

# Trigonella foenum- graecom L. Anti-Glycemic and Anti-Hypertensive Effects in Healthy Men

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## Abstract

Introduction: Fenugreek (Trigonella foenumm- graecum L.) is widely used against several diseases, particularly against diabetes. It owned great interest because of copious biologically active substances that it contains. In this work, the in vivo effect of fenugreek seeds' intake on hemodynamic, blood sugar level and hematological parameters was evaluated in healthy volunteers. Materials and Methods: Ten healthy volunteer men had been included in the experiment. Their overnight fasting blood sugar level, hemodynamic and hematological parameters were evaluated before, and one hour after the intake of 10 g of powdered fenugreek seeds in a form of water suspension. Results: The T-paired test showed significant decrease in the arterial blood pressure (from 9.20  $\pm$  0.65 to 8.43  $\pm$  0.31 cmHg for the mean arterial pressure; and 7.80  $\pm$  1.03 to 6.7  $\pm$  0.67 cmHg for the arterial diastolic pressure) and heart frequency (from 77.3 ± 3.23 to 75.40 ± 3.37 bits/min), and an increase in total white blood cell (8.24 ± 2.29 and 8.79 ± 2,30.10<sup>3</sup>/µL; p ≤0.01) and granulocytes (4.87 ± 0.37 to 4.97 ± 0.40 .10<sup>3</sup>/µL, p ≤0.01) counts, one hour after fenugreek seeds intake. In addition the overnight- fasting blood sugar level was diminished from  $5.71 \pm 0.37$  to  $5.37 \pm 0.44$  mmol/L, at p  $\leq 0.001$ . Conclusion: The present work demonstrates the anti-hypertensive and antihyperglycemic effects of fenugreek seeds, and consolidates its usage as alternate remedy against these chronic pathologies. It is suggested to realize specific allergic tests before its application.

Keywords: Fenugreek; Seeds; Anti-hyperglycemia; Anti-hypertension

## 1. Introduction

Recently, great interest is brought back to therapeutic plants' usage as nutritional supplement or medication to prevent and manage several chronic diseases. Current researches highlighted that fenugreek (Trigonella foenum- graecum L.), a Mediterranean annual Fabaceae herb, exerts beneficial effects on human and animal health. It is suggested to counteract obesity, cancer, diabetes, cardiovascular diseases, bacterial and fungal infestation, and reproductive disorders, as well as much other pathology [1]. The main phyto-therapeutic effects of *T. foenum- graecum* result from various bioactive compound that it contains. Particularly, this plant is highly rich in proteins, amino acids, saponins, flavonoids, polyphenols, fiber, minerals and polysaccharides [2,3]. The steroidal saponins (diosgenin, eugenol, gingenol, zingenone, cedrene) found in *T. foenum- graecum* seeds are of great concern because of their anti-neoplastic activities [4-8]. Other *T. foenum- graecum* fractions modulate blood sugar levels and insulin secretion and thereby ameliorate the wound healing and prevent diabetes [9-12]. The anti- obesity effect of fenugreek might be bypassed through repressing adipocytes' proliferation and lipids metabolism [13,14]. It also stimulates anti-oxidative enzymes activities and decreases the ROS release, a major protective pathway against several pathologies [15,16]. In contrary, some case reports outlined that using fenugreek or its extract induced allergic reaction which was much pronounced in asthma patients [17].

This work aimed to evaluate the effect of fenugreek intake on some clinic parameters, particularly blood glucose levels and arterial blood pressure, in healthy volunteers.

## 2. Material and Methods

Fenugreek preparation: a commercialized indigenous fenugreek (*Trigonella foenum-graecum* L, Fabacae family) seeds were purchased from a local vendor. After washing using distillated water and dried into ambient temperature (20°C), 200 g of seeds were thinly powdered and mixed with drinking water in order to obtain a final solution's volume of 2 L.

Subjects: ten healthy men were admitted in the experiment. After being informed, they signed a written contentment for participation. All participants confirmed their usual consumption of fenugreek as food ingredient. Their anthropometric profile is shown in TABLE 1. Our experimental design was in conformity with the guidelines of the Declaration of Helsinki and Tokyo for humans and was approved by a local ethical comity at the Laboratory of Pharmacology of the Medicine Faculty of Sfax.

Age (years)	34,40 ± 3,23
Tall (m)	$1,71 \pm 0,04$
Weight (kg)	76,64 ± 4,81

TABLE 1. Anthropometric parameters of the study-included volunteers.

#### 2.1 Study design

All subjects were kept fasting before and throughout the experimentation. Volunteers' arterial blood pressure and hematological parameters, in addition to their blood sugar levels were diagnosed at admission and one hour after 100 ml of *T*. *foenum- graecum* solution's intake. All diagnostic measurements were carried out by an unaware Physician, and were accomplished at a Local Hospital.

The blood pressure (Systolic [SAP] and Diastolic [DAP] and mean arterial [MAP] pressures) and heart frequency were recorded using arm cuff- stethoscope, at a setting position, after at least 15 minutes of rest. Thereafter, withdrawal of venous blood samples were carried out, in order to assess hematological parameters (Mindray BC-3000 plus automated apparatus, Shenzhen Mindray Bio-medical Electronics Co., Ltd.) and glucose level (Mindray BA-88A automated apparatus, Shenzhen Mindray Bio-medical Electronics Co., Ltd.), at each time- point of the experimentation. Two hours after the experiment termination, subjects did not experience any sign of intoxication and felt well.

#### 2.2 Statistical analysis

T- Paired test was used to compare the obtained results between the baseline and 60 minutes after the *T. foenum- graecum* solution's intake. SPSS for Windows 11 software was used to carry out the statistical analysis. All results are expressed as mean values  $\pm$  standard deviation.

#### 3. Results

Our results showed that the mean arterial blood pressure significantly decreased from  $9.20 \pm 0.65$  cmHg at T0 to  $8.43 \pm 0.31$  cmHg at T1 (p <0.001). Similarly, a significant lowering was observed in DAP (7.80 ± 1.03 and 6.70 ± 0.67 cmHg, respectively at T0 and T1) and heart frequency (77.30 ± 3.23 and 75.40 ± 3.37 bits/min, respectively at T0 and T1); but no significant change was observed in the systolic pressure (FIG. 1). The Fenugreek- postprandial level of blood sugar diminished significantly from  $5.71 \pm 0.37$  mmol/L to  $5.37 \pm 0.44$  mmol/L, at p ≤ 0.001 (FIG. 2).



FIG. 1. Variation of the arterial pressure and the cardiac frequency following *T. foenum-graecum* intake. (\*) significant difference at  $p \le 0.01$ .



FIG. 2. Variation of the granulocytes and white blood cells (WBC) counts and blood glucose level following *T. foenum-graecum* intake. (\*) significant difference at  $p \le 0.01$ .

The analysis of the hematological profile did not exhibit any significant modification in erythrocytes and thrombocytes numerations and indices, except for the mean thrombocytes' volume (VMP). This later decreased from  $8.85 \pm 0.62$  fL to  $8.54 \pm 0.51$  fL at the end of the experiment ( $p \le 0.01$ ) [TABLE 2]. The FIG. 2 shows a significant increase in granulocytes number (from  $4.87 \pm 0.37 \ 10^3/\mu$ L at T<sub>0</sub> to  $4.97 \pm 0.40 \ 10^3/\mu$ L at T<sub>1</sub>,  $p \le 0.01$ ); and in the total count of white blood cells ( $8.24 \pm 2.29 \ 10^3/\mu$ L and  $8.79 \pm 2.30 \ 10^3/\mu$ L; respectively before and 60 minutes after fenugreek intake;  $p \le 0.001$ ). Other immune cell parameters were unchanged [Table 2].

	T0 (at admission)	T1 (1 Hr after treatment)
RBC (10 <sup>6</sup> /µL)	4,97 ± 0,37	5,06 ± 0,34
HGB (g/dL)	15,69 ± 2,15	15,76 ± 1,75
HCT (%)	48,20 ± 7,07	48,05 ± 5,60
CCMH (g/dL)	32,44 ± 3,27	32,31 ± 3,03
TMH (pg)	30,70 ± 2,26	30,55 ± 1,81
VGM (fL)	89,19 ± 14,10	88,67 ± 12,93
PCT (%)	$0,237 \pm 0,023$	$0,228 \pm 0,024$
IDP	$15,67 \pm 0,18$	$15,54 \pm 0,23$
MPV (fL)	$8,85 \pm 0,62$	8,54 ± 0,51 (*)
Lymphocytes (10 <sup>3</sup> /µL)	2,30 ± 0,39	2,40 ± 0,41
Lymphocytes (%)	$32,08 \pm 4,00$	30,35 ± 4,70

TABLE 2. Hematological parameters of healthy volonteers before and following T. foenum-graecum intake.

## 4. Discussion

*Trigonella foenum-graecum* L has been used as a spices and medication against various diseases in folkloric medicine. Recently, it owned great attention, particularly for its anti-diabetic and anti-tumor effects. In this work, some clinical hematological and hemodynamic outcomes are investigated in healthy volunteers following the intake of a water- suspension of powdered fenugreek which is a traditional meal consumed by local Tunisian populations.

At the assayed dose ( $\approx$ 10 g of fenugreek seeds/ subject), there was a significant decrease in the mean arterial blood pressure which is attributed to the lowering of the diastolic event and heart frequency. Although several studies reported the use of this Fabacae plant as antihypertensive [18], few clinical works were reported, in such concern. Talpur et al [19] found that a combination of various essential plants' oils, including which of *T. foenum- graecum*, exerts continual lowering of the arterial blood pressure, in fatty rats. The blood pressure decrease might result from the inhibitory effect of *T. foenum- graecum* is seed extracts limit the angiotensinergic vascular contractility [20]. It was also shown that *T. foenum- graecum* is seed extracts limit the angiotensin I conversion to its vasoconstrictor form (angiotensin II) by conformational docking to ACE site of action and its dislocation [7], thus reduces the systemic blood pressure.

As expected, substantial hypoglycemia was checked after fenugreek seeds intake. The modulation of carbohydrate metabolic key enzymes, such as the repression of  $\alpha$ -amylase and maltase activities and the enhancement of which of the phosphor-fructo-kinase in intestine mucosa and liver are the main modus operandi of the anti-hyperglycemic effect. In addition, it was evidenced that fenugreek (extracts) stimulates insulin secretion and/or activity and its receptor expression, and thereby improves diabetes mellitus wound healing [11,21,22]. Eidi and her colleagues [23] found that fenugreek seeds anti-glycemic effect is dose dependent and much more potent in diabetic rats than in healthy ones.

In our experimental series, granulocytes and total white blood cell counts were augmented. This event might be explained by Patil et al, [17] reported allergic reaction following fenugreek usage, in some clinical cases. Galactomannan, a polysaccharide found in *T. foenum- graecum* extracts, was shown to enhance the dentretic cells maturations [24]. It also stimulates phagocytosis and macrophages proliferation [25]. Some subsets of immune cells' mobilization / proliferation have been also observed in long-time treatment of Humans using a fenugreek extract [26].

This event might bring substantial explanation for the observed mobilization of immune cell lineages in our work. Other authors reported that it exerts anti-inflammatory and anti-nociceptive action [27,28]. Such divergence could be a consequence of the variability of the used part and extracts of the plant, and perhaps the applied posology and individual response to the treatment (dose and duration of administration).

In exception of the mean platelets' volume decrease, we did not find significant changes in erythrocytes and thrombocytes parameters one hour after fenugreek intake. The decline in thrombocytes volume might be related to anti-aggregative effect of the plant [29]. In long treatment using the phyto-therapeutic plant several reports outlined that it ameliorates hemoglobin synthesis and counteract anemia. Its richness in several metabolites and cofactors for hemoglobin synthesis such as iron, folate and ascorbate is sought as patent effectors against the pathology [28,30].

## 5. Conclusion

Our findings highlight the potential of fenugreek seeds to improve wound healing of several diseases; and that is almost safe. In raison of its hypoglecymic and anti- hypertensive effects, *Trigonella foenum graecum* consumption is suggested to wound heal diabetes associated to hypertension. It is suggested that it could be used as dietetic supply against diabetes complicated by hypertension. Because of the immune system activation by its extracts, particular measurement should be considered for allergic patients. Much deeper investigations are envisaged to better evaluate its usage as remedy for complicated diseases.

## 6. Acknowledgment

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## 7. Conflict of Interest

Authors declare that there are no conflicts of interest.

## REFERENCES

- 1. Sheikhlar A. Trigonella foenum- graecum L. (fenugreek) as a medicinal herb in animals growth and health. Sci Int. 2013;1(6):194-8.
- Acharya S, Srichamreon A, Basu S, et al. Improvement in the nutraceutical properties of fenugreek (Trigonella foenum- graecum L.). Songklanakarin J Sci Technol. 2006;28(suppl.1):1-9.
- 3. Sulieman A-ME, Ahmed HE, Abdelrahim AM. The chemical composition of fenugreek (Trigonella foenum graecum L) and the antimicrobial properties of its seed oil. Gezira J Eng Appl Sci. 2008;3(2):52-71.
- Taylor WG, Zaman MS, Mir Z, et al. Analysis of steroidal sapogenins from amber fenugreek (Trigonella foenumgraecum) by capillary gas chromatography and combined gas chromatography/ mass spectrometry. J Agric Food Chem. 1997;45(3):753-9.
- 5. Taylor WG, Elder JL, Chang PR, et al. Microdetermination of diosgenin from fenugreek (Trigonella foenumgraecum) seeds. J Agric Food Chem. 2000;48(11):5206-10.
- 6. Alizadeh S, Jahanmehr SA-H, Ardjimand AR, et al. Antineoplastic effect of fenugreek (Trigonella foenum graecum) seed extract against acute myeloblastic leukemia cell line (KG-1). Iran J Blood Cancer. 2009;1(4):139-46.
- 7. Priya V, Jananie RK, Vijayalakshmi K. Molecular docking analysis of compounds present in Trigonella foenum graecum with angiotensin converting enzyme insilico analysis. J Chem Pharm. Res. 2011;3(4):129-39.
- Khalil MIM, Ibrahim MM, El-Gaaly GA, et al. Trigonella foenum (fenugreek) induced apoptosis in hepatocellular carcinoma cell line, HepG2, mediated by upregulation of p53 and proliferating cell nuclear antigen. BioMed Res. Inter. 2015.
- 9. Goplapura PB, Jayanthi C, Dubey S. Effect of Trigonella foenum graecum seeds on the glycemic index of food: a clinical evaluation. Int J Diab Dev Ctries. 2007;27(2):41-5.
- Damodaran C, Koduru S, Kumar R, et al. Diosgenin targets Akt-mediated signaling in human breast cancer cells. Int J Cancer. 2009;25(4):961-7.

- Ali NM, Zamzami MA, Khoja SM. Regulation of hepatic and mucosal 6- phosphofructo-1-kinase activity by Trigonella foeum- graecum Linn (fenugreek) seeds of streptozoticin- induced diabetic rats. J Diab Res Clin Metabol. 2013;2:18.
- 12. Robert SD, Ismail AAS, Wan-Rosli WI. Trigonella foenum- graecum seeds lowers postprandial blood glucose in overweight and obese individuals. J Nutr Metabol. 2014.
- 13. Sharma RD, Sarkar A, Hazra DK, et al. Hypolipidaemic effect of fenugreek seeds: a chronic study in non- insulin dependent diabetic patients. Phytotherapy Res. 1996;10(4):332-4.
- 14. Ilavenil S, Arasu MV, Lee JC, et al. Trigonelline attenuates the adipocyte differentiation and lipid accumulation in 3T3-L1 cells. Phytomed. 2014;21(5):758-65.
- 15. Bukhari SB, Bhanger MI, Memon S. Antioxidant activity of extracts of fenugreek seeds (Trigonella foenumgraecum). Pak J anal Environ Chem. 2008;9(2):78-83.
- 16. Devi R, Nandhini J, Madhavan M, et al. The effect of fenugreek (Trigonella foenum- graecum ) intake on the oxidative stress in hypercholesterolaemic subjects. Nat J Lab Med. 2013;2(1):5-7.
- 17. Patil SP, Niphadkar PV, Bapat MM. Allergy to fenugreek (Trigonella foenum graecum). Ann Allergy Asthma Immunol. 1997;78(3):297-300.
- Ziyyat A, Legssyer A, Mekhfi H, et al. Phytotherapyof hypertension and diabetes in oriental Morocco. J Ethnopharmacol. 1997;58(1):45-54.
- 19. Talpur N, Echard B, Ingram C, et al. Effects of a novel formulation of essential oil on glucose insulin metabolism in diabetic and hypertensive rats: a pilot study. Diabetes Obes Metab. 2005;7(2):193-9.
- 20. Vaez-Mahdavi MR, Roghani M, Baluchnejadmorjarad T. The role of adrenergic and angiotensinergic systems in vascular effect of alcoholic extract of Trigonella foenum- graecum seed in diabetic rats. Iran J Pharm Res. 2010;10(1):83-8.
- 21. Robert SD, Ismail AAS, Wan-Rosli WI. Trigonella foenum- graecum seeds lowers postprandial blood glucose in overweight and obese individuals. J. Nutr. Metabol. 2014.
- 22. Amin A, Alkaabi A, Al-Falasi S, et al. Chemoprotective activities of TRigonella foenum graecum (fenugreek) against breast cancer. Cell Biol Int. 2005;29(8):687-94.
- 23. Eidi A, Eidi M, Sokhteh M. Effect of fenugreek (Trigonella foenum- graecum L) seeds on serum parameters in normal and streptozotocin- induced diabetic rats. Nutri Res. 2007;27(11):728-33.
- 24. Santander SP, Aoki M, Pombo M, et al. Galactomannan from Caesalpina spinosa induces phenotypic and functional maturation of human dendretic cells. Int Immunopharmacol. 2011;11(6):652-60.
- Ramesh HP, Yamaki K, Tsushida T. Effect of fenugreek (Trigonella foenum-graecum L.) galactomannan fractions on phagocytosis in rat macrophages and on proliferation and IgM secretion in HB4C5 cells. Carbohydrate Polymers. 2002;50(1):79-83.
- 26. Maheshwari A, Verma N, Swaroop A, et al. Efficacy of Furosap<sup>™</sup>, 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.
- 27. Mandegary A, Pourmamdari M, Sharififan F, et al. Alkaloid and flavonoid rich fractions of Fenugreek seeds with antinociceptive and anti-inflammatory effects, Food Chem Toxicol. 2012;50(7):2503-07.
- 28. Suresh P, Kavitha Ch N, Babu SM, et al. Effect of ethanol extract of Trigonella foenum graecum (fenugreek) seeds

on Freund's adjuvant- induced arthritis in albino rats. Inflammation. 2012;35(4):1314-21.

- 29. Tej Eldin I, Abdulmutalab MM, Bikir HE. An in vitro anticoagulant effect of fenugreek (Trigonella foenum graecum) in blood samples of normal Sudanese individuals. Sudan J Pediatr. 2013;13(2):52-6.
- 30. Doshi M, Mirza A, Umarji B, et al. Effects of Trigonella foenum- graecum (fenugreek / methi) on hemoglobin levels in females of child bearing age. Biochem Res. 2012;23(1):47-50.