21,8±1,5mg/dL and 18.9 ± 1.4 mg / dL [11].The Egyptian study conducted by Gamal R et al. proved the fenugreek modulating effect of lipid parameters disturbed by the treatment of rats with alloxan and by a diet rich in lipid, in fact, they cause a significant increase in total lipids, total cholesterol, triglycerides and atherogenic index compared to the control group. The use of fenugreek has improved these parameters whose effect is dose-dependent; indeed, better modulation is induced by the high dose of fenugreek seeds [12]. Mukthamba P performed similar results in his study in high-fat lipid-fed Wistar rats after 8 weeks of treatment with fenugreek and oil separately or in combination. The increase in serum triglycerides caused by the lipid diet was bypassed by taking 20% fenugreek and 20%, and the increase in total cholesterol and LDL cholesterol was corrected by 24% and 38%, respectively increased HDL-cholesterol by 17%, these corrections are more marked in the case of the combination of fenugreek and oil [15].A Moroccan study by Harchane H et al. on a group of 40 Wistar rats shows that prolonged treatment with aqueous extract of fenugreek seeds improves the lipid profile resulting in a 34% decrease in total cholesterol, 32% in triglycerides, 38% in LDL-cholesterol with a 36% increase in HDL-cholesterol [16].In Tunisia, Khlifi S et al. conducted a study of the effect of a 2.5 and 5g dose of fenugreek for 30 days on the serum lipid profile of a population of type 2 diabetics, they found a significant dose dependent decrease triglyceride levels and non-significant reductions in total cholesterol and HDL-cholesterol were recorded [17].Ethan Basch attributed these effects on the lipid parameters of fenugreek to its sapogenins [7], these effects seem to be related to the ability of diosgenin to inhibit the absorption of cholesterol, to lower the concentration of hepatic cholesterol and to increase secretion gallbladder [19].Regarding the anthropometric parameters that were compared before and after taking the fenugreek extract, we found a good evolution of the different measures. Indeed, there has been a decrease in BMI, TT respectively -5.56 ± 1.42 Kg / m2 and -10.46 ± 5.92 cm. Linear regression analysis introducing blood glucose as a dependent variable and BMI, waist circumference, insulin and resistin as explanatory variables show a strong correlation between blood glucose and BMI and insulin, which explains significant

reduction in BMI after treatment with extract fenugreek. Another study by Wan-Li Xue Ph.D. et al. in China, in a group of 70 male mice weighing between 100 and 110 g and made diabetic by treatment with streptozotocin, in addition to a diet rich in lactose and lipid for 8 weeks to induce insulin resistance. After 6 weeks of treatment with metformin and the aqueous extract of fenugreek at different doses, weight gain was noted in this group of mice treated against a remarkable weight loss in the group of untreated mice, this is in favor of the fenugreek extract attenuates the streptozocin-induced toxicity especially at high doses [39]. Ikeuchi et al. evaluated the dose-dependent efficacy of fenugreek extract due to 300mg / kg body mass in a group of male mice, on endurance capacity in swimming over a 4-week period. The administration of fenugreek has therefore resulted in a significant increase in training time, these results have shown that this improvement is due to the increase in the use of fatty acids as a source of energy [40].In addition to Kumar et al. reported a significant weight loss, a reduction of body mass index, plasma lipids and cardiac risk factors in rats consuming aqueous extract of fenugreek, and this by the regulation of appetite by reducing the level of leptin in adipose tissue [22].The likely mechanism of fenugreek in weight loss and fat reduction may be the removal of carbohydrates from the body before they enter the bloodstream resulting in weight loss [19].Some studies show that consumption of fenugreek has led to a change in eating behavior in humans, which can help better weight management, consider the new sedentary lifestyle, poor eating habits high in calories and by consequently the rising epidemic of obesity worldwide [25].In addition to the high proportion of soluble fiber that has a gelatinous structure slowing the digestion and absorption of food which gives a sensation of fullness thus suppressing appetite and promoting weight loss [37].

CONCLUSION

Type 2 diabetes is a disease in its own right that can lead to many complications affecting quality of life. Its increase and frequency are a public health problem in our country. It would be wise to seek effective therapeutic means, other than allopathy, to improve anthropometric, biochemical and hormonal parameters and thus reduce the risk of morbidity. Therapeutic means with fewer side effects and lower cost. In our study, we tried to prove the role of fenugreek seeds associated with a regular physical activity in the improvement of parameters disturbed by type 2 diabetes. There was a clear improvement in anthropometric, biochemical and hormonal parameters. In fact, there was a significant decrease in BMI and waist circumference, an increase in HDL-C and a decrease in LDL-C levels, as well as a decrease in fasting blood glucose and insulin levels. The reduction of resistin would, therefore, be

beneficial to the health of our patients by its detrimental effects on insulin sensitivity and its pro-inflammatory role. From these results, our work approves the benefits of consuming fenugreek seeds in obese patients with type 2 diabetes and especially its association with regular physical activity. It is therefore important to promote the phytotherapy that is starting to fit into the health system as part of the therapeutic arsenal of diabetes

REFERENCES

1. Ronald G, Zubin P. Définition, classification et diagnostic du diabète, du prédiabète et du syndrome métabolique. Can j Diabetes. 2013; 37 Suppl 5: 369-72.
2. Wild S, Roglic G, Green A, Scree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004; 27 (5): 1047-53.
3. Hiba AB, Sofyan NM, Rabab FT, Reema FT. The Postprandial Hypoglycemic Activity of Fenugreek Seed and Seeds' Extract in Type 2 Diabetics: A Pilot Study. Phcog Mag. 2009 ; 5 (18) : 134-8.
4. Schlienger JL. Diabète et phytothérapie : les faits. Médecine des Maladies Métaboliques. 2014; 8 (1): 101-6.
5. Kassaian N, Azadbakht L, Forghani B, Amini M. Effect of fenugreek seeds on blood glucose and lipid profiles in type 2 diabetic patients. Int J Vitam Nutr Res. 2009; 79 (1): 34-9.
6. Madar Z, Abel R, Samish S, Arad J. Glucose-lowering effect of fenugreek in non-insulin dependent diabetics. Eur J Clin Nutr.1988; 42 (1): 51-4.
7. Basch E, Ulbricht C, Kuo G, Szapary P, Smith M. Therapeutic applications of fenugreek. Altern Med Rev. 2003; 8 (1): 20-7.
8. Gupta A, Gupta R, Lal B. Effect of Trigonella foenum-graecum (fenugreek) seeds on glycaemic control and insulin resistance in type 2 diabetes mellitus: a double-blind placebo controlled study. J Assoc Physicians India. 2001; (49): 1057-61.
9. Winiarska H, Dworacka M, BoroWsKA M, Bobkiewicz KT, Gorecki P, Mscisz A, et al. The effects of plant extracts of Medicago sativa and Trigonella foenum-graecum on postprandial glucose levels in type 2 diabetic rats. Herba Polonica. 2007; 53 (4): 34-44.
10. Abdel-Barry JA, Abdel-Hassan IA, Al-Hakiem MH. Hypoglycaemic and antihyperglycaemic effects of Trigonella foenum-graecum leaf in normal and alloxan induced diabetic rats. J Ethnopharmacol. 1997; 58 (3): 149-55.
11. Annida B, Stanely-Mainzen P. Supplementation of fenugreek leaves lower lipid profile in streptozocin-induced diabetic rats. J Med Food. 2004; 7 (2): 153-6.
12. Ramadan G, El-Beih NM, Abd-El-Kareem HF. Anti-metabolic syndrome and immunostimulant activities of Egyptian fenugreek seeds in
diabetic/obese and immunosuppressive rat models. Br J Nutr. 2011; 105 (7):995-1004.
13. Haghani K, Bakhtiyari S, Doost-Mohammadpour J. Alterations in plasma glucose and cardiac antioxidant enzymes activity in streptozocin-induced diabetic rats: Effects of Trigonella foenum-graecum extract and swimming training. Can J Diabetes. 2016 ; 40 (2) : 135-42.
14. Hannan JM, Ali L, Rokeya B, Khaleque J, Akhter M, Flatt PR et al. Soluble dietary fibre fraction of Trigonella foenum-graecum (fenugreek) seed improves glucose homeostasis in animal models of type 1 and type 2 diabetes by delaying carbohydrate digestion and absorption and enhancing insulin action. Br J Nutr. 2007; 97 (3): 514-21.
15. Neelakantan N, Narayanan M, Souza RJ, Dam RM. Effect of fenugreek (Trigonella foenum-graecum L.) intake on glycemia: a meta-analysis of clinical trials. Nutr J. 2014; 13 (7): 13-7.
16. Rios JL, Francini F, Schinella GR. Natural products for the treatment of type 2 diabetes millitus. Planta Med. 2015; 81 (12-13): 975-94.
17. Sauvaire Y, Petit P, Broca C, Manteghetti M, Baissac Y, Fernandez- Alvarez J, et al. 4-Hydroxyisoleucine: A novel amino acid potentiator of insulin secretion. Diabetes. 1998; 47: 206-10.
18. Haber SL, Keonavong J. Fenugreek use in patients with diabetes mellitus. Am J Health Syst Pharm. 2013; 70: 1196-1203.

19. Al-Naim JN. Therapeutic use of fenugreek (Trigonella foenum-graecum L.). AJSIH. 2014; 5(29): 21-36.
20. Zafar MI, Gao F. 4-Hydroxyisoleucine: A potential new treatment for type 2 diabetes mellitus. BioDrugs. 2016; 30(4): 255-62.
21. Broca C, Brevil V, Cruciani-Guglielmacci, Manteghetti M, Rouault C, Derouet M, et al. Insulinotropic agent ID-1101 (4-hydroxyisoleucine) activates insulin signaling in rat. Am J Physiol Endocrinol Metab. 2004; 287(3): 463-71.
22. Nagulapalli-Venkata KC, Swaroop A, Bagchi D, Bishayee A. A small plant with big benefits: Fenugreek (Trigonella foenum-graecum Linn.) for disease prevention and health promotion. Mol Nutr Food Res. 2017; 61(6).
23. Swaroop A, Bagchi M, Kumar P, Preuss HG, Tiwari K, Marone PA, et al. Safety, efficacy and toxicological evaluation of a novel, patented antidiabetic extract of Trigonella Foenum-Graecum seed extract (Fenfuro). Toxicol Mech Methods. 2014; 24 (7): 495-503.
24. Saravanan G, Ponmurugan P, Deepa P, Senthilkumar B. Modulatory effects of diosgenin on attenuating the key enzymes activities of carbohydrate metabolism and glycogen content in streptozocin-induced diabetic rats. Can J Diabetes. 2014; 38 (6): 409-14.
25. Perla V, Jayanty SS. Biguanide related compounds in traditional antidiabetic functional foods. Food Chem. 2013; 138 (2-3): 1574-80.
26. Yadav UC, Baquer NZ. Pharmacological effects of Trigonella foenumgraecum L. in health and disease. Pharm Biol. 2014; 52(2): 243-54.
27. Aditya G, Varsha D, Yash B. In vitro α-amylase and α-glucosidase inhibitory potential of Trigonella foenum-graecum leaves extract. Ayu.2013; 34(1): 109-12.
28. King K, Lin NP, Cheng YH, Chen GH, Chein RJ. Isolation of positive modulator of glucagon-like peptide-1 signaling from Trigonella foenumgraecum (Fenugreek) seed. J Biol Chem. 2015; 290 (43): 26235-48.
29. Gaddam A, Galla C, Thummisetti S, Marikanty RK, Palanisamy UD, Rao PV. Role of fenugreek in the prevention of type 2 diabetes mellitus in prediabetes. J Diabetes Disord. 2015; 14 (74): 1186-96.
30. Sharma RD, Raghuram TC, Rao NS. Effect of fenugreek seeds on blood glucose and serum lipids in type I diabetes. Eur J Cln Nutr. 1990; 44: 301-6.
31. Sharma RD, Sarkar A, Hazra DK. Toxicological evaluation of fenugreek seeds: a long term feeding experiment in diabetic patients. Phytother Res. 1996; 10: 519-20.
32. Sowmya P, Rajyalakshmi P. Hypocholesterolemic effect of germinated fenugreek seeds in humain subjects. Plant Foods Hum Nutr. 1999; 53: 359-65.
33. Sharma RD. An evaluation of hypocholesterolemic factor of fenugreek seeds (T foenum-graecum) in rats. Nutr Res Int. 1986; (33): 669-77.
34. Bordia A, Verma SK, Srivastara KC. Effect of ginger (Zingiber officinale Rosc.) and fenugreek (Trigonella foenumgraecum L.) on blood lipids, blood sugar and platelet aggregation in patients with coronary artery disease. Prostaglandins Leukot Essent Fatty Acids. 1997; (56): 379-84.
35. Mukthamba P, Krishnapura S. Hypolipidemic and antioxidant effects of dietary fenugreek (Trigonella foenum-graecum) seeds and garlic (Allium satvum) in high-fat fed rats. Food Biosc. 2016 ; 14(1) : 1-9.
36. Harchane H, Addas H, Amasaguine S, El-Amrani N, Radallah D. Effets de l'extrait aqueux des graines du fenugrec (Trigonella foenum graecum) sur l'amélioration du profil lipidique et la prise de poids chez le rat. Phytothérapie. 2012 ; 10 (6) : 357-62.
37. Khlifi S, Abaza H, Ben-Jemaa H, Benhmad H, Abid A, Guemira F, et al. Effet du fenugrec sur le profile lipidique sérique d'une population tunisienne de diabétiques type 2. Nutrition clinique et métabolisme. 2013 ; 27 (1) : 100.
38. Handa T, Yamaguchi K, Sono Y, Yazawa K. Effects of fenugreek seed extract in obese mice fed a high-fat diet. Biosci Biotechnol Biochem. 2005 ; 69 (6) : 1186-8.
39. Xue WL, Li XS, Zhang J, Liu YH, Wang ZL, Zhang RJ. Effect of Trigonella foenum-graecum (fenugreek) extracts on blood glucose, blood lipid and hemorheological properties in streptozocin-induced diabetic rats. Asia Pac J Clin Nutr. 2007; 16 (1): 422-6.
40. Anuj M, Narsingh V, Anand S, Manashi B, Harry GP, Kiran T, et al. Efficacy of Furosap, a novel Trigonella foenum-graecum seed extract, in enhancing testosterone level and improving sperm profile in male volunteers. Int J Med Sci. 2017; 14(1): 58-66.