



## Effect of Fenugreek (*Trigonella foenum-graecum*) Seed Extract and Glibenclamide in Albino Rats with Diabetic

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**T**RIGONELLA *foenum* is using for therapeutic purposes in different cultures, which has an antidiabetic effect by reducing blood sugar concentrations. This work is aimed to determine the properties of antioxidant and poly phenol content of ethanolic fenugreek (*Trigonella foenum-graecum*) seed extract (FSE). Additionally, glibenclamide, a common medication, was contrasted with the antihyperglycemic Wister albino rats. Total flavonoid and total phenolic contents in FSE ( $\text{mg g}^{-1}$ ) accounted for 126.50 as QE and 325.07 as GAE; respectively whereas DPPH and ABTS (83.11 and 72%) were used to measure antioxidant activity. Six phenolic and five-flavonoid components were found in the FSE after examined using HPLC. Thirty rats were split up into five groups for the in vivo experiment. Group 1 was the normal control, whereas diabetic rats (caused by a single 100 mg/kg b.w. alloxan dose) were found in Group 2. Group three contained diabetic rats that received an oral dose of 10 mg/kg of glibenclamide. Group four contained diabetic rats orally administrated with 100 mg/kg FSE daily. Group 5 received an oral dose of with 200 mg/kg FSE. The study had 56 days. Administration of both dosages (100 and 200 mg/kg) with FSE diabetic rats significantly reduced blood glucose, total lipid, total cholesterol and LDL levels in diabetic rats, as well as increasing levels of high density lipoprotein cholesterol and enhancing kidney and liver functions.

**Keywords:** DPPH, Diabetes, Glibenclamide, Fenugreek extract.

### Introduction

Diabetes is a chronic disease, that threatens 500 million humans worldwide and it is expected to rise by 51% higher in 2045 (Saeedi et al., 2019). It causes harmful effects in the body's systems if not controlled, including micro and macrovascular events. Type 2 diabetes (T2DM) varies according to the sociodemographic characteristics of population groups (including the level of urbanization, employment, education, and income), and it has been rising quickly in developing countries (Misra et al., 2019).

*Trigonella foenum*, a member of Fabaceae family is an historical and widely used food and medicine plant in Egypt, China, India, and northern and eastern Africa (Acharya et al., 2006). Seeds, leaf extract have been studied for possible health and nutritional characteristics.

Phytochemical analysis reveals that leaves of fenugreek contain  $\beta$ -carotene, ascorbic acid and saponins. However, flavonoids and phenolic are the main components observed in various parts of fenugreek that are supposed to be responsible for all of its antioxidant properties (Sharma et al., 2017). A variety of metabolites, including polysaccharide, galactomannan, alkaloids such as choline and trigonelline, lipids, flavonoids, apigenin, luteolin, and quercetin, and numerous saponins like diosgenin and yamogenin, were observed in the seed extract (Seasotiya et al., 2014).

Various reports have indicated that hypoglycemic, hypo cholesterol emic and hyperactive insulinomic properties in Feungreek seed effects on those who have type 1 and type 2 as well as diabetic test animals (Khosla et al.,

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1995; Puri et al., 2002). In addition to saponins and 4-hydroxyisoleucine, which have hypoglycemic and antidiabetic properties, Trigonella seeds contain the following nutrients: ascorbic acid, tryptophan, arginine, nicotinic acid, niacin, chromium, copper, quercetin (flavonoid) and alkaloids, choline (Anuradha and Ravikumar, 2001). Besides this, a few longer-term fenugreek studies have shown reductions in plasma glucose during fasting (FPG and PPG) and glycated haemoglobin (HbA1c) (Madar et al., 1988; Gupta et al., 2001), while other research produced negative findings (Chevassus et al., 2009; Mathern et al., 2009). 45–60% of the carbohydrates in fenugreek seed consist of mucilaginous fiber (galactomannans); twenty to thirty proteins rich in tryptophan and lysine, 5–10% fixed oils (lipids), pyridine-type alkaloids just choline (0.5%), trigonelline (0.2–0.36%), gentianine, and flavonoids, carpaine, free amino acids, glycosides, cholesterol and sitosterol, vitamins and volatile oils (Shang et al., 1998; Blumenthal et al., 2000; Das & Sharangi, 2021). Fenugreek seed extract is extensively used to treat diabetes mellitus (DM) because numerous prior researches have been shown its antidiabetic activity and to be highly effective at removing free radicals and preventing oxidative stress (Belguith-Hadriche et al., 2013). The purpose of this study was to ascertain how fenugreek seed (FS) affected the function of the liver, kidneys, and serum blood glucose in rats suffering from type 2 diabetes mellitus (T2DM).

## Material and Methods

### Plant and animals

We bought fenugreek seeds from local market. Male albino rats with body weights of 120±10 g were acquired from Egyptian Drug Authority, EL-Manial, Cairo, Egypt.

### Determination of total phenolic compounds

Utilizing an AUV spectrophotometer (SM1600UV-vis Spectrophotometers, Azzota, USA) and following the instructions for colorimetric oxidation/reduction (Muntana and Parsing, 2010). The total amount of phenol contained was determined in the ethanolic extracts. 0.5 ml of the diluted extract (10 mg in 10 ml solvent) was combined with 2.5 ml of the Folin-Ciocalteu reagent and 2 ml of sodium carbonate (75 g/l). After incubating at 50°C for five minutes, the samples were cooled. The control samples were distilled water (0.5 ml). At 760 nm the absorbance was analyzed. The gallic acid equivalent (GAE) is used to express the total phenolic content.

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### Determination of total flavonoids

The method of Ordon et al. (2006) was applied with minor modifications to determine the total flavonoid content. 1.5 ml of the 20 g/l AlCl<sub>3</sub> ethanolic solution was mixed with 0.5 ml of the extract solution (10 mg in 10 ml solvent). The absorbance was analyzed at 420 nm at room temperature an hour after addition. The presence of flavonoids is indicated by a yellow colour. Extract samples were assessed at a final concentration of mg/ml. The QE (quercetin equivalents) is used to express the total flavonoid content.

### DPPH radical-scavenging activity

The purple-colored DPPH solution was bleached using the method of Hanato et al. (1988) to determine the extracts' electron donating capacity. 100 µL of the extract (10 mg extract/10 ml solvent) was added to 3 ml of 0.1 mM DPPH dissolved in ethanol. Following a half-hour incubation time the absorbance at 517 nm at room temperature, in comparison to the control. The following equation was used to calculate the percentage of antioxidant activity:

$$\text{Antioxidant activity (inhibition) \%} = \left[ \frac{A_{\text{control}} - A_{\text{sample}}}{A_{\text{control}}} \right] \times 100$$

where:  $A_{\text{control}}$  is the absorbance of the control reaction and  $A_{\text{sample}}$  is the absorbance in the plant extract.

### 2.5. ABTS•+ radical scavenging activity

The cation decolonization test was used to make the determination as described by Zielinski et al. (2014). 7 mM ABTS•+ and 2.4 mM K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> (1:1, v/v) stock solution mixture was diluted with methanol to give 0.706 absorbance at 734 nm after being left in the dark for 12–16 hr at room temperature. After incubating in a dark area for two hours, 150 µl of the sample was added to 2.85 ml of ABTS solution, and the absorbance was measured at 734 nm.

$$\text{ABTS radical scavenging activity \%} = \left[ \frac{A_{\text{control}} - A_{\text{sample}}}{A_{\text{control}}} \right] \times 100$$

where Abs sample and Abs control are the absorbance values of ABTS•+ control and sample; respectively.

### HPLC analysis

HPLC system HP1100 (Agilent Technologies, Palo Alto, CA, USA) equipped with a diode array detector (DAD, Hewlett Packard 1050), quaternary pump, and autosampler was utilized, to identify the phenolic chemicals in FSE according

to Kim et al. (2006). The system made use of an Altima C18, 5 × 150 mm, 4.6 mm ID column and an Altima C18, 5 mm guard column (Alltech). The concentrations of acetic acid in the solvent system were A (2.5%), B (8%) and C (acetonitrile). The extraction process involved applying 70% methanol to a freeze-dried sample (1:10), allowing the extremely clear extract to evaporate under the N stream, resolving it in methanol, filtering it, and injecting it. The methanolic extracted samples 70% were administered ten microlitres at a millilitre per minute flow rate.

#### *Extract preparation for biological experiments*

Seeds of Fenugreek were clean and dried at 40°C and mechanically grinding, dissolved a ratio of ethanol 80% (1:10) in a Soxhlet for 72 h. Filtration was done on the mixture using a Büchner funnel with filter paper in and then concentrated until it was dry using a rotary evaporator. The experimental animal was then given the extract orally after it had been diluted in distilled water to treat hyperglycemia (Eidi et al., 2007; Al-Timimi, 2019).

#### *Biological design for experiment*

Thirty adult male wister strain albinos weighed 120 grams. They were housed at room temperature in a cage made of stainless steel with a wire bottom. Rats were fed a basal diet and kept in normal health conditions for a period of 14 days. Animals were then divided into two major groups. First main group (group 1), consisting of six rats, was treated as a healthy control. The second biggest group (24 rats) were the group of diabetes. Just one injection dosage of 100 mg kg<sup>-1</sup> body weight of alloxan solution was given to rats (Buko et al., 1996). After 24 hr of alloxan injection, the presence of diabetes was examined, (glucose blood level was exceeding than 180 mg dl<sup>-1</sup>) and then they were established into four subgroups (six rats each). Group (2) was given a basal diet for 8 weeks while being maintained as (positive control) for a diabetic. For eight weeks, Group (3) was given a basal diet and a dosage of glibenclamid (10 mg/kg body weight per day). Group (4) was given a basal diet and 100 mg kg<sup>-1</sup> body orally. Group (5) was given a normal diet and received orally fenugreek seed extract (200 mg/kg body weight/day) for 8 weeks. The decoction was administered at a doses of 100 and 200 mg/kg<sup>1</sup> body weight FSE (fenugreek seed extract) for eight weeks using a Sondi needle (Osman et al., 2020; Bafadam et al., 2021).

#### *Blood sampling, biochemical analysis and Histological evaluation*

Using tiny capillary heparinized tubes, samples of blood were taken from each rat's retro-orbital plexus veins at the end of the experiment. Serum was used for investigation the biochemical markers, such as the lipid profile and tests for liver and kidney function. The following protocols were followed to evaluate the activities of serum albumin, total protein, and the enzymes of liver, including AST, ALT and ALP (Reitman, and Frankel (1957); Tietz et al., 1983; Doumas et al., 1971; Doumas et al., 1973), respectively. By calculating albumin from serum total protein, the globulin was estimated. Urea, uric acid and creatinine were among the kidney function indicators that were evaluated using the procedure described in Amer et al. (2007). The methods of Ramadan et al. (2008) were used to determine the lipid profile, which included (TAG, total TC, HDL and LDL).

In addition, a histological assay was used to examine the samples of pancreatic tissue. Rats in each group provided the tissue samples, which were quickly preserved by fixing them with neutral buffered formalin at 10%. Following conventional protocols, thin paraffin slices were made and assessed under a microscope. Hematoxylin after that, eosin (H&E) stain was used to the sections in accordance with the recommendations given by Suvarna et al. (2018). Each experimental group's pancreatic tissue architecture and cellular morphology could be thoroughly evaluated thanks to this histological examination.

#### *Statistical analysis*

One-way ANOVA was used to analyses all the data. The differences between the treatments means has been eliminated using Duncan's new multiple-range test. The statistical program SPSS 11.0 (SPSS Ltd., Surrey, UK) was used for all statistical analyses. A p50.05 was considered statistically significant. Ratio values were not arcsin transformed before statistical analysis (Steel et al., 1997).

## **Results**

#### *Total phenolic, total flavonoid and antiradical activities of fenugreek seed extract (FSE)*

Total flavonoid and phenolic content results are shown in Fig. 1. FSE had a high content of total flavonoid (126.50 mg QE/1g) and phenolic compounds (325.07 mg GAE/g). This study showed that, FSE demonstrated the highest

activity in DPPH and ABTS 83.11 and 72.01%. The data presented matches with what was reported by Osman et al. (2020).

*Using HPLC, some of antioxidant components of the ethanolic extract were identified*

Metabolomics profiling has been investigated to assess the biological activities of the ethanolic extract of FSE. Eleven polyphenolic compounds (phenolic and flavonoid fractions) were found, their quantities were assessed by HPLC, as shown in Table 1 and Fig. 2 (a & b). This percentage of polyphenols has a major effect on human health. An ethanol extract was selected for the toxicity study given the fact that it contains several potent bioactive phytoconstituents that distinguish it from more extractions that are solvent as additional pharmacological research using the FS-EOH. Table 1 shows that the main identified phenolic compounds and their contents ( $\mu\text{g/ml}$ ) in FSE were Ellagic (14.39), followed by pyrogallol (8.12). The main compounds of flavonoid ( $\mu\text{g/ml}$ ) was Querestin (12.69) followed by Kampherol

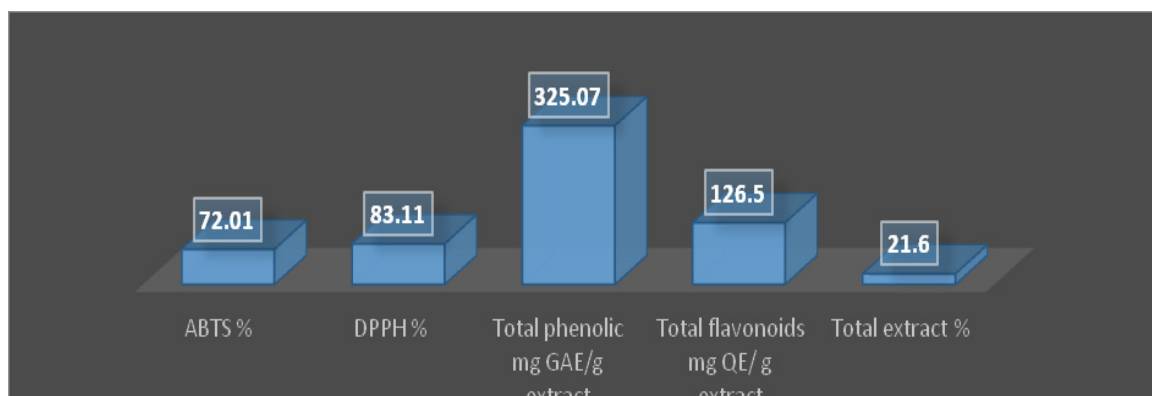
(4.33). The data presented matches with what was reported by Varsha and Jain (2018) and Benziane et al. (2019).

*Biological evaluation*

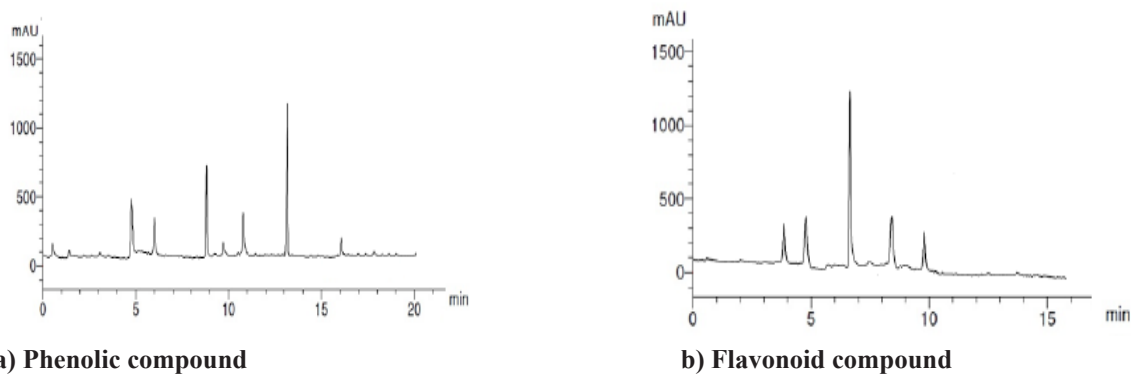
After 56 days Serum glucose, liver function lipid profile, and kidney function were assessed

*Effect of FSE treatment on blood glucose*

Table 2 shows the result of fasting blood sugar level. Significant ( $p < 0.001$ ) increasing in blood glucose levels in the positive group ( $370.4 \text{ mg dl}^{-1}$ ), than those of the normal group ( $125.3 \text{ mg dl}^{-1}$ ). After a 56-day administration of FSE (100 and 200  $\text{mg/kg}$ ) or (10  $\text{mg/kg}$ ) glibenclamide, rats with diabetes had blood glucose levels that were lowered to 140.9, 131.4, and 121.5  $\text{mg dl}^{-1}$ ; respectively. These results are agreement with those reported by Thakran, et al. (2004); Baset, et al (2020); Bafadam et al. (2021) and Dahab et al. (2024), who reported that blood glucose levels in all treated groups rats administered fenugreek extraction, was considerably less than that of the diabetic group.



**Fig.1. Antiradical activities, total phenolic and flavonoid of fenugreek seed extract.**



**Fig. 2. Antioxidant components in an ethanolic extract were identified using HPLC.**

**TABLE 1. Identification of some antioxidant components of the seed ethanolic extract by utilizing HPLC:**

Components	RT	Conc. ( $\mu\text{g/ml}$ )
<b>Phenolic compounds</b>		
1. Syringic acid	4.8	4.22
2. P-Coumaric	6	2.55
3. Pyrogallol	9	8.12
4. Gallic	10	5.66
5. Ferulic acid	11	3.21
6. Ellagic	13	14.39
<b>Flavonoid compound</b>		
1. OH-Flavon	3.9	2.3
2. Rutin	5.0	4.12
3. Querestatin	6.8	12.69
4. Kampherol	8.2	4.33
5. Apegenin	9.9	2.05

**TABLE 2. Effects of FSE and glibenclamide treatments on blood glucose levels in both positive and negative groups**

G	Serum glucose			
	Before injection	After injection	After 4 weeks	After 8 weeks
1 Control negative	124.1 <sup>a</sup> $\pm$ 4.9	123.5 <sup>b</sup> $\pm$ 2.4	124.2 <sup>c</sup> $\pm$ 2.5	125.3 <sup>bc</sup> $\pm$ 1.0
2 Diabetic (100 mg/kg alloxan)	123.4 <sup>a</sup> $\pm$ 3.2	340.7 <sup>a</sup> $\pm$ 13.4	343.3 <sup>a</sup> $\pm$ 24.8	370.4 <sup>a</sup> $\pm$ 12.8
3 10 (mg/kg) GLI + Diabetic	123.5 <sup>a</sup> $\pm$ 3.0	329.7 <sup>a</sup> $\pm$ 10.0	220.3 <sup>b</sup> $\pm$ 9.3	121.5 <sup>c</sup> $\pm$ 3.8
4 100 (mg/kg) FSE + Diabetic	123.4 <sup>a</sup> $\pm$ 2.7	323.9 <sup>a</sup> $\pm$ 7.2	242.3 <sup>b</sup> $\pm$ 7.8	140.9 <sup>b</sup> $\pm$ 5.4
5 200 (mg/kg) FSE + Diabetic	124.0 <sup>a</sup> $\pm$ 0.7	326.5 <sup>a</sup> $\pm$ 8.8	237.7 <sup>b</sup> $\pm$ 2.5	131.4 <sup>bc</sup> $\pm$ 4.2

SD: Each group's standard deviation, n = 6; FSE: Fenugreek Seed Extract; GLI: Glibenclamide; **Note:** Differentiated letters (a, b, c and d) indicate significant statistical differences ( $p < 0.001$ ) among the values in every column.

#### *Effects of FSE at different dose on lipid profile:*

The profile of lipid in serum of rats with diabetes is shown in Table 3. Serum levels of T. Lipid, Total C., TG and LDL were significantly ( $p < 0.001$ ) higher in diabetic rats. Rather, HDL decrease in comparison to the control normal. The lipid profile of serum (TC, TG and LDL) was improved in groups 3, 4 and 5 after they received 100 and 200 mg/kg FSE and glibenclamide 10 mg/kg for 56 days. This is because their levels decreased in comparison to rats with diabetes. Group 5, which was administered 200 mg/kg of FSE, illustrated a significantly ( $p < 0.001$ ) increase in high density lipoprotein level in comparison to the rats with diabetes. These results are consistent with those reported by Geberemeskel et al. (2019) and Dahab et al. (2024).

#### *Effect of FSE at different dose on liver and kidney functions of rats after 56 day*

Table 4 data acquired indicating a significant ( $p < 0.001$ ) enhance in liver enzyme levels (aspartate

aminotransferase, alanine transaminas, and ALP) between the diabetic rats and the normal control group. According to El-Hadary and Ramadan (2019) and Salim et al. (2023), the increase in activities of liver enzymes may be related to the hepatotoxic effects of alloxan caused by liver cell leakage into the bloodstream. When compared to control diabetic rats (group 2), the effect of FSE on liver enzyme in (group 4 & 5) which have diabetic rats showed a significant improvement in liver enzymes levels (Table 5). These results are uniform with Geberemeskel, et al. (2019).

Urea, uric and creatinine levels in rats with diabetes (group 2) were significantly higher than those in group one (Fig 3). Diabetes can cause abnormal renal function, as illustrated by decreased glomerular filtration and higher serum urea and creatinine, as well as damage to the blood vessels (arteries the kidneys) (Bamanikar et al., 2016; Dahab et al., 2024). When comparing the serum levels of urea and creatinine in diabetic

rats (groups 4, 5) treated with FSE to diabetic control rats, the data shown in Fig. 3 show a significant decrease. These results are accurate with (Berroukche, et al., 2018).

#### Histological assay

Examined serial sections of the negative control group's pancreas (G1) showed that, the acinar epithelium and its secretory granules were healthy, and both the exocrine and endocrine counterparties were normal. Endocrine Islets of Langerhans are the lighter staining areas. They were diffusely scattered throughout the body of the pancreas. Three significant cell types are present in the islets: Glucagon is formed by alpha ( $\alpha$ -cells) and elevates the concentration of plasma glucose. Primarily found on the outer edge of the islets, they are smaller than  $\beta$ -cells and have a deep eosinophilic cytoplasm. Insulin is produced by  $\beta$ -cells and lowers plasma glucose by encouraging absorption by the liver, skeletal muscle and adipose tissue (Fig. 4.1). Fragments of pancreatic tissue from alloxan induced diabetic

rats, (G2) recognized characteristic changes represented by moderate decrease in densities of the islets cells, degenerative changes in the  $\beta$ -cells of the islets, mainly cloudy swelling and hydropic degenerations. Necrotic and apoptotic changes in a moderate numbers of  $\beta$ -cells was a pathognomonic lesion as the necrotic cells completely or partially lost their nuclear and or the cytoplasmic components, sometimes with a ballooning changes in affected cells (Fig. 4.2). On the other hand, Rats given Glibenclamide 10 mg/kg (G3), demonstrated an almost normal exocrine pancreas including several cystically dilated pancreatic ducts that had accumulated intraductal secretory materials (Fig. 4.3). Compared with changes in the pancreatic tissue of diabetic administered rats (G2), serial sections from pancreas of administered rats which were treated with 100 and 200 mg/kg FSE alcoholic extracts (G 4, 5 ); respectively revealed degenerative changes (hydropic degeneration) in a few number of  $\beta$ -cells particularly in treated rats (G4).

**TABLE 3. Effect of glibenclamide and FSE treatment on lipid profile in both negative and positive groups.**

G	Lipid profile				
	Total Lipid	Triglyceride (mg/dl)	T. Cholesterol (mg/dl)	HDL (mg/dl)	LDL (mg/dl)
1 Control negative	475.9 <sup>b</sup> ± 2.5	150.2 <sup>d</sup> ± 1.0	151.6 <sup>c</sup> ± 1.4	55.3 <sup>a</sup> ± 0.6	74.3 <sup>d</sup> ± 1.23
2 Diabetic (100 mg/kg alloxan)	598.3 <sup>a</sup> ± 6.7	169.3 <sup>a</sup> ± 1.1	193.3 <sup>a</sup> ± 0.5	38.1 <sup>d</sup> ± 1.0	123.8 <sup>a</sup> ± 1.55
3 10 (mg/kg) GLI + Diabetic	403.3 <sup>c</sup> ± 4.9	156.1 <sup>c</sup> ± 3.5	151.0 <sup>c</sup> ± 1.9	47.3 <sup>b</sup> ± 2.1	84.8 <sup>c</sup> ± 0.31
4 100 (mg/kg) FSE + Diabetic	473.0 <sup>b</sup> ± 20.5	161.6 <sup>b</sup> ± 1.2	165.2 <sup>b</sup> ± 1.1	42.6 <sup>c</sup> ± 0.6	90.2 <sup>b</sup> ± 0.30
5 200 (mg/kg) FSE + Diabetic	482.6 <sup>b</sup> ± 5.1	155.4 <sup>c</sup> ± 5	143.5 <sup>d</sup> ± 3.0	49.7 <sup>b</sup> ± 0.5	83.5 <sup>c</sup> ± 0.61

SD: Each group's standard deviation, n = 6; FSE: Fenugreek Seed Extract; GLI: Glibenclamide; **Note:** Differentiated letters (a, b, c and d) indicate significant statistical differences ( $p < 0.001$ ) among the values in every column.

**TABLE 4. Treatment effect of glibenclamide and (FSE) on liver both negative and positive groups.**

G	ALT	AST	ALP	T. Protein	Albumin
1 Control negative	46.4 <sup>a</sup> ± 0.7	22.3 <sup>c</sup> ± 1.7	89.4 <sup>bc</sup> ± 0.87	7.03 <sup>ab</sup> ± 0.25	3.68 <sup>b</sup> ± 0.19
2 Diabetic (100 mg/kg alloxan)	65.6 <sup>a</sup> ± 16.2	59.5 <sup>a</sup> ± 0.7	129.2 <sup>a</sup> ± 0.86	7.45 <sup>a</sup> ± 0.33	4.22 <sup>a</sup> ± 0.11
3 10 (mg/kg) GLI + Diabetic	54.5 <sup>a</sup> ± 1.4	42.8 <sup>c</sup> ± 3.1	85.6 <sup>cd</sup> ± 0.67	6.95 <sup>ab</sup> ± 0.14	3.48 <sup>b</sup> ± 0.17
4 100 (mg/kg) FSE + Diabetic	60.3 <sup>a</sup> ± 1.1	51.1 <sup>b</sup> ± 1.1	92.6 <sup>b</sup> ± 2.64	6.59 <sup>b</sup> ± 0.24	2.37 <sup>c</sup> ± 0.24
5 200 (mg/kg) FSE + Diabetic	53.3 <sup>a</sup> ± 2.8	33.2 <sup>d</sup> ± 1.0	84.0 <sup>d</sup> ± 1.58	7.05 <sup>ab</sup> ± 0.28	3.37 <sup>b</sup> ± 0.04

SD: Each group's standard deviation, n = 6; FSE: Fenugreek Seed Extract; GLI: Glibenclamide; **Note:** Differentiated letters (a, b, c and d) indicate significant statistical differences ( $p < 0.001$ ) among the values in every column.

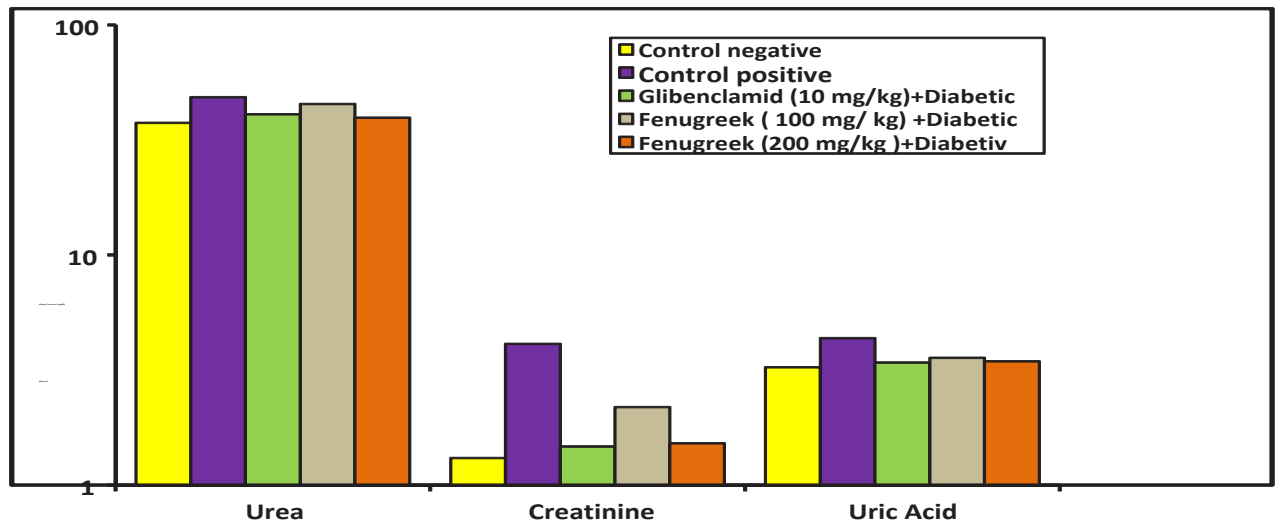


Fig. 3. Treatment effect of (FSE) and glibenclamide on kidney function in both negative and positive groups.

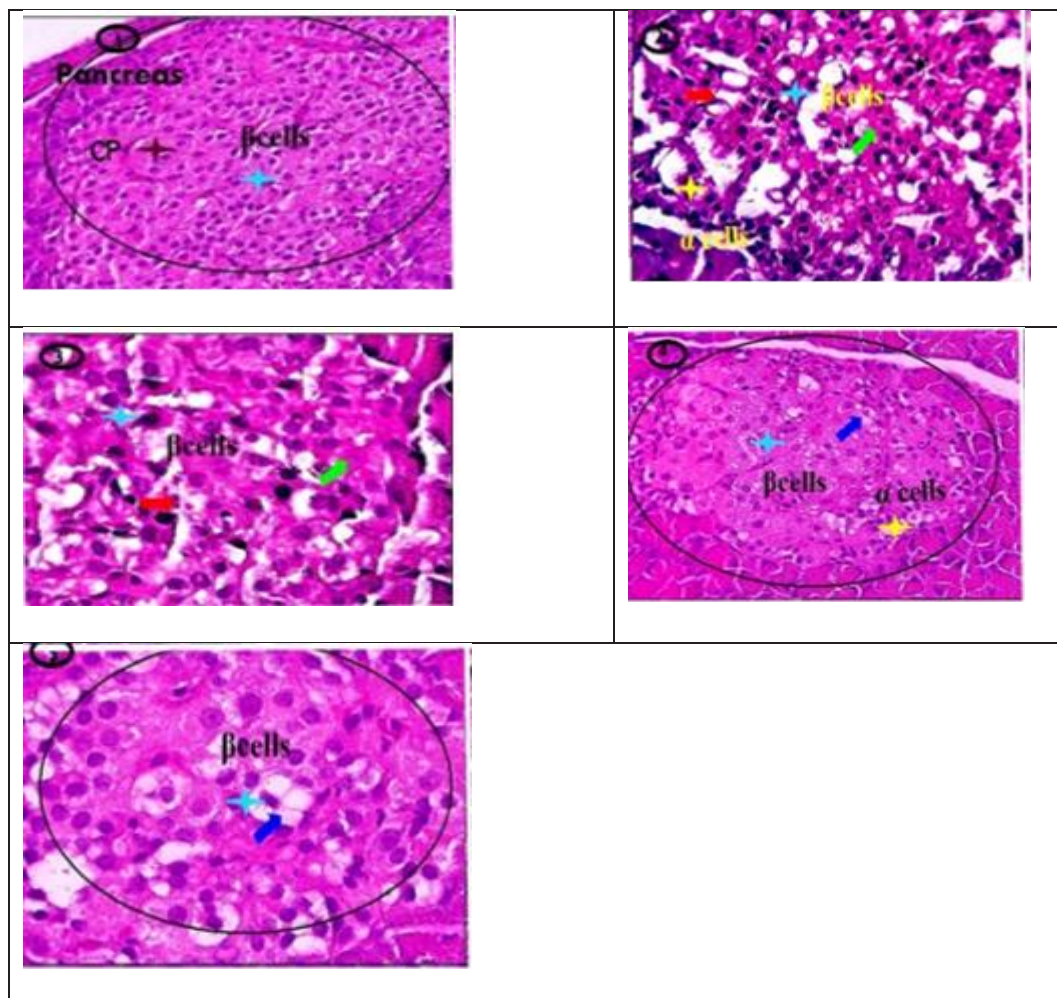


Fig. 4. (1, 2, 3, 4 and 5) Photomicrographs from pancreas of different experimental groups. H&E X 100, 200, 400.

## Discussion

Multiple interruptions in the body's metabolic processes, which are directly related to an abnormal accumulation of insulin, are the characteristics of diabetes. The aim of this research is to investigate the effects of fenugreek seed extract on blood glucose levels in rats with alloxan diabetes at its human therapeutic dose. Additionally, to demonstrate how fenugreek and alloxan diabetes for eight weeks of treatment effected the functional biochemical changes of the kidney and liver as well as the related histopathological alternations in the pancreas. By evaluating the extract's polyphenol content, its capacity as free radicals scavenger and its hypoglycemic effect in rats, the current study was able to evaluate the antioxidant and antidiabetic potential of FSE.

Higher polyphenol contents, significant blood sugar reduction potential and free radical scavenging activity were all demonstrated by the ethanol extract of FSE seeds. Although phenolic compounds are assumed to be produced by plants to protect them from biotic and abiotic stresses, they also help humans when they are released to oxidative stress carried on by disease. Rats that were given a significant amount of sugar effect of promoting induce hyperglycemia were used to evaluate the extract's glucose in the event of hyperglycemia. The 100 and 200 mg/kg extract doses were effective.

All the doses of FSE showed good activity in improving blood glucose levels compared with diabetic group as shown in Table 2. These results are similar to the findings on anti-diabetic studies that showed treatments significantly decreased elevated serum glucose levels in rats with diabetes (Thakran et al., 2004). It is commonly known that uncontrollable appearance of type 2 diabetes mellitus rises LDL and triglycerides while reducing HDL and increasing the risk of coronary artery disease (Geberemeskel et al., 2019). In our study, comparison to the normal control rats, alloxan treatment resulted in a significant increase in total cholesterol (TC), TG, and a decrease in HDL levels. Moreover, a significant reduction in TC, TG and an elevation of HDL was noticed in treated diabetic rats with FSE extract 200 mg/kg as shown in Table 3.

Table 4 illustrates that, alloxan treatment had a significant rise in ALT, AST and ALP, compared with control rats. Moreover, a significant reduction

in enzymes of liver were noticed in diabetic rats given treatment with 200 mg/kg FS extract. Figure 3 shows that, alloxan treatment had a significant increase in urea, Creatinine and Uric acid compared with control rats. Moreover, a significant reduction in kidney enzymes were noticed in diabetic rats given treatment with 200 mg/kg FS extract. When compared to the control group, rats given fenugreek treatment showed a non-significant increase in serum total protein and albumin.

## Conclusion

Ethanol extracts from fenugreek seeds have been investigated to enhance diabetic therapies; they have no unfavorable effects on lipid profiles, liver, or kidney function. Because of the antioxidant potential of the extract bio constituents (phenolics and flavonoids), the FSE was probably protective against hyperglycemia in albino rats. This indicates utilizing antioxidants found naturally in herbs to treat in vivo diabetes mellitus. Natural substances, such as quercetin, which aids in the treatment of type 2 diabetes, or the whole or particular active compounds of medicinal plants, are significant in preventing pathogenesis, which includes diabetes.

## Abbreviations

FSE: Fenugreek Seed Extract; GLI: Glibenclamide; ABTS: 2, 2'-Azino-bis (3-Ethylbenzothiazoline-6-Sulfonic); DPPH: 1, 1-Diphenyl-2-Picrylhydrazyl; acid; GAE: Gallic acid Equivalent; QE: Quercetin Equivalent; LDL: low-density lipoprotein; HDL: high density lipoprotein; TFC: total flavonoid content's; aspartate amino ferase: TPC: total phenolic content; ALT: alanine transaminase.

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