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RESEARCH ARTICLE

Therapeutic Role of Methanolic Extract of *Ocimum basilicum* L. Seeds and its Isolated Compound as Potent Antidiabetic and Antihyperlipidemic Agents

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ARTICLE HISTORY

Received: July 05, 2018
Revised: October 26, 2018
Accepted: January 03, 2019

DOI:
10.2174/2210315509666190117145617

Abstract: ***Background*:** *Ocimum basilicum* seed, commonly also known as Takhmaria in Gujarat. The seed of O. basilicum traditionally used to treat diabetes. This activity is related to the presence of flavonoids, the major compounds of the crude extract.

***Objective*:** The present study was planned to examine the antidiabetic and antihyperlipidemic potential of *Ocimum basilicum* Linn seed, used as a traditional treatment for diabetes mellitus.

***Method*:** The methanolic extracts of *O. basilicum* seed (40 mg/kg) and isolated compound apigenin (10 mg/kg) were administered orally for 15 days to streptozotocin (STZ)-induced diabetic rat. Anti diabetic activity, oral glucose tolerance test, change in body weight and lipid profile of diabetics rat treated with methanolic extracts of O. basilicum seed and isolated apigenin were assessed and which was further compared with normal, diabetic control and standard drug-treated rat. Histological examination was carried out on 15 days of treatment.

***Results*:** Methanolic extract of *O. basilicum* seed (40 mg/kg) and apigenin (10 mg/kg) produced a significant reduction in fasting blood glucose level ($p<0.01$) and ($p<0.001$) respectively in the streptozotocin-induced diabetic rat. Significant differences were observed in oral glucose tolerance test, serum lipid parameters and body weight for methanolic extract of *O. basilicum* and apigenin-treated diabetic rat as compared to diabetic, normal and standard drug-treated rat. The outcome of the histological examinations of the pancreas treated with a methanolic extract of *O. basilicum* and apigenin showed comparable regeneration of the cells, which were earlier necrosed by streptozotocin. Methanolic extract of *O. basilicum* and isolated compound apigenin exhibit significant antihyperglycemic and antihyperlipidemic activities in streptozotocin-induced diabetes in the rat.

***Conclusion*:** From above findings, it can be concluded that the *O. basilicum* seed and isolated compound apigenin must be considered as a potential candidate for the treatment of diabetes and lipid-lowering activities in streptozotocin-induced diabetes in the rat.

Keywords: Antidiabetic activity, Antihyperlipidemic activity, Methanolic extracts of *Ocimum basilicum* seed (MEOBS), Apigenin, Streptozotocin.

1. INTRODUCTION

Diabetes mellitus (DM), characterized by increased fasting and postprandial blood sugar levels, is a chronic disorder of carbohydrate, fat and protein metabolism [1]. The incidence of diabetes is alarming and has exceeded epidemic proportion particularly among the upper age group. It has been predicted by the World Health Organization (WHO) that the major burden will occur in developing countries. Several studies conducted in the last decade, have emphasized that not only the prevalence of diabetes is high but is also increasing rapidly in urban population [2].

According to the International Diabetes Federation's (IDF) statistics of the year 2017,425 million adults (20-79 years) were living with diabetes; by 2045, this will rise to 629 million. Diabetes is related to micro- and macro-vascular complications, along with hyperglycemia and abnormalities in serum lipids, which are the major causes of morbidity and death in diabetic subjects. Patients suffering from cardiovascular diseases generally have increased blood cholesterol and low-density lipoprotein (LDL), with an increased activity of lipid peroxidation, which are the hallmarks of hypercholesterolemia [3].

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2210-3155/20 $65.00+.00

Long-term damage and dysfunction of various organs including the eyes, kidneys, nerves, and blood vessels have been found with abnormal increase of blood glucose in diabetes [4]. People with diabetes are more probable to have retina damage, nephropathy, amputation and stroke [5]. Currently, diabetes mellitus is amongst one of the ten foremost causes of death and one of the most costly chronic diseases worldwide [6]. Therefore, there is an urgent need to investigate antidiabetic drugs by considering safety and efficacy aspects. Synthetic drugs including biguanides, sulphonylureas, thiazolidinediones-glycosidase inhibitors, insulin, *etc.* are available as modern medicines for the management of DM [7]. However, these synthetic drugs have undesired side effects connected with their usage [8].

Ocimum basilicum L. (Lamiaceae), commonly known as sweet basil is an important medicinal plant found throughout India. *O. basilicum* leaves possess antimicrobial, anti-inflammatory, antioxidant, anti ulcerogenic, analgesic, cardiac stimulant, chemomodulatory, CNS depressant, hepatoprotective, hypoglycemic, larvicidal and hypolipidemic activities. *O. basilicum* seeds, also known as Takhmaria in Gujarat, India, possess antioxidant, antimicrobial, aphrodisiac, α-glucosidase and α-amylase diuretic and antidysenteric actions [9] and also possess antidiabetic activity [10].

The purpose of the present research was to evaluate the antidiabetic and antihyperlipidemic potential of methanolic extract of *O. basilicum* seeds (MEOBS) and its isolated compound apigenin in streptozotocin (STZ)-induced diabetic rats along with glibenclamideas as reference standard to generate scientific data with justification to support the activity.

2. MATERIALS AND METHODS

2.1. Collection and Authentication of Plant Material

The *O. basilicum* seeds were collected from the local market, Ahmedabad, Gujarat, and were authenticated by Dr. Bhasker L. Pungani (Head of P. G. Centre in Botany, Smt. S. M. Panchal Science College, Talod, Gujarat). An authenticated voucher herbarium specimen of the seeds was deposited at the Pharmaceutical Analysis laboratory of Institute of Pharmacy, NU for future reference.

2.2. Instrument

A Shimadzu (Kyoto, Japan) model, 1800 double beam UV-Visible spectrophotometer with a spectral width of 2 nm, wavelength accuracy of ± 0.5 nm and a pair of 10 mm matched quartz cells, A Sartorius CP224S (Gottingen, Germany) analytical balance, and Glucometer ATICO Medical Pvt. Ltd (Ambala, India) were used for the study.

2.3. Chemicals and Reagents

Glucose was procured from S.D fine chemicals, Ahmedabad, India. Glibenclamide and streptozotocin (STZ) were purchased from Orchid Chemicals & Pharmaceuticals Ltd., Chennai, India. Glucose kit, urine analysis kit, triglycerides kit and total cholesterol kit were purchased from Span Diagnostics, Surat, India. Solvents and other chemicals required for the experiment were of analytical grade.

2.4. Preparation of Methanolic Extract of *O. basilicum* Seeds (MEOBS)

Air- dried powder (100 gm) of *O. basilicum* seeds was defatted by refluxing with 250 mL petroleum ether (60-80°C) for 4 h. The residue was air dried and subjected to Soxhlet extraction using methanol for 4 h and filtered through Whatman filter paper No 41. The above procedure was repeated three times to get complete extraction from the powder. All extracts were combined and evaporated using vacuum-assisted rotary evaporator at 40°C. Residues were weighed and the dried extract was stored in an air-tight container protected from light and air.

2.5. Preliminary Phytochemical Analysis

Preliminary phytochemical screening was carried out to find the presence of active chemical constituents in methanolic extract such as alkaloids, flavonoids, tannins, phenolic compounds, saponins steroids, fixed oils and fats. In general, tests for the presence of phytochemical compounds involve the addition of appropriate chemical reagent(s) to the extract in test tubes. The mixture was then shaken and/or heated as the case may be. The alkaloids were tested using Mayer test. The flavonoids were tested by alkaline reagent test and the presence of tannins was checked by ferric chloride test. The total phenolic content in extract was also determined by ferric chloride test, and saponin content was determined by froth formation test. The steroids and triterpenoids were tested by salkowski test. The presence of carbohydrate was determined by molisch test.

Densitometric evaluation was carried out on pre-coated silica gel G60 F HPTLC plates using toluene–acetone–formic acid (5:4:1, *v/v*) as the mobile phase. Scanning and densitometric evaluations were done at 340 nm [11].

2.6. Acute Toxicity Study

The MEOBS was administered orally in doses of 20, 100, 250, 500 and 1000 mg/kg to groups of Wistar Albino rats (n = 6) as per OECD 423 guidelines and the percentage mortality was noted 24 h later. A dose of 1000 mg/kg showed the toxic symptoms, so according to the OECD guideline 423, it is considered as a LD cut off value [12].

2.7. Selection of Dose

Doses selected for pharmacological studies by fixed dose methods were 20 mg/kg and 40 mg/kg. The dose of apigenin was selected on the basis of previous reports where apigenin was used as a protective agent used in hepatocarcinogenesis [13].

2.8. Isolation and Identification of the Active Compound

Isolated flavonoid compound was purified and separated by column chromatography method. The column was packed with silica gel-H (60-120#, Spectochem Pvt. Ltd). Slurry of silica gel was added into a glass column having 45 cm length and 3 cm width. The flavonoid extract was bound with silica gel and loaded on top of the column. The column was eluted with a solvent system of toluene-acetone-formic acid system 5:4:1 (v/v/v) until all fractions were collected. The purified compound obtained by column chromatography from the

seed of *O. basilicum* was characterized using various spectroscopic techniques and the structure was confirmed.

2.9. Experimental Animals

Wistar Albino rats (200-250 gm) of either sex were procured from Zydus Cadila Health care, Ahmedabad, India. They were housed at the animal house of Arihant School of Pharmacy, Ahmedabad, India. The animals were housed in standard cages and kept under standard condition. The protocol for the experimental study was approved by the institutional animal ethics committee of Arihant School of Pharmacy & Bio-research Institute, Ahmedabad, India. (Protocol No: ASP&BRI/AH/2016/01)

2.10. Induction of Diabetes

Diabetes was induced in rats by intraperitoneal (i.p.) injection of streptozotocin (STZ) dissolved in 0.1 M cold citrate buffer (pH=4.5) at a dose of 65mg/kg bodyweight. Diabetes was confirmed by the determination of fasting blood glucose level on the second day post administration of STZ. After 48 h, animals with fasting blood glucose levels greater than 200 mg/dL were considered diabetic and included in this study.

2.11. Animal Grouping for OGTT

For a week, the animals were allowed to acclimatize at laboratory environment, and randomly divided into five groups (n = 6) as mentioned below:

Group I: (Control) animals were administered with distilled water (10 mL/kg p.o.)

Group II: (Standard) animals were administered with glibenclamide (standard drug) (1.5 mg/kg p.o.)

Groups III: (MEOBS I) animals were administered with MEOBS at dose of (20 mg/kg p.o.)

Groups IV: (MEOBS II) animals were administered with MEOBS at dose of (40 mg/kg p.o.)

Groups V: Apigenin (API) animals were administered with isolated marker apigenin (10 mg/kg p.o.)

OGTT was carried out after 15 days of treatment, during which the animals were fed with normal diet. After the treatment of 15 days, glucose (2.5 gm/kg) was fed 30 min after the administration of extracts. The rats fasted overnight and blood was withdrawn from tail-vein just prior to the drug administration (normal fasting) and at 0, 30, 60 and 120 min of glucose loading. Blood glucose level was measured immediately by using glucometer [14].

2.12. Animal Grouping for STZ Induced Diabetes

For a week, the animals were allowed to acclimatize at laboratory environment, and randomly divided into six groups (n = 6) as mentioned below

Group I, Control rats (Control): Animals were administered with normal saline for (p.o.) 15th days.

Group II, Diabetic control rats (DC): Animals were administered with STZ (65 mg/ kg, i.p.) on the 1stday.

Groups III, (MEOBS -I): Animals were administered with MEOBS (20 mg/kg, p.o) treated diabetic rats, for 15 days from 3rd day onwards of STZ administration.

Groups IV, (MEOBS -II): Animals were administered with MEOBS (40 mg/kg, p.o) treated diabetic rats, for 15 days from 3rd day onwards of STZ administration.

Groups V, (API), Animals were administered with apigenin (10 mg/kg, p.o) treated diabetic rats, for 15th days from 3rd onwards of STZ administration.

Group VI, (Standard): Animals were administered with glibenclamide, (1.5 mg/kg, p.o) treated diabetic rats, for 15 days from 3rd day onwards of STZ [15].

2.13. Effect on Body Weight

Change in body weight was assessed in the diabetic animals treated with MEOBS and apigenin and compared with diabetic control and normal rats after the 15th day of the study [16].

2.14. Estimation of Serum Biochemical Parameters

At the end of the experimental period (on day 15), animals were sacrificed after an overnight fast, anesthetized by diethyl ether and blood samples were collected by a direct cardiac puncture. Serum was separated after coagulation at room temperature for 30 min and centrifuged at 3000 rpm for 10 min, which was stored at -20^{o}C until biochemical parameters were determined. Serum lipid profile was assessed in the diabetic animals treated with MEOBS and apigenin and compared with diabetic control and normal rats [17].

2.15. Collection of Blood Samples and Glucose Determination

Blood samples were retrieved one hour after drug administration from the retro-orbital plexus in overnight fasted and anesthetized rats using diethyl ether solution inhalation. Blood glucose levels were measured on day(s) 1, 5, 10 and 15 of the study by glucose oxidation method. Plasma triglycerides levels, and plasma cholesterol levels were measured on 15 days of the study using commercially available kits (Span Diagnostics).

2.16. Histological Examination of the Rat Pancreas and Livers

At the end of the experimental period (on day 15), the animals were sacrificed after an overnight fast, and anesthetized with diethyl ether. Pancreatic tissues from all groups of the rats were subjected to histopathological studies. A pancreas of the rat had been taken and fixed in 10% neutral formalin, dehydrated by a graded alcohol series, embedded in paraffin and cut into sections. Sections of about 4 µm thickness of pancreases were stained with hematoxylin and eosin, which were further evaluated under a light microscope [18].

2.17. Statistical Analysis

The results are expressed as mean ± SEM. Statistical analysis was done using one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests. In all tests, the criterion for statistical significance was

Table 1. Effect of methanolic extract of *O. basilicum* seed and apigenin on oral glucose tolerance test.

Treatment	Blood Glucose Concentration mg/dL			
(n=6)	0 min	30 min	60 min	120 min
Control	178.56 ± 4.12	302.13 ±5.12	265.65 ±5.31	176.78 ± 4.36
Standard	183. 32 ± 5.65 $	238.46±6.43$	164.45±6.41$	145.32 ±4.32$
MEOBS I	1861.32 ±4.67	285.34±5.34*	234.54±7.23*	204.32 ±6.76*
MEOBS II	190.45 ±5.63	260.43±7.24*	214.56±6.34*	158.47 ±5.67*
API	181.41 ±7.76	240.39±6.34*	170.45±7.65*	143.67 ±6.56*

Values are expressed as mean ± SEM NS –Non Significant, $<0.05, **$<0.1, ***$<0.01, ****$<0.001
The Comparison was made between Group I Vs group III, IV, V at 0 min, 30 min, 60 min, and 90 respectively.
Values are expressed as mean ± SEM NS –Non Significant, *p<0.05, **p<0.1, ***p<0.01, ****p<0.001
The Comparison was made between Group II Vs group III, IV, V, V at 0 min, 30 min, 60 min, and 90 respectively.

considered as p<0.05 (95%level). The analysis was performed by using Graph-Pad Prism 6.

3. RESULTS

3.1. Percentage Yield of Crude Extracts

The percentage yield of MEOBS was found to be 2.00 (w/w).

3.2. Phytochemical Tests

Presence of flavonoids, saponins, phenolic compounds, tannins, and carbohydrates was revealed by a preliminary phytochemical screening of the MEOBS.

3.3. Acute Toxicity Study

The result of the acute oral administration of MEOBS in various doses of 20, 100, 250 and 500 mg/kg indicated that there were no changes in normal behavioural pattern and no signs and symptoms of toxicity and mortality were observed. At dose 1000 mg/kg, changes in normal behavioural pattern and signs and symptoms of toxicity and mortality were observed. On the basis of the above study results, the biological evaluation was carried out at doses of 20 and 40 mg/ kg body weight.

3.4. Identification of the Compound

By isolation of the MEOBS, a yellow crystalline powder was obtained. Structural interpretation of the compound was done using spectroscopy techniques and it was confirmed as apigenin. The compound was identified based on the following evidences: Molecular weight: 270.24 g/mole; ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance II 400 spectrometer (at 400 MHz and 100 MHz, respectively) at 25 °C, using TMS as an internal standard using DMSO-d_6. ^{1}H NMR: δ 12.91, 10.43, 7.85, 6.94, 6.64, 6.43 and 6.19; ^{13}C NMR: δ 181.59, 163.99, 163.62, 161.48, 161.02, 157.24, 128.03, 121.19, 115.81, 103.73, 102.72, 98.76 and 93.75. ESI-MS m/z: 271.38 $[M+H]^+$. Mass spectra (ESI-TOF) was measured on a Q-TOF MICROMASS (LC-MS) spectrometer. The molecular formula of apigenin is $C_{15}H_{10}O_5$ (4,5,7-trihydroxyflavone) and the structure is shown in Fig. (**1**).

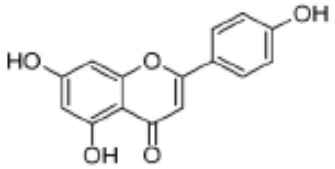

Fig. (1). The structure of apigenin.

3.5. Oral Glucose Tolerance Test

Administration of glucose (2.5 gm/kg,) produced a significant change in blood glucose level of a normal rat. Treatment with MEOBS (20 and 40 mg/kg, p.o.), apigenin (10 mg/kg) and glibenclamide (1.5 mg/kg, p.o.) significantly reduced serum glucose level in normal fasting group, at 0 min, 30 min, 60 min and 120 min compared to normal control group as shown in Table **1**. The effect of oral glucose tolerance test is shown in Fig. (**2**).

3.6. Body Weight

The body weight of diabetic control group was decreased after 15 days, whereas body weight was significantly recovered toward normal level by treatment with MEOBS (40 mg/kg), apigenin (10 mg/kg) as shown in Table **2**. The effects of body weight on STZ – induced diabetic rats are shown in Fig. (**3**).

3.7. Anti-diabetic Activity

The results of the present study clearly indicated that MEOBS (40 mg/kg) and apigenin (10 mg/kg) showed a significant decrease (P <0.05) in blood sugar level. After 15 days of treatment with standard drug glibenclamide, blood sugar level was decreased as shown in Table 3. The effects of oral administration of 20 mg/kg and 40 mg/kg MEOBS and apigenin (10 mg/kg) on blood glucose in STZ-induced diabetic rats are shown in Fig. (**4**).

3.8. Effect on Lipid Profile

Serum lipid profile was measured at initial and at 15 days of treatment as given section 2.10 and the results are shown in Table **4**.

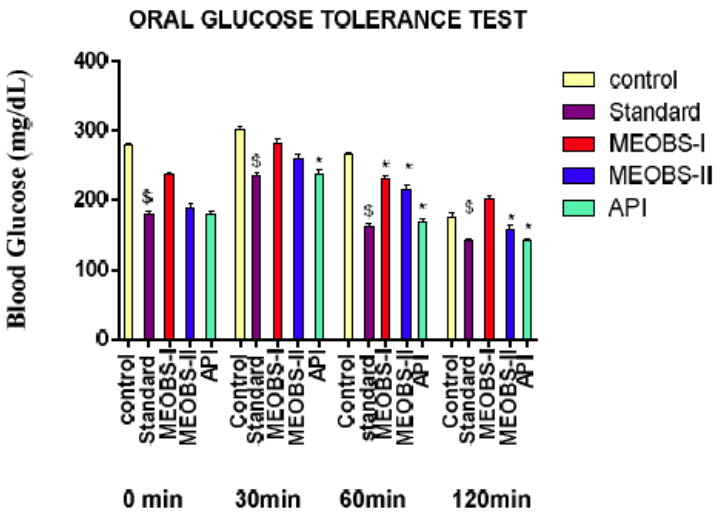

Fig. (2). Effect of methanolic extract *O. basilicum* seed and apigenin on serum glucose levels.

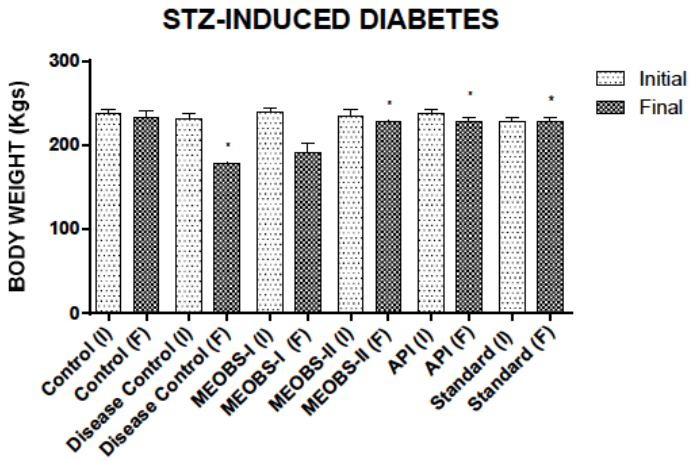

Fig. (3). Effect of methanolic extract of *O. basilicum* seed & Apigenin on body weight Each value are expressed as mean ± SEM *p<0.05, Comparison were made between initial body weight and final body weight respectively.

Table 2. Effect of methanolic extract of *O. basilicum* seed and apigenin on body weight.

Group	Initial Body Weight	Final Body Weight
Normal	240.3 ± 12.3	238.4 ± 12.3
DC	235.75±12.6	181.6 ± 10.4*
Standard	234.7 ± 14.8	234.5 ± 12.8 *
MEOBS -I	241.1 ± 13.4	202.6 ± 10.1
MEOBS -II	238.7±9.54	233.6± 08.6*
API	240.8 ± 8.6	234.3 ± 09.8 *

Values are expressed as mean ± SEM NS –Non Significant, $<0.05, **$<0.1, ***$<0.01, ****$<0.001
The Comparison was made between Group I Vs group III, IV, V, VI after the 15th day of study.
Values are expressed as mean ± SEM NS –Non Significant, *p<0.05, **p<0.1, ***p<0.01, ****p<0.001
The Comparison was made between Group II Vs group III, IV, V, VI after the 15th day of study.

A significant (P <0.05) reduction in TG, TC, LDL and VLDL was found in diabetic rats treated with MEOBS & apigenin (40 mg/kg & 10 mg/kg, p.o) as compared to diabetic control.. However, a significant (P <0.05) elevation of HDL in MEOBS (40 mg/kg) & apigenin (10 mg/kg) treated diabetic rats was found after 15 days as compared to the diabetic control as shown in Fig. (**5.1**-**5.5**).

3.9. Effects of MEOBS and Apigenin on Pancreas Histology

Histological structure of pancreas of normal rats (A) having normal sized islets is shown in Fig. (**6**). The normal structure of the islets in the diabetic rats was found to be shrunken in diabetic rats which is shown in Fig. (**B**). Animals treated with MEOBS (20 mg/kg), MEOBS (40 mg/kg) and apigenin (C, D and E), the restoration of the normal cellular population and structure and appearance of islets were noted to be restored to the original, especially in the central β-cell region. These results were comparable to the rats treated with standard diabetic drug Glibenclamide.

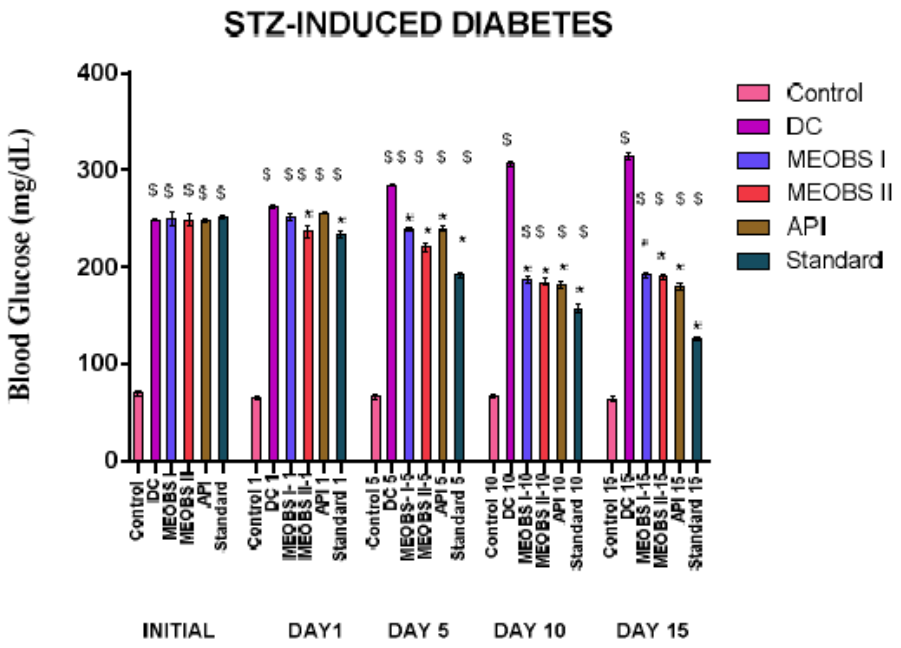

Fig. (4). Effects of methanolic extract of *O. basilicum* seed and apigenin on blood glucose in STZ-induced diabetic rats.

Table 3. Anti-diabetic activity of methanolic extract of *O. basilicum* seed and isolated compound (apigenin) against STZ –induced diabetic rats.

Group	Blood sugar level in Group (15 days) mg/ dL (mean ± SEM)				
	Initial	Day 1	Day 5	Day 10	Day 15
Control	70.34± 2.94	65.12±1.38	66.30±2.17	67.05±1.23	64.36±1.26
DC	249.05±1.20 $	262.9±1.90 $	285.1±1.92 $	306.6±2.70 $	314.3±3.52$
MEOBS -I	250.2±3.19 $	252.21±1.31 $	239.0±1.79* $	187.5±3.51*$	192.5± 2.72* $
MEOBS -II	249.1±5.78 $	236.3±5.80 * $	221.3±4.58* $	184.83±3.449* $	190.3±2.71* $
API	248.5±1.71 $	256.0±1.39 $	239.7±2.50* $	182.34±3.56* $	180.16±3.67*$
Standard	251.8±1.66 $	233.7±2.78* $	192.2±2.15* $	157.4±3.69* $	126.64 ±2.12* $

Values are expressed as mean ± SEM NS –Non Significant, $<0.05, **$<0.1, ***$<0.01, ****$<0.001
The Comparison was made between Group I Vs group III, IV, V, VI at day 1, day 5, day 10 and day 15 respectively
Values are expressed as mean ± SEM NS –Non Significant, *p<0.05, **p<0.1, ***p<0.01, ****p<0.001
The Comparison was made between Group II Vs group III, IV, V, VI at day 1, day 5, day 10 and day 15 respectively.

4. DISCUSSION

The present study discussed the antidiabetic and anti-hyperlipidemic effects of MEOBS and isolated compound apigenin on STZ-induced-diabetic rats. The MEOBS (40 mg/kg) and isolated compound apigenin (10 mg/kg) showed significant improvement in glucose tolerance in the glucose-fed hyperglycaemic normal rat. Such an effect may be accounted for, in part, by a decrease in the rate of intestinal glucose absorption, achieved by an extra pancreatic action including the stimulation of peripheral glucose utilization or enhancing glycolytic and glycogenic process with a concomitant decrease in glycogenolysis and glyconeogenesis [19].

The present study indicated that the MEOBS (40 mg/kg) and apigenin 10 mg/Kg) exhibited a marked antidiabetic activity in the STZ-induced-diabetic rat by lowering the blood glucose levels as compared to the rats treated with MEOBS (20 mg/kg). STZ, a naturally occurring nitrosamide, damages pancreatic β-cells possibly by generating excess reactive oxygen species and thus is widely used for the

Table 4. Effect of methanolic extracts of *O. basilicum* seed and apigenin on lipid profile of normal and STZ rats.

Groups	TC (mg/dL)	TG (mg/dL)	HDL-C (mg/dL)	LDL-C (mg/dL)	VLDL –C (mg/dL)
Control	88.9±2.94	47.59±1.37	42.69±3.17	34.36±5.25	9.51±0.27
DC	132.01±3.53	94.29±1.36 $	15.42±1.46$	97.72±3.92 $	18.79±0.27$
MEOBS -I	122.4±31.5	86.57±1.75$	21.66±1.49$	83.5±2.22 $	17.31±0.3$
MEOBS -II	104.1±2.83*	60.92±2.02*$	33.78±1.26 *	58.16±2.93*	12.18±0.40*$
API	97.17±1.72*	58.60±2.52*	38.23±0.52*	48.42±1.86*	11.71±0.50*
Standard	118.27±3.15^	88.73±1.26	18.37±0.50$	82.14±3.33$	17.73±0.25

Values are expressed as mean ± SEM NS –Non Significant, $<0.05, **$<0.1, ***$<0.01, ****$<0.001
The Comparison was made between Group I Vs group III, IV, V, VI on day 15.
Values are expressed as mean ± SEM NS –Non Significant, *p<0.05, **p<0.1, ***p<0.01, ****p<0.001
The Comparison was made between Group II Vs group III, IV, V, VI on day 15.

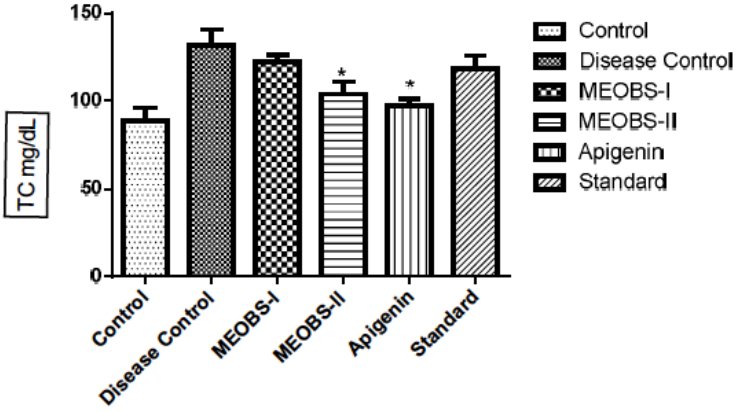

Fig. (5.1). Effect of methanolic extract of *O. basilicum* seed and apigenin on TC-C.

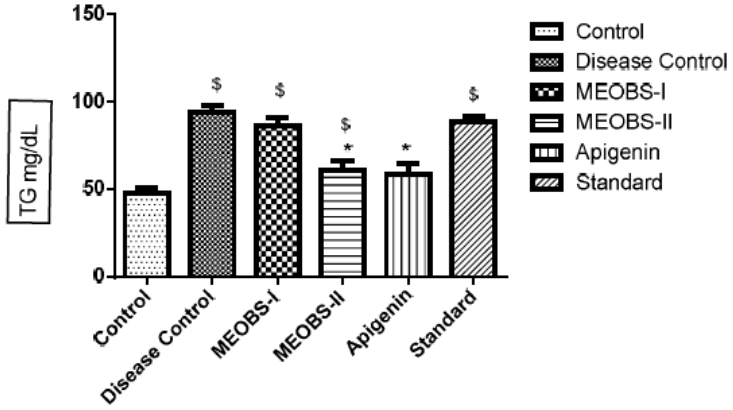

Fig. (5.2). Effect of methanolic extract of *O. basilicum* seed extract and apigenin on TGC.

induction of diabetes mellitus in experimental models. STZ generated lipid peroxidation and DNA breaks in pancreatic islet cells have been demonstrated. From the results, it is assumed that the MEOBS and apigenin could be responsible for stimulation of insulin release. Further, the observed reduced blood glucose lowering effect of the MEOBS could also possibly be due to increased utilization of peripheral glucose [20].

Induction of diabetes by STZ results in loss of body weight because of increased muscle waste and loss of tissue proteins [21]. After 15 days of treatment with MEOBS and apigenin, remarkable recovery in the body weight was observed in the diabetic rat and the results were comparable with that of the standard drug glibenclamide. The results obtained with the MEOBS treatment in chronic diabetic model further supported the antidiabetic effect of the MEOBS (40 mg/kg) and apigenin (10 mg/kg).

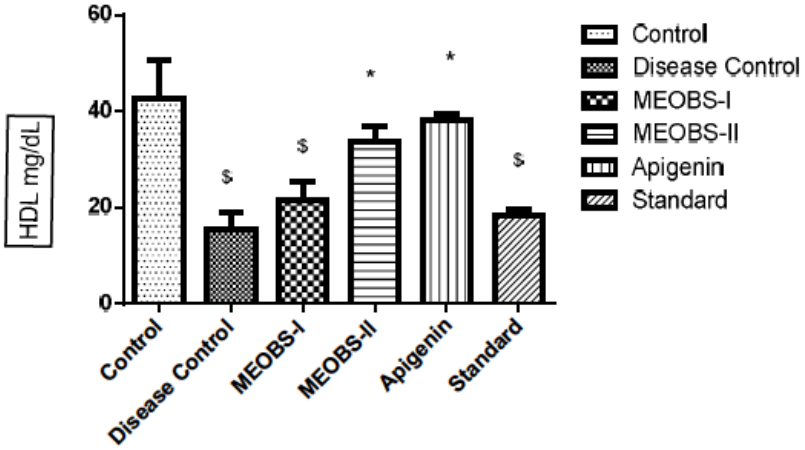

Fig. (5.3). Effect of methanolic extract of *O. basilicum* seed and apigenin on HDL-C.

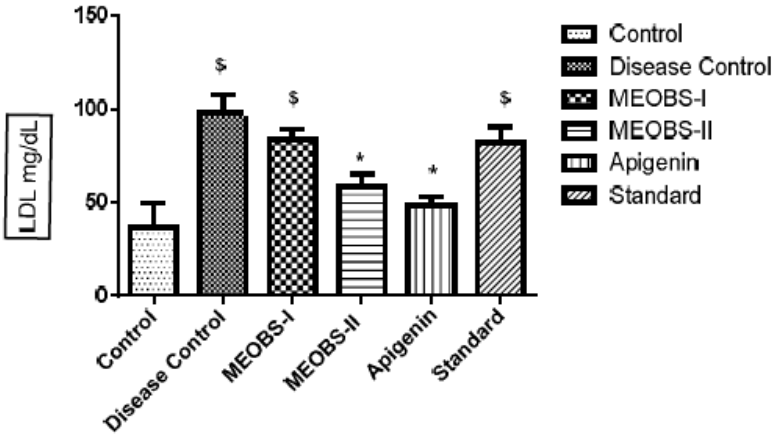

Fig. (5.4). Effect of methanolic extract of *O. basilicum* seed and apigenin on LDL-C.

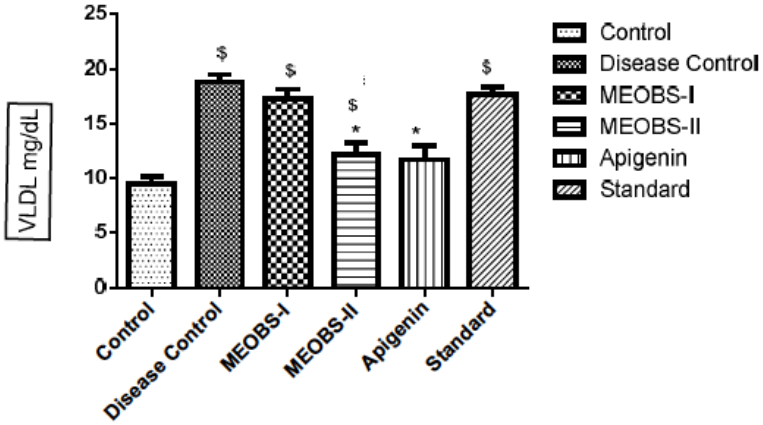

Fig. (5.5). Effect of methanolic extract of *O. basilicum* seed and apigenin on VLDL-C.

In this study, the damage of pancreas in STZ-treated diabetic control rat and regeneration of islets of Langerhans by glibenclamide was observed. The regeneration and restoration of the normal cellular size of the islet with hyperplasia were also shown by MEOBS (40 mg/kg) and apigenin(10 mg/kg) and were found to be remarkably comparable. The antidiabetic effect may be attributed to the regeneration of islet of Langerhans which may confirm the efficiency of the given MEOBS and apigenin in the management of diabetes.

A marked increase in serum concentrations of TG, TC, VLDL, LDL, and decreased HDL level were observed with a diabetic rat than the control group which can be related to hyperlipidemia. During diabetic state, insulin deficiency contributes to derangements of various metabolic and regulatory mechanisms in the body. At normal state, insulin activates the lipolytic hormones action on the peripheral fat depots which hydrolyses triglycerides and prevents mobilization of free fatty acids. However, insulin deficiency inactivates the

lipoprotein lipase which promotes liver conversion of free fatty acids into phospholipids and cholesterol and finally discharges into blood which results in elevated serum phospholipid level. The administration of the MEOBS (40 mg/kg) and apigenin (10 mg/kg) to the STZ induced diabetic rat significantly decreased TG, TC, VLDL, and LDL-C levels whereas HDL-C level was significantly increased. This implied that MEOBS and apigenin may possess insulin-like activity which would be helpful to reduce the incidence of lipid born complications. Methanol extract showed the presence of flavanoids, saponins, phenolic compounds and tannins. It is reported that flavanoids constitute the active biological principle of most medicinal plants with hypoglycemic and anti-diabetic properties. The significant antidiabetic and anti hyperlipidemic activity of the MEOBS and isolated compound apigenin in our study may be attributed to its principle constituent flavanoid.

CONCLUSION

Seeds of *O. basilicum* and isolated compound apigenin would be a good candidate as alternative and /or complementary medicine in the management of diabetes mellitus. The results of the present study indicate that the MEOBS (40 mg/kg) and isolated compound apigenin (10 mg/kg) are capable of exhibiting significant anti-diabetic activity in STZ-induced diabetic rat as compared to MEOBS (20 mg/kg). The extracts and isolated compound also showed improvement in parameters like oral glucose tolerance, body weight, and lipid profile as well as regeneration of pancreatic islets of Langerhans and hence might be valuable in diabetes treatment.

LIST OF ABBREVIATIONS

API	=	Apigenin
DMSO	=	Dimethyl sulfoxide
HDL-C	=	High density lipoprotein cholesterol
IDF	=	International Diabetes Federation's
LDL-C	=	Low density lipoprotein cholesterol
MEOBS	=	Methanolic extract of *O. basilicum* seeds
NMR	=	Nuclear magnetic resonance
STZ	=	Streptozotocin
TC	=	Total cholesterol
TG	=	Triacylglycerol
VLDL	=	Very low density lipoprotein
WHO	=	World health organization

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No animals/humans were used for studies that are the basis of this research.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

SUPPLEMENTARY MATERIAL

Supplementary material is available on the publishers web site along with the published article.

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