



Original article

Role of *Moringa Oleifera* leaves extract against the side effects of diabetes mellitus induced by STZ in male albino ratsSara Ebrahiem¹, Mona M.M, Eltonsy^{1*}, Mahmoud M. Salem², Doaa Gewily¹, Ahmed Nabeeh²¹Department of Zoology and Entomology, Faculty of Science (Girls), Al-Azhar University, Cairo, Egypt²Department of Zoology and Entomology, Faculty of Science (Boys), Al-Azhar University, Cairo, Egypt

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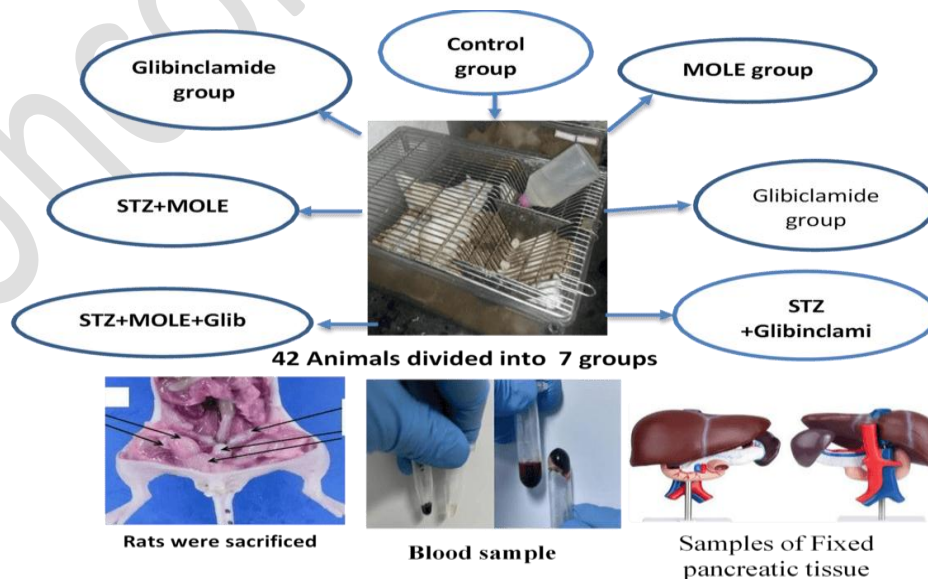
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Diabetes mellitus
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ABSTRACT

Diabetes is a chronic hyperglycemic condition requiring regular insulin and blood sugar monitoring. The goal of this study was to find out whether or not the extract of *Moringa Oleifera* leaves (MOLE) can prevent male albino rats from developing diabetes mellitus as a result of streptozotocin (STZ). Forty-two male albino rats were divided into seven groups at random: Group I, control rats; Group II, rats received oral glibenclamide (5 mg/kg b.wt./day); Group III, normal rats received oral MOLE (200 mg/kg b.wt./daily); Group IV (the diabetic group) received a single intraperitoneal injection of STZ (45 mg/kg diluted in saline solution); Group V, diabetic rats received oral MOLE (200 mg/kg b.wt./daily); Group VI, diabetic received glibenclamide at a dose of 5 mg/kg body weight; and Group VII, received both oral MOLE and glibenclamide. All of the animals were sacrificed after 45 days. The results showed that STZ dramatically decreased final body weights and increased HbA1c and HOMA-IR levels. Compared to the STZ group, the blood insulin levels of the treated group also increased. Additionally, compared to the STZ-diabetic group, HDL cholesterol, VLDL, LDL/HDL cholesterol, TC/HDL, triglycerides, and LDL cholesterol serum levels in the treated groups were significantly lower. Histopathological examination of pancreatic tissue of diabetic rats showed degenerative abnormalities, such as hazy swelling, hydropic degeneration, necrosis, and apoptotic alterations. However, the treated groups displayed a significant recovery. According to existing research, using glibenclamide and MOLE in combination is more effective than each alone. These findings suggest that MOLE may help prevent metabolic and biochemical alterations associated with type 2 diabetes.

Graphical abstract



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1. Introduction

DM is a metabolic condition marked by chronic hyperglycemia with changes in metabolism of fat, carbohydrates, and proteins, due to defects in insulin hormone secretion or action [1]. There are two forms of diabetes: diabetes mellitus, both types 1 and 2 [1]. Numerous consequences, such as diabetic ketoacidosis, hyperglycemia, and even mortality, can result from untreated diabetes [2]. The severe long-term complications include eye damage, foot ulcers, chronic renal failure, stroke, and cardiovascular disease [3].

A glucosamine-nitroso-urea compound called STZ primarily harms and kills cells through DNA damage caused by nitric oxide [4]. Because STZ damages the beta cells that create insulin in the pancreatic islets of Langerhans, it is frequently used to support diabetes studies in animals. [4] Medicinally, it has been established that plant materials contain a range of phytochemicals in various concentrations [5]. Plants can regulate blood glucose levels in various ways, and these phytochemicals are significant in the pharmacological and non-medicinal properties of plant materials [6]. Certain plants may have properties similar to those of insulin, increase the number of beta cells in the pancreas by promoting cell regeneration, or act as antioxidants by lowering oxidative stress brought on by free radicals [6]. Folk medicine has made use of MOLE, a traditional plant. or as a food additive for a long time [7]. Thyroid hormone regulators, antihypertensives, laxatives, anti-diabetics, and antibiotics are only a few of the pharmacological actions of MOLE [8]. Considering that MOLE contains polyphenols including rutin, kaempferol, quercetin-3-glycoside, and glycosides, it may be able to reduce blood sugar levels after meals [8].

This study aimed to investigate how glibenclamide and extract from *Moringa oleifera* leaves (MOLE) affected male albino rats' diabetes mellitus brought on by streptozotocin (STZ). The research focused on assessing changes in body weight, glucose levels, insulin levels, and lipid profile parameters associated with diabetes. MOLE was evaluated as a standalone treatment for diabetes due to its antidiabetic activity when used alone and in combination with the established antidiabetic drug glibenclamide.

2. Materials and methods

Animals used in the experiment:

Forty-two male albino rats weighing between 170 and 190 g were used in this experiment.

They came from the El-Nile Company for Pharmaceutical Products' farm for animals in El-Nile, Cairo, Egypt. The rats were kept in metal cages for the duration of the experiment and maintained under regular circumstances, including temperature and humidity, as well as a 12-hour cycle of light and dark. Throughout the experiment, free food and beverages were offered. The rats were given time to adapt a week before the study began.

Reagents

All used chemicals and reagents, including STZ and

glibenclamide, were obtained from Sigma Aldrich, Germany; glucose test strips/kits (i-QARE DS-W AL International CO., Ltd, Taiwan); and test strips.

Preparation of plant alcoholic extractions

The Egyptian Scientific Society of *Moringa Oleifera* leaves, National Research Center, Dokki, and Giza in Egypt, provided two kilograms of fresh, green *Moringa oleifera* leaves in total

According to Tuorkey *et al.* [9] an ethanolic extract of *Moringa oleifera* leaves was produced. Before being ground into powder, fresh leaves were frequently thoroughly cleaned with distilled water to get rid of dust and filth. They were then allowed to dry completely at room temperature. For 48 hours, the powder was steeped in 70% ethanol at room temperature (22 °C) while being gently shaken. A semisolid crude extract weighing 250 g and having a crude percentage of 12.5% was created after the contents were filtered using filter paper (Whatman size No. 1) and left to air dry at room temperature. The extract was maintained at 4 °C in an airtight container.

Experimental design

Induction of diabetes

Rats that had been fasting for 16–18 hours were given a single intraperitoneal injection of streptozotocin (STZ) (45 mg/kg body) (Sigma Chemical Co., St. Louis, USA) dissolved in 0.1 mol/L citrate buffer, pH 4.5, to induce diabetes, according to Guo *et al.* [10]. To avoid initial drug-induced hypoglycemia mortality, the STZ-treated rats were housed in their cages for the following twenty-four hours and given a 5% glucose solution as a supplement. Blood samples were taken using the tail snip method 96 hours after the STZ injection, and each animal's blood sugar level was ascertained. According to Guo *et al.*[10]. All rats with a fasting blood glucose level higher than 240 mg/dL (11.1 mmol/L) were deemed hyperglycemic and were chosen for the studies.

The forty-two animals used in this study were split up into seven groups, each of which had six male albino rats:

G1: normal control rats that received a basal diet.

GII: normal rats were given Glibenclamide (5 mg/kg b.wt/day).

GIII: MOLE (200 mg/kg b.wt/day) was administered to normal rats.

GIV: rats in the diabetic group received single intraperitoneal injections of streptozotocin (45 mg/kg).

GV: diabetic rat given an oral MOLE dosage of 200 mg/kg body weight.

GVI: diabetic rats given Glibenclamide (5 mg/kg body weight/day).

GVII: diabetic rats given glibenclamide and MOLE (5 mg/kg b.wt. +200 mg/kg b.wt./day)

All animals were sacrificed after 45 days of treatment.

Blood sample collection

Heparinized capillary tubes were used to extract blood samples from the retro-orbital plexus of the animals fasting for 12 hours after the experiment and under diethyl ether anesthesia. For 30 minutes, the blood was centrifuged at 3000 rpm. As soon as the clear supernatant sera were collected, they were stored at -20°C for further biochemical parameter analysis.

Histopathological investigation

After sacrificing each rat, samples of fixed pancreatic tissue were cleansed with xylene, embedded in paraffin wax, and dehydrated in increasing alcohol concentrations. Hematoxylin and eosin were used to stain tissue slices 5–6 µm thick after cutting them with a rotary microtome.

Body weight measurement

Weekly measurements of body weight were taken starting at zero time (the time before treatment) and continued until the end of the experiment.

Assessment of biochemical parameters

Assessment of insulin resistance using the homeostasis model (HOMA-IR)

As Zhang and colleagues [11] stated, a glucometer (Acu-Chek Active, Germany) was used to measure blood glucose levels after fasting for the entire night.

Immuno-enzymatic assay kits for the quantitative detection of insulin in serum were used to measure the serum insulin level, per Bergmeyer *et al.* [12].

HOMA-IR was calculated using the following formula

Genovesi *et al.*¹⁴ state the $HOMA-IR = \text{fasting insulin (U/L)} \times \text{fasting glucose (mg/dL)} / 405$.

Determination of blood glucose level and HbA1C

The enzymatic glucometer technique assessed serum glucose level and HbA1C, Matthew *et al.* [13].

Determination of lipid profile levels

Serum lipid profile levels were measured, including Triglycerides, high-density lipoprotein cholesterol (HDL), total cholesterol, and low-density lipoprotein cholesterol (LDL-C). All parameters were assessed using French BioMérieux SA kits. Following the calculation of serum LDL-C (low-density lipoprotein cholesterol) and VLDL (very low-density lipoprotein cholesterol), serum TC-C/HDL-C (risk factor 1) and LDL-C/HDL-C (risk factor 2) ratios were determined as follows: Trinder equation

Risk factor 1 = TC-C/HDL-C

Risk factor 2 = LDL-C/HDL-C. Trinder *et al.* [14]

VLDL-C was calculated following Friedewald's equation:

$LDL-C \text{ (mg/dl)} = TC - \{HDL + [TG/5]\}$.

$VLDL-C = TG/5$. Friedewald *et al.* [15]

Statistical investigation

The mean ± standard error (SE) of the mean was used to express all values. With Graph Pad Prism (Version 5.01,

Graph Pad Software, San Diego, USA), the differences between the groups were examined using one-way analysis of variance (ANOVA) and post hoc, Tukey's test for intergroup comparisons. A probability of less than 0.05 was deemed significant.

3. Results

1. % of Body weight change

Rats treated with MOLE and glibenclamide did not differ significantly from control rats. Animals administered STZ significantly decreased body weight ($p < 0.05$) compared to control rats. The body weight of diabetic rats treated with MOLE and glibenclamide, or both, increased significantly ($p < 0.05$) in comparison to the STZ group (Table 1).

2. Biochemical findings: blood glucose and HbA1C

Blood glucose and HbA1C levels were significantly higher ($p < 0.05$) than in the control group, as shown in Table 2. Serum glucose and HbA1C activity did not significantly differ between animals treated with MOLE and glibenclamide and those without. Blood glucose and HbA1C concentrations were significantly ($p < 0.05$) lower in rats treated with MOLE, glibenclamide, and their combination than in the diabetic group.

Insulin, HOMA-IR

Rats treated with glibenclamide and MOLE and control rats displayed discernible differences in insulin and HOMA-IR levels, as indicated by the findings in Table 2. Comparing the STZ group to the control group revealed a substantial decrease ($p < 0.05$) in blood insulin and a significant increase ($p < 0.05$) in HOMA IR values. In contrast, as given to diabetic rats, MOLE, glibenclamide, and their combination resulted in a substantial increase ($p < 0.05$) in insulin levels and a significant decrease ($p < 0.05$) in HOMA IR levels as compared to the diabetic group's identical values.

Lipid profile

According to the data in Table 3, serum HDL-C, TC-C, TG-C, VLDL-C, and LDL-C concentrations in rats treated with glibenclamide and MOLE did not change significantly from those in control groups. In animals given STZ, TC-C, TG-C, VLDL-C, and LDL-C levels were significantly higher ($p < 0.05$) than the control group's equivalent values. Compared to the control group, our data revealed a significant ($p < 0.05$) decrease in HDL concentration in rats who received STZ.

When diabetic rats were given MOLE, there was no discernible change in their HDL, VLDL, and LDL levels. However, a significant ($p < 0.05$) reduction in triglyceride and TC-C levels was noted when compared to the diabetic group (Table 3).

The group administered with glibenclamide showed a considerable increase ($p < 0.05$) in HDL-C levels and a significant decrease ($p < 0.05$) in TC, C, TG, VLDL-C, and

LDL-C levels when compared to the diabetic group (Table 4). When compared to the diabetic group, rats treated with STZ showed a substantial rise ($p<0.05$) in HDL but a significant decrease ($p<0.05$) in TC, TG, VLDL, and LDL after receiving MOLE and glibenclamide together.

Serum LDL-C/HDL-C and TC-C/HDL-C

Statistics indicated that rats given glibenclamide and MOLE had no significant difference in serum TC-C/HDL-C and LDL-C/HDL-C from those in the control groups. Serum levels of TC-C/HDL-C and LDL-C/HDL-C were considerably ($p<0.05$) higher in STZ-induced rats than in control rats (Table 4). Treatment with MOLE led to no significant changes in LDL-C/HDL-C and TC-C/HDL-C levels compared to diabetic rats (Table 4). TC-C/HDL-C and LDL/HDL in STZ-treated rats were significantly ($p<0.05$) lower when treated with glibenclamide than in the diabetic group (Table 4).

TC-C/HDL-C and LDL/HDL values in STZ-treated rats were considerably ($p<0.05$) lower than those in the diabetic group when glibenclamide and MOLE were given simultaneously.

Table 1: The body weight of adult male albino rats.

Parameters	First day	Last day	% change
Teams			
control rats	170±4.2 ^a	182±2.9 ^a	4.6
GLI	173±4.1 ^a	186.4.8 ^a	4.89
MOLE	177±2.4 ^a	181±2.4 ^a	2.7
Diabetic group or STZ	180±8.5 ^b	148±5.1 ^c	-15.3
STZ+MOLE	182±6.4 ^b	165±7.3 ^b	-9.3
STZ+ GLI	187±12.3 ^b	182±17.1 ^c	-2.1
STZ+GLI+MOLE	189±5.5 ^b	186.5±1.9 ^d	1.5

Table 2. Show the level of HB A1C, Glucose, Insulin and HOMA-IR level in adult male albino rats were given various treatments.

Parameters	HbA1C %	Glucose mg/dL	Insulin μ IU/dl	HOMA IR
Teams				
Control rats	5.08±0.4 ^a	93.5±5 ^a	4.7±0.1 ^a	1.07±0.1 ^a
GLI	5.3±0.8 ^a	86.5±1.8 ^a	5.4 ±0.18 ^b	1.15 ±0.15 ^a
MOLE	5.32±0.1 ^a	87±1.9 ^a	4.75±0.18 ^a	0.79±0.18 ^a
Diabetic group or STZ	9.1±0.1 ^b	484 ±14 ^b	1.74±0.2 ^c	2.07±0.4 ^c
STZ+MOLE	7.6±0.2 ^e	388± 15 ^e	2.39±0.16 ^d	2.28±0.19 ^d
STZ+GLI	6.6±0.1 ^e	382± 17 ^e	3.03±0.26 ^d	2.85±0.19 ^d
Diabetic rat + MOLE+ GLI	4.7±0.0.3 ^f	228± 35 ^e	3.1±0.2 ^d	2.20±0.2 ^d

The average of six records $\pm$ SE was used. Each number, grouped with different letters, shows a substantial change compared to all, where groups with the same letter mean no significant variation. STZ or streptozotocin. TC: cholesterol, TG: triglyceride, HDL-C: high density lipoprotein – cholesterol and LDL-C: low density lipoprotein – cholesterol

Table 3. Lipid profile (VLDL-C, TC, TG, HDL-C, and LDL-C mg/dl) of adult male albino rats exposed to various treatment.

Parameters	Total Cholesterol mg/dl	Tri Glyceride mg/dl	VLDL mg/dl	High Density Lipoprotein mg/dl	Low Density Lipoprotein mg/dl
Team					
Untreated rats	143±0.9 ^a	140±2.5 ^a	28±1.3 ^a	39.8±0.4 ^a	66.1±1.3 ^a
Glibenclamide	129±0.6 ^a	149±0.8 ^a	29.8±1.1 ^a	39.9±0.3 ^a	58.1±1.1 ^a
MOLE	135±0.8 ^a	142±1.2 ^a	28.4 ±1.2 ^a	39.6±0.4 ^a	67.2±1.2 ^a
Diabetic rats or STZ	216±9.7 ^b	294±0.7 ^b	58.8±4.3 ^b	23.9±1.3 ^c	133.1±4.3 ^b
Diabetic rat + MOLE	188±15 ^e	205±5.6 ^e	41±6.2 ^a	23.63±1.37 ^a	126±6.2 ^a
Diabetic rat + GLI	167±7 ^e	242.2± 1.7 ^e	48.4±6 ^e	29.61±0.7 ^d	93.5±6 ^e
Diabetic rat + MOLE+ GLI	161±5.4 ^e	203±6.2 ^e	40.6±4.6 ^e	31.5±1.69 ^d	89.2±4.6 ^e

The average of six records $\pm$ SE. was used. Each number, grouped with different letters, shows a substantial change compared to all, where groups with the same letter mean no significant variation. STZ or streptozotocin. TC: cholesterol, TG: triglyceride, HDL-C: high-density lipoprotein–cholesterol, and LDL-C: low-density lipoprotein–cholesterol

Table 4. Lipid profile (VLDL-C and LDL/HDL) in adult male albino rats subjected to different treatment conditions

Parameters	TC/HDL	LDL/HDL
Teams		
Control rats	3.6±2.1 ^a	1.66±0.4 ^a
GLI	3.2±1.1 ^a	1.48 ±0.3 ^a
MOLE	3.5±1.2 ^a	1.69±0.4 ^a
Diabetic group or STZ	9.3±4.3 ^b	5.7±0.4 ^b
Diabetic rat + MOLE	8±6.2 ^a	5.34±0.2 ^a
Diabetic rat + GLI	5.6±6. ^e	3.2±0.3 ^e
Diabetic rat + MOLE+ GLI	5.2±4.6 ^e	2.8±0.32 ^e

The average of six records $\pm$ SE. was used. Each number, grouped with different letters, shows a substantial change compared to all, where groups with the same letter mean no significant variation. STZ or *streptozotocin*. TC: cholesterol, TG: triglyceride, HDL-C: high density lipoprotein – cholesterol and LDL-C: low density lipoprotein – cholesterol

Histopathology of the pancreas

Control group

The negative control group's (C) pancreatic serial slices showed densely packed acinar cells, including secretory cells, and normal organization in both exocrine and endocrine counterparts. The lighter staining spots are endocrine islets of Langerhans, evenly distributed throughout the pancreas. Three types of cells are found in the islets: alpha cells, which secrete glucagon, are smaller than β -cells and have a deeply eosinophilic cytoplasm. They are mostly found in the islet's periphery. β -cells, which produce insulin, have a pale basophilic cytoplasm and are found in the center of the islets. Delta-cells generate somatostatin, which suppresses insulin and glucagon release. Delta cells are the smallest cell type in the islets, with ovoid or ellipsoid nuclei and a thin ring of eosinophilic cytoplasm. (Fig. 1A, B).

Glibenclamide-treated rats

In sections of this group, the pancreas exhibited apparently normal pancreatic structures, including the exocrine and endocrine counterparts, with actively secretory acinar cells. Apparently, normal sizes and distribution of islet cells, alpha and delta, were observed with normal capillary networks; however, some cells revealed mild cytoplasmic vacuolations, particularly in beta cells (Fig.2A, B).

Moringa oleifera leaf extract-treated rats.

Sections from the pancreas of this group revealed ostensibly normal pancreatic structures, including the exocrine and endocrine counterparts, with active secretory acinar cells, relatively normal sizes and distribution of islet cells, and a normal capillary network. However, in some rats, newly transformed proliferated islet cells with comparatively smaller nuclei and a thin rim of cytoplasm were seen. (Fig. 3A, B).

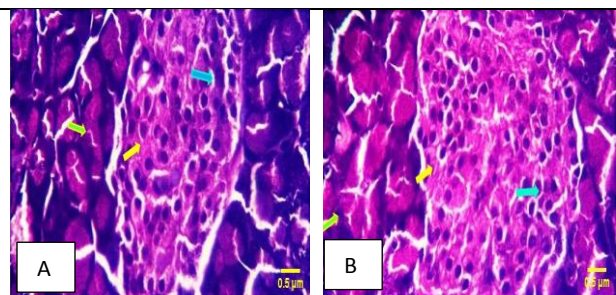


Fig. 1: Photomicrograph of pancreas (A, B) of control rats showing normal structure of pancreatic exocrine and endocrine glands. The exocrine consists of acinar epithelial cells loaded with secretory granules (green arrows). Islets of Langerhans are the lighter staining areas containing three types of cells: α -cells (light blue arrow), β -cells with a deep eosinophilic cytoplasm (yellow arrow), and D-cells (H&E x200, 400).

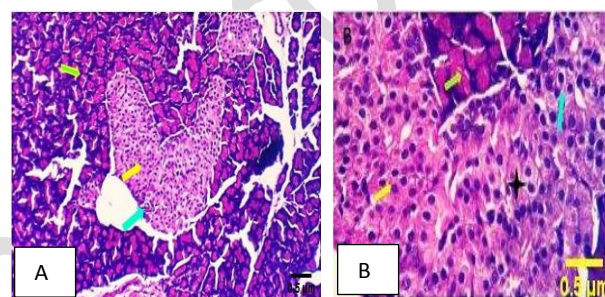


Fig. 2. Photomicrograph of pancreas (A, B) of Glibenclamide-treated rats showing normal pancreatic structures, including the exocrine and endocrine, with actively secretory acini cells (green arrows). Relatively normal sizes and distribution of alpha cells in islets of Langerhans (yellow and light blue arrows) are observed with a normal capillary network. However, some cells show mild cytoplasmic vacuolations, particularly in beta cells (black star). (H&E.x200, 400)

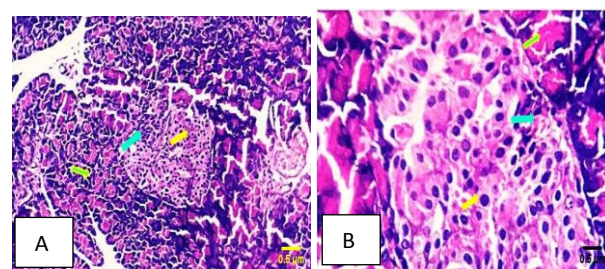


Fig. 3. photomicrograph of pancreas (A, B) of *Moringa oleifera* leaf extract-treated rats showing apparently normal pancreatic structures, including the exocrine and endocrine counterparts, with normal secretory acini cells (green arrows) and relatively normal sizes, distribution, and structure of the beta and alpha islet cells (yellow and light blue arrows) (H&E $\times$ 200, 400)

Control positive, STZ-induced diabetic rats

Serial sections from diabetic pancreatic tissue, 45 mg STZ/kg BW (single IP), revealed characteristic changes

such as a moderate decrease in islet cell densities, degenerative changes in islet β -cells, primarily cloudy swelling, and hydropic degeneration. A pathognomonic lesion was seen, and a small percentage of β cells had necrotic and apoptotic changes, as necrotic cells entirely or partially lost their nuclear and/or cytoplasmic components, occasionally with ballooning changes in afflicted cells. Apoptotic cells have tiny nuclei and reduced deep eosinophilic cytoplasm. α -cells, on the other hand, were compensatory or substantially expanded in the breadth of the reduced cell population. The exocrine pancreas had cystic dilatation, localized lymphocyte aggregations, occasionally assuming a follicular appearance, and ductal wall fibrosis (Fig. 4 (A, B)).

Induced diabetic rats treated with *Moringa oleifera* leaf extract.

Sections from pancreas of this group exhibited apparently normal pancreatic structures including the exocrine and endocrine counterparts with active secretory acini cells, and comparatively normal alpha, beta, and delta islet cell counts, sizes, and distributions, as well as a typical capillary network between them, however in some rats a newly transformed proliferated acinar cells with comparatively large hyperchromatic nuclei and large cytoplasm were seen. Mild interstitial edema and vascular dilatation were recorded (Fig. 5 (A, B)).

Induced diabetic rats treated with glibenclamide

Structures, including the exocrine and endocrine counterparts, showed active secretory acini cells, and a relatively normal population, size, and distribution of islet cells with a normal structure of alpha, beta, and delta cells and a normal capillary network among them; however, very few beta cells were apoptotic. In some sections, the exocrine pancreas revealed cystically dilated excretory ducts with peri-ductal fibrotic changes (Fig. 6 A, B)

STZ-induced diabetic rats treated with *Moringa oleifera* leaf extract and Glibenclamide

Sections from pancreas of this group revealed apparently normal pancreatic structures including the exocrine and endocrine counterparts with active secretory acini cells, and relatively normal populations, sizes and distribution of islets cells with a normal structure of alpha, beta and delta cells and normal capillary network among them. Moreover the sizes and cellular populations of Islet cells were apparently more sizable and more countable than other groups (Fig. 7 A, B).

4. Discussion

The current research examined the potential of *Moringa oleifera* as a treatment to reduce the adverse effects of Type 2 diabetes in albino rats. These findings aligned with Genovesi *et al.* [16], who assert that a lack of amino acid and glucose entry into cells is associated with muscle mass reduction, causing a biosynthetic deficit. However, when MOLE was given to diabetic rats, weight gain was

observed. Diabetes mellitus significantly decreased the rats' final body weight. These findings were consistent with those of Zhan Zhang [7].

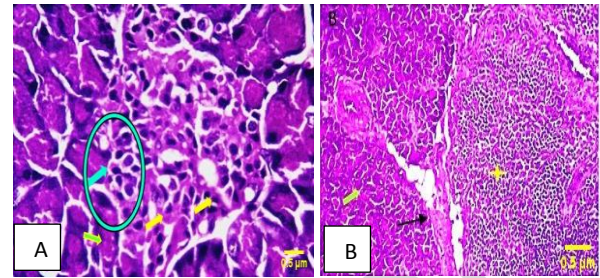


Fig. 4: Photomicrograph of the Pancreas (A&B) of STZ-induced diabetic rats showing necrotic and apoptotic changes in β cells. Some necrotic cells exhibit ballooning modifications; others have lost their cytoplasmic components and/or nucleus entirely or partially (red arrow). Apoptotic cells have tiny nuclei and shrunken, deep eosinophilic cytoplasm (yellow arrows). On the other hand, α -cells show a relatively normal distribution (light blue circle and arrow). The exocrine pancreas (green arrow) shows cystic dilatation, focal lymphocytic aggregations (yellow star), and fibrosis of the affected ductal walls (black arrow). (H&E. x200, 400)

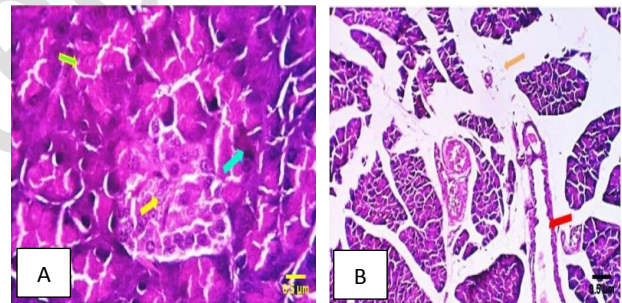


Fig. 5. photomicrograph of pancreas (A&B) of diabetic rats treated with *Moringa oleifera* leaf extract showing apparently normal pancreatic structures, including the exocrine and endocrine glands with normal secretory acini cells (green arrows) and apparently normal populations, sizes, distribution, and morphology of the beta cells (yellow arrow). Newly transformed proliferated acinar cells with comparatively large hyperchromatic nuclei and prominent cytoplasm (light blue arrow). Mild interstitial edema and vascular dilatation are also observed (orange and red arrows), (H&E x200, 400).

The increase in weight may be caused by the MOLE effect on blood glucose levels, which is explained by lower insulin resistance in this group [18-19].

Glibenclamide was given to diabetic rats to compensate for the body weight loss caused by STZ injection; these findings are comparable to those of Olayaki *et al.* [20], who revealed that the significance of glibenclamide's antioxidant activity may explain diabetes management.

Diabetes changed the lipid profile; HDL was reduced while triglycerides, total cholesterol, and low-density lip-

oprotein significantly increased. These findings align with Zafar *et al.* [21], who found dyslipidemia due to excessive lipolysis produced by hypoglycemia, which elevated lipid parameter levels in blood with aberrant metabolism [22]. As a result, the larger the amount of lipids returning to the liver, the more triacylglycerols are formed and produced in VLDL. It has also been found that lipoprotein activity causes diabetic hypertriglyceridaemia [23-24]. These findings are consistent with Cullen *et al.* [25].

In diabetic rats, MOLE showed a hypolipidemic effect, consistent with previous findings by Tété-Bénissan *et al.* [26]. In the current investigation, blood total lipids in the STZ-diabetic rats treated with glibenclamide significantly decreased. These results are consistent with those of Kondo *et al.* [27], who show that this improvement is caused by the effect of sulfonyl urease on high-density lipoproteins (HDL-C and LDL-C) [28].

Our results align with those of Rajanandh *et al.* [29], who found that the increased glucose level might be connected to the death of pancreatic β -cells by STZ, which causes a significant decrease in the amount of insulin released by pancreatic β -cells. Rats with STZ-induced diabetes had significantly higher blood glucose and HbA1C levels than control rats.

The current study investigated that diabetic rats who were administered MOLE and glibenclamide had significantly lower blood glucose levels and HbA1C than diabetic rats. This was consistent with the findings of Mastan *et al.* [30], who discovered that MOLE and glibenclamide have a glucose-lowering effect in diabetic rats.

The current study investigated whether diabetic rats given glibenclamide and MOLE had significantly lower blood glucose levels and HbA1C than non-diabetic rats. This was consistent with the findings of Mastan *et al.* [30], who discovered that MOLE and glibenclamide had a glucose-lowering impact on diabetic rats.

The current study's findings showed that glibenclamide considerably increased blood insulin levels [32], aligning with those of Gupta *et al.* [31], who evaluated the impact of gliclazide medication on the severity of diabetes in rats. Dupas *et al.* [33] claimed that increased insulin resistance is a consequence of type 2 diabetes. Carnevale *et al.* [34] found that HOMA-IR is a good indicator of how sensitive a tissue is to insulin production, especially in the liver. According to Schianca *et al.* [35], who ascribed this effect to the antihyperglycemic properties of MOLE, which enable insulin resistance to recover, this finding was consistent with Tuorkey *et al.* [36]'s previous results.

Our results agreed with those of Rajala *et al.* [37]. This may explain *Moringa Oleifera* leaves' potential to inhibit adipocytes' ability to resist via their active components, particularly estrogenic compounds [38]. Histopathological study data backs up the biochemical marker results. There was atrophy and necrosis of beta-cells and a decrease in

pancreatic cells in diabetic rats. These findings agreed with Shah *et al.* [39], who found that diabetic rats had necrotic cells.

Yagihashi *et al.* [40] also found that β -cell mass was decreased in individuals with diabetes. STZ causes hyperglycemia by damaging pancreatic cells with a cytotoxic effect. One of the intracellular mechanisms for its cytotoxicity is the generation of free radicals. [41]. The results demonstrated that treating rats with MOLE, glibenclamide, or MOLE and glibenclamide alleviated the histological abnormalities in the liver caused by STZ [41].

This showed that MOLE, glibenclamide, or MOLE had a therapeutic effect on rats with STZ-induced diabetes [42]. Following histological analysis of the pancreas from diabetic rats, Kimoto *et al.* found that MOLE therapy significantly improved the histoarchitecture of the islet cells [43].

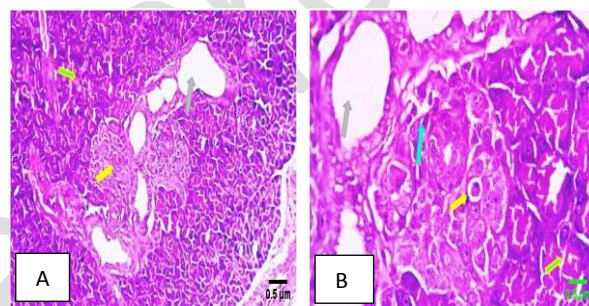


Fig. 6. photomicrograph from pancreas (A, B) of diabetic rats treated with Glibenclamide showing apparently normal pancreatic structures including the exocrine and endocrine counterparts with active secretory acini (light green arrows) and apparently normal populations, sizes, distribution and beta, alpha islets cells (A, yellow and light blue arrows) a very few beta cells are apoptotic (B, yellow arrow), cystically dilated excretory ducts with peri-ductal fibrotic changes are seen (dark green arrows) (H&E x200, 400).

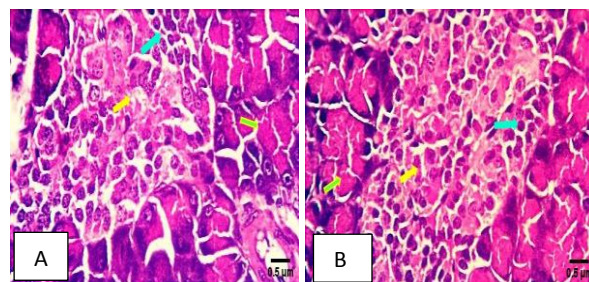


Fig. 7. photomicrographs (A, B) from the pancreas of diabetic rats given glibenclamide and extract from *Moringa oleifera* leaves. Normal pancreatic structures, including the exocrine and endocrine parts with active secretory acini cells (green arrows) and the normal structure of beta and alpha islet cells (yellow and light blue arrows) (HE x200, 400)

Glibenclamide therapy considerably preserved the islets of Langerhans and acinar cells in diabetic rats compared

to the diabetic group. According to Kimoto *et al.* [43], glibenclamide may shield pancreatic cells from oxidative damage [44], which our findings support.

5. Conclusion

The results of this study show that MOLE leaf extracts significantly lower the risk of diabetes in rats. The traditional use of MOLE leaf for treating type 2 diabetes is supported by pharmacological evidence thanks to these findings. More research is needed to identify the active ingredient responsible for the leaf extract's anti-diabetic effects.

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