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Antioxidant and Antidiabetic Effects of *Mondia whitei* Root Extract in Streptozotocin-Induced Diabetic Wistar Rats

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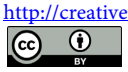

Abstract

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia and is a major contributor to global morbidity and mortality. Although *Mondia whitei* has been traditionally used for its antidiabetic and antioxidant effects, scientific evidence supporting these claims remains limited. This study aimed to evaluate the therapeutic potential of *Mondia whitei* root extract in a streptozotocin (STZ)-induced diabetic Wistar rat model. Phytochemical screening of *M. whitei* root extract revealed the presence of saponins, phenols, flavonoids, tannins, alkaloids, glycosides, coumarins, steroids, and terpenoids. Antioxidant activity was assessed using 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging and ferric reducing antioxidant power (FRAP) assays. DM was induced with 65 mg/kg body weight STZ. Rats were grouped into normal control, diabetic control, 200 mg/kg extract, 400 mg/kg extract, and 100 mg/kg metformin treated groups. Treatments were administered orally for 21 days. Fasting blood sugar (FBS) and body weight were measured weekly. At termination, blood and liver tissues were collected for analysis. *M. whitei* extract exhibited strong antioxidant activity *in vitro*. The 400 mg/kg dose significantly reduced FBS levels, nearing metformin's hypoglycemic effect when compared to diabetic control. The extract also significantly lowered serum gamma-glutamyl transferase (GGT), alanine aminotransferase (ALT), alkaline phosphatase (ALP), lipids, and malondialdehyde (MDA), while increasing FRAP values in liver and plasma while serum creatinine and urea levels were reduced, though not significantly. The phytochemical-rich *M. whitei* root extract showed significant antidiabetic, antioxidant, hypolipidemic, and hepatoprotective activities, supporting its potential as a natural alternative for managing DM and its complications.

Subject Areas

Biochemistry, Diabetes and Endocrinology, Medicinal Chemistry

Keywords

Mondia whitei, Diabetes Mellitus, Wistar Rat, Streptozotocin, Phytochemicals

1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disease characterized by elevated blood glucose levels, which over time can lead to serious complications affecting the heart, blood vessels, eyes, kidneys, and nerves [1]. Type 2 diabetes mellitus (T2DM) accounts for over 90% of all DM cases and arises primarily from a combination of insulin resistance and impaired insulin secretion by pancreatic β-cells [2]. T2DM is strongly associated with obesity, particularly central adiposity, which contributes significantly to its pathogenesis [2].

Globally, diabetes and its complications pose a major public health challenge. Nearly half a billion people currently live with diabetes, with projections estimating a 25% increase by 2030 and a 51% rise by 2045 [3]. According to the International Diabetes Federation (IDF), 11.1% of adults (20 - 79 years)—about 590 million people—will be living with diabetes by 2025, a number expected to rise to 853 million by 2050. The burden is expected to be highest in low- and middle-income countries undergoing economic transitions [4]. According to IDF Diabetes Atlas, 10th Edition, 2021, in 2021 alone, DM caused an estimated 6.7 million deaths and accounted for global healthcare expenditures of approximately USD 966 billion.

Although modern medicine offers treatments such as insulin and oral hypoglycemic agents, these are often associated with side effects including insulin resistance, weight gain, gastrointestinal disturbances, liver dysfunction, and increased risk of hypoglycemia [5] [6]. Other pharmacological options like amylin analogs and alpha-glucosidase inhibitors (e.g., acarbose, miglitol, voglibose) are also limited by adverse effects such as lactic acidosis and diarrhea. Thus, there is a growing need for alternative therapeutic agents that are effective, affordable, and present minimal side effects.

In recent years, medicinal plants have gained attention as viable sources of antidiabetic compounds. Phytochemicals such as flavonoids, tannins, phenolics, and alkaloids have been shown to enhance insulin secretion, improve insulin sensitivity, and reduce glucose absorption [7] [8]. Other non-essential bioactive compounds, including carotenoids and stilbenes, possess antioxidant, anti-inflammatory, and antiviral properties, further supporting their potential in managing diabetes and its complications [9] [10].

Mondia whitei, a plant traditionally used across Africa, has been employed for treating various ailments, including diabetes, hypertension, infertility, stomachache, and rheumatism [1] [11]. Virtual screening studies have identified antidia-

betic compounds such as 5-chloropropacin and 7-hydroxy-4,8-dimethoxypropacin in *M. whitei* [12]. Additionally, 2-hydroxy-4-methoxy benzaldehyde, a compound found in *M. whitei*, has demonstrated antioxidant and antidiabetic potential [13].

Despite its ethnomedicinal use, scientific validation of *M. whitei's* pharmacological properties remains limited. This study was therefore designed to evaluate the antidiabetic and antioxidant effects of *M. whitei* root extract in streptozotocin (STZ)-induced diabetic Wistar rats. Male rats were selected due to their lower hormonal variability and greater sensitivity to STZ compared to females [14]. The STZ model is widely used in diabetes research due to its rapid and reproducible induction of hyperglycemia [15].

The objectives of this study were to 1) qualitatively assess the phytochemical composition of *M. whitei* root extract, 2) evaluate its *in vitro* antioxidant activity, and 3) investigate its effects on fasting blood glucose, body weight, liver and kidney function markers, lipid profile, lipid peroxidation, and *in vivo* antioxidant capacity in diabetic rats.

2. Materials and Methods

2.1. Materials

Cryovials, vacutainers for storage of processed blood samples, needles, syringes (2 mL), microfine needles (0.5 mL), dissecting kit, glucometer (Gluco Rx type), glucose strips (Gluco Rx strips) and automatic pipettes and pipette tips were bought from Bridge Well Scientific, Eldoret, Kenya. Rat pellets (chow) were commercially bought from Maraba Agro Vet in Eldoret, Kenya. Streptozotozin (STZ) was obtained from Nacalai Tesque, Inc, Kyoto, Japan. Thiobarbituric acid (TBA) was obtained from (Sigma Aldrich, St. Louis, Missouri, USA) and Tetramethoxypropane (TMP) was bought from Kobian Scientific, Nairobi, Kenya. DPPH was acquired from Avonchem Wellingtine House, Macclesfield, UK. Metformin (Glucophage) was obtained from Lipha Pharma Ltd, UK. All other commercial reagents used were of analytical grade.

2.2. Plant Collection and Identification

Fresh roots of *M. whitei* were obtained from 0˚35'28.0"N 34˚35'42.6"E, Bungoma County, Kenya and in situ identification was done by a local herbalist. *M. whitei* roots were then transported to the University of Eldoret where they were botanically identified by Mr. Dennis Onyango a taxonomist in the Department of Biological Sciences, University of Eldoret, Kenya and was assigned herbarium label number MUH/MOW/03/95.

2.3. Plant Crude Extract Preparation

The roots of *M. whitei* were washed to remove any debris then chopped into small pieces, followed by drying at room temperature and crushed into homogenous powder using an electric mill (Disk Mill FFc-23, China). Hexane crude extract of

M. whitei roots was prepared according to [16] whereby the powdered plant (200 g) was soaked in 6 L of CH_2Cl_2:MeOH (1:1) mixture at room temperature for 72 h and then filtered. The mixture was then concentrated under reduced pressure at 45˚C using a Rotary Evaporator (Rotavapor type EL 30, model AG CH-9230, Germany) and extracted for 30 min in 500 mL of hexane and filtered. The solvent was removed as previously to obtain crude extract which was weighed. Aqueous crude extract of *M. whitei* roots was prepared by dissolving 200 g of the powdered roots in 1.3 L of distilled water and kept for 72 h at 4˚C and occasionally stirred. After filtration, the solution obtained was evaporated in an oven (50˚C) for 72 h and the residue weighed. *M. whitei* methanol extract was obtained through maceration of powdered roots using methanol (1:5 w/v) for 72 hours with regular stirring [17]. The mixture was then filtered and concentrated under reduced pressure at 50˚C using a Rotary Evaporator (Rotavapor type EL 30, model AG CH-9230, Germany), followed by incubation at 50˚C for 48 hours to obtain the final residue. Methanolic extract after solvent removal, yielded about 17.8 g (8.91% w/w) while aqueous extract yielded 13.7 g (6.85% w/w) and the hexane extract yielded 3.7 g (1.85% w/w). For oral dosing, the extract was reconstituted in normal saline (0.9% NaCl).

2.4. Qualitative Phytochemical Screening of the Crude Extract

Analysis of phytochemicals in hexane, methanol and aqueous root extracts was done in accordance to [18]-[20] using standard chemical tests.

2.5. *In Vitro* Antioxidant Analysis of Crude Extract

2.5.1. DPPH Scavenging Activity

DPPH scavenging assay was done according to [21]. 6 mg of a stable free radical, 1,1-diphenyl-2-picryhydrazyl (DPPH), was accurately weighed and dissolved in 50 mL of analytical grade methanol and made to 0.3 mM solutions. One mL of the methanolic solution of 0.3 mM DPPH was added to 2.5 mL of each of the methanol and aqueous extract concentrations (10, 50, 100, 200, and 400 µg/mL). The mixtures were shaken and incubated for 15 minutes in the dark, at room temperature. Methanol (2.5 mL) plus sample solution (1 mL) was used as a blank. In addition, L-ascorbic acid at concentrations equivalent to that of the test samples was used as positive control. After incubation, absorbance (A) was measured at 517 nm in triplicate using a spectrophotometer (Spectro Scan 30, Biotech Engineering Management Co. ltd, UK). Percentage of the radical scavenging activity (% RSA) was calculated using the following formula below.

$$\%\ \text{DPPH radical scavenging activity} = \frac{\text{Abs of control} - \text{Abs of test sample}}{\text{Abs of control}} \times 100$$

2.5.2. Ferric Reducing Antioxidant Power Assay

The ferric reducing antioxidant power of the aqueous and methanolic root extracts of *M. whitei* were evaluated according to the methods described by [21]. The reaction mixtures which incorporated 1 mL of different concentrations of

methanolic extract, aqueous extracts and L-ascorbic acid as a positive control (0.2, 0.4, 0.6, 0.8, 1.0, and 5.0 mg/mL), 2.5 mL of phosphate buffer (200 mM, pH 6.6), and 2.5 mL of potassium ferricyanide (30 mM) was prepared. The mixtures were then incubated at 50˚C for 20 minutes after which 2.5 mL of trichloroacetic acid (600 mM) was added, mixed, and centrifuged at 3000 rpm for 15 minutes. Thereafter, 2.5 mL of the supernatants was aspirated and mixed with 2.5 mL of distilled water and 0.5 mL of $FeCl_3$ (6 mM). Blank was prepared by taking 1 mL of distilled water and treating it as the samples. The absorbance values of samples and standard were measured in triplicates against blank at 700 nm using a spectrophotometer (Spectro Scan 30, Biotech Engineering Management Co. ltd, UK).

2.6. Experimental Animals

Thirty male Wistar albino rats (*Rattus norvegicus*) of 6 - 8 weeks' old were purchased from Zoology Department, Chiromo Campus, University of Nairobi, Kenya. The animals were housed in wire cages with sawdust and soft grass placed at the bottom of the cages. The animals were housed in cages in groups of 6 rats under standard laboratory conditions (Temperature, 25˚C, 40% - 60% humidity and 12 h light and 12 h dark cycle) and cleanliness was maintained in the cages. All animals had free access to food and drinking water. The rats were allocated two weeks for acclimatization before initiation of the experiments.

2.7. Induction of Diabetes Mellitus

Diabetes mellitus was induced according to [22] with slight modification whereby twenty four overnight fasted male rats were given a single intraperitoneal injection of 65 mg/Kg bwt of STZ [23] prepared in 100 µL ice cold 0.1 M sodium citrate buffer (pH 4.5). The normal control rats were injected intraperitoneally with 100 µL of 0.1 M sodium citrate buffer. The STZ induced experimental groups were given 5% glucose solution overnight to overcome drug- induced hypoglycemia. Three days after the injection, hyperglycemia was confirmed by the elevated glucose levels in the blood drawn from the tail end using a glucometer. Those whose fasting blood sugar levels were ≥150 mg/dl (8.3 mmol/L) [14] were considered diabetic and suitable for study.

2.8. Experimental Design

The experimental design was set according to [24] with slight modification. The animals were placed in five groups randomly with each group containing six rats as outlined below.

Group I: Normal control administered with normal saline daily

Group II: Diabetic control administered with normal saline daily.

Group III: Diabetic rats administered with 200 mg/Kg bwt of crude extract.

Group IV: Diabetic rats administered with 400 mg/Kg bwt of crude extract.

Group V: Diabetic rats administered with 100 mg/Kg bwt of metformin (Standard drug).

Rats were assigned to experimental groups via a computer-generated randomization sequence. Doses of 200 mg/kg and 400 mg/kg of extracts were chosen in accordance with earlier research highlighting the efficacy and safety of plant-derived extracts in diabetic rodent models [17] [22].

M. whitei crude extract (200 mg/kg bwt and 400 mg/kg bwt) and metformin (100 mg/kg bwt) were administered orally to each rat daily for 21 days. Fasting body weights were recorded on days 0, 7, 14, and 21 to monitor changes before and after treatment and to adjust weekly dosages accordingly. Fasting blood glucose levels were also measured on the same days to assess the effects of the treatments.

2.9. Animal Sacrifice and Collection of Samples

The animals were sacrificed according to [25] [26] and the rats were fasted overnight prior to terminal sacrifice. On the 22nd day, all the rats were weighed and FBS determined. The animals were then placed under terminal anesthesia using chloroform and sacrificed. Blood was collected via cardiac puncture using a sterile needle and syringe, with careful extraction from the ventricle to prevent heart collapse.

One portion of the blood was put in vacutainers containing ethylene diamine tetra acetic acid (EDTA) to prevent coagulation and centrifuged at 1500 rpm for 15 minutes to obtain plasma for subsequent *in vivo* antioxidants assay. Blood sample for biochemical tests was collected in vacutainers with no EDTA and kept at 4˚C for 4 hours to clot and then centrifuged at 1500 rpm for 15 minutes to obtain serum. The serum was refrigerated at −22˚C prior to usage for biochemical assays. The sacrificed animals were laid on a dissecting board after blood sample collection. Vertical midline was cut with a pair of scissors running from the neck to the pelvis to open the peritoneum. The liver was excised, washed in ice cold normal saline and stored at −20˚C for lipid peroxidation and ferric chloride reducing power assay analyses.

2.10. Biochemical Serum Analyses of Lipid Profile and Indices of Liver and Kidney Function

The serum obtained after animal sacrifice was used for lipid profile analysis that is total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C) and triglycerides (TG). Liver function tests that is serum GGT, ALP, AST, ALT, total bilirubin, bilirubin direct, total proteins (TP), and albumin (ALB) were analyzed. Serum urea and creatinine were assessed to determine kidney function. All these tests were done according to standard operating procedures of Cobas Integra 400 plus auto-analyzer (Roche Diagnostics, Mannheim, Germany) at Moi Teaching and Referral Hospital (MTRH), Eldoret.

2.11. *In Vivo* Antioxidant Capacity Analyses

2.11.1. Analysis of *M. whitei* Extracts on Plasma's Ability to Reduce Ferric Ions

Effect of extracts on plasma reducing power was determined according to [27]. 1

mL of plasma was mixed with 0.5 mL phosphate buffer (0.2 M, pH 6.6) and 0.5 mL potassium ferricyanide (1% w/v). The mixture was incubated at 50˚C for 20 min. After terminating the reaction by adding 2 mL trichloroacetic acid (10% w/v), the mixture was centrifuged at 3000 rpm for 10 min. 0.5 mL supernatant of the solution was mixed with 0.5 mL distilled water and 0.1 mL $FeCl_3$ (0.1% w/v). After 5 min, the absorbance was measured at 700 nm using a spectrophotometer (Spectro Scan 30, Biotech Engineering Management Co. ltd, UK). A mixture containing all the above reagents except the sample was used as blank. Absorbance values were interpreted as the concentration of ferrous ions (Fe^{2+}) formed from reduction of ferric ions (Fe^{3+}) since Fe^{2+} forms a colored complex with ferric chloride, which can be measured spectrophotometrically at 700 nm.

2.11.2. Analysis of *M. whitei* Extract on Liver's Ability to Reduce Ferric Chloride

This assay was done according to [28] with little modifications. 10% (w/v) liver homogenate was prepared in Tris HCL buffer (pH 7.4). The homogenate was centrifuged at 4000 rpm at 4˚C for 15 min and the supernatant collected. 1mL of supernatant was mixed with 0.5 mL phosphate buffer (0.2 M, pH 6.6) and 0.5 mL potassium ferricyanide (1% w/v). The mixture was incubated at 50˚C for 20 min. After terminating the reaction by adding 2 mL trichloroacetic acid (10% w/v), the mixture was centrifuged at 3000 rpm for 10 min. 0.5 mL supernatant of the solution was mixed with 0.5 mL distilled water and 0.1 mL $FeCl_3$ (0.1% w/v). After 5 min, the absorbance was measured at 700 nm using a spectrophotometer (Spectro Scan 30, Biotech Engineering Management Co. ltd, UK). A mixture containing all the above reagents except the sample was used as blank.

2.12. Lipid Peroxidation Analysis of Liver Tissues

Determination of malondialdehyde (MDA), an index of lipid peroxidation in liver tissues after extract treatment was determined as described by [22] with a little modifications. Liver tissues initially frozen at −20˚C were removed and allowed to thaw for one hour to attain room temperature. One gram of the liver tissue in 9 mLs of 1.15% cold potassium chloride (KCl) was homogenized with mortar and pestle and then centrifuged at 2000 rpm for 10 minutes. The resultant supernatant (0.1 mL) was then be mixed with 0.2 mL of 8.1% sodium dodecyl sulfate (SDS), 1.5 mL of 20% acetic acid, and 1.5 mL of 8% thiobarbituric acid (TBA). The volume of the mixture was made to 4 mL with distilled water and then heated at 95˚C on a water bath for 60 minutes using boiling chips. After incubation, the tubes were cooled to room temperature and final volume made to 5 mL in each tube. Five mL of butanol: pyridine (15:1) mixture was added and the contents vortexed thoroughly for 2 minutes. After centrifugation at 4000 rpm for 10 minutes, the upper organic layer was taken and its optical density measured using a spectrophotometer (Spectro Scan 30, Biotech Engineering Management Co. ltd, UK) at 532nm. The MDA levels were obtained from a standard calibration curve generated using hydrolyzed 1,1,3,3-tetramethoxypropane (TMP) as a standard. The ref-

erence blank was 0.1 mL of 1.15% KCl treated in the same way as the samples and standards by addition of the same reagents. The level of malondialdehyde in samples was finally expressed in μM.

2.13. Data Management and Statistical Analysis

Statistical analysis was performed using MS Excel and R software. Means and standard error of means (SEM) were calculated. Statistical differences were done by paired Student's t test and One Way Analysis of Variance (ANOVA) at the confidence limit of 95%.

3. Results

3.1. Qualitative Phytochemical Analysis of *M. whitei* Crude Root Extract

Crude extracts of *Mondia whitei* roots were obtained using aqueous, hexane, and methanol solvents, and subjected to qualitative phytochemical screening. The results, summarized in Table 1, indicate distinct phytochemical profiles across the different solvents. The aqueous extract tested positive for saponins, phenols, tannins, flavonoids, glycosides, coumarins, steroids/sterols, and terpenoids, while alkaloids and anthraquinones were absent. The hexane extract contained saponins, phenols, tannins, glycosides, coumarins, steroids/sterols, and terpenoids, but lacked alkaloids, flavonoids, and anthraquinones. In contrast, the methanol extract exhibited the broadest phytochemical spectrum, with the presence of saponins, phenols, tannins, alkaloids, flavonoids, glycosides, coumarins, steroids/sterols, and terpenoids; only anthraquinones were not detected. These findings suggest that methanol was the most effective solvent for extracting a wide range of phytochemical constituents from *M. whitei* roots.

Table 1. Qualitative phytochemical analysis of *M. whitei* crude root extract.

Phytochemicals	Aqueous extract	Hexane extract	Methanol extract
Saponins	+	+	+
Phenols	+	+	+
Tannins	+	+	+
Alkaloids	−	−	+
Flavonoids	+	−	+
Glycosides	+	+	+
Coumarins	+	+	+
Steroids/sterols	+	+	+
Terpenoids	+	+	+
Anthraquinones	−	−	−

Presence (+), *Absence* (−).

3.2. *In Vitro* Anti-Oxidant Properties of the *M. whitei* Crude Root Extract

3.2.1. DPPH Scavenging Activity

Methanolic and aqueous extracts exhibited remarkable concentration-dependent increase in percentage of DPPH scavenged as indicated in Figure 1. Across all tested concentration L—ascorbic acid (positive control) had highest absorbance, followed by methanolic extract and finally aqueous extract. Inhibitory concentration (IC_{50}) values, representing the concentration required to scavenge 50% of the DPPH radicals, were 23.00 µg/mL, 42.71 µg/mL and 116.79 µg/mL for ascorbic acid, methanol extract and aqueous extract respectively.

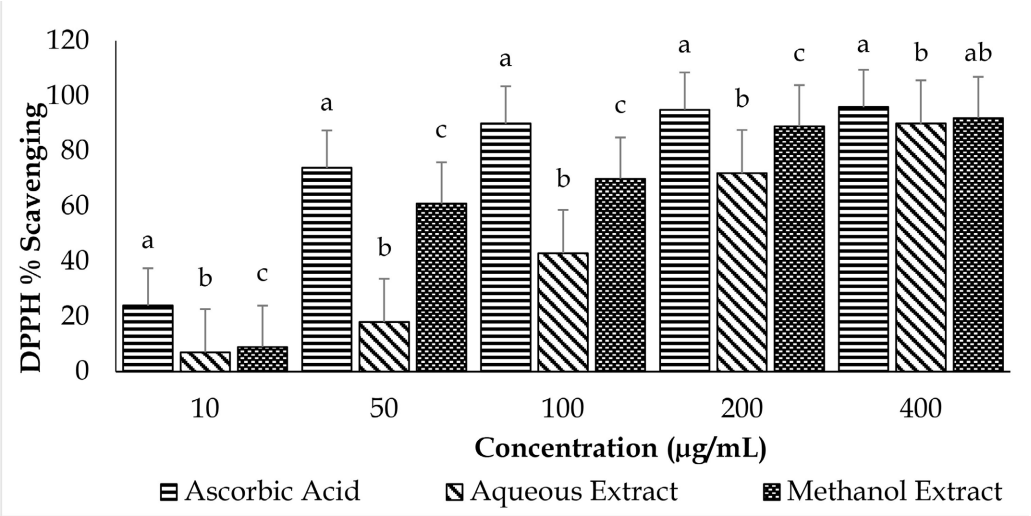

Figure 1. DPPH scavenging activity of *Mondia whitei* root extracts. Values are expressed as mean ± SEM; n = 3. Bars with different letters are significantly different ($p < 0.05$, ANOVA). DPPH; 1,1-diphenyl-2-picrylhydrazyl.

3.2.2. Ferric Ions Reducing Antioxidant Power Assay

Methanolic and aqueous extracts exhibited concentration-dependent increases in values at wavelength 700 nm as shown in Figure 2 which was an indication of the extracts' reducing power. Inhibitory concentration (IC_{50}) values, representing the concentration required to achieve 50% reduction in ferric ions, were 0.23 mg/mL, 24.13 mg/mL and 29.5 mg/mL for ascorbic acid, methanol extract and aqueous extract respectively. Ascorbic acid had the lowest IC_{50}, while that of methanol was lower than aqueous extract. The methanolic extract showed significantly higher reducing power compared to the aqueous extract, reflecting its greater antioxidant capacity and based on this methanol was selected to obtain extract used in subsequent animal studies.

3.3. Effects of *M. whitei* Crude Root Extract on Fasting Blood Sugar and Body Weight

At day 0 (Before treatment), all STZ-injected rats were diabetic with FBS levels significantly higher than normal control rats ($p < 0.05$) as shown in Figure 3.

Upon treatment with 200 and 400 mg/kg bwt of *M. whitei* root extract, and 100 mg/kg bwt of metformin for 21 days, there was significant reduction in the mean FBS levels when compared with diabetic control group ($p < 0.05$). The mean body weights for the normal control rats had an overall trend of increase across the study period while the diabetic induced groups had a declining trend, with more decline being observed in diabetic control group as shown in Table 2.

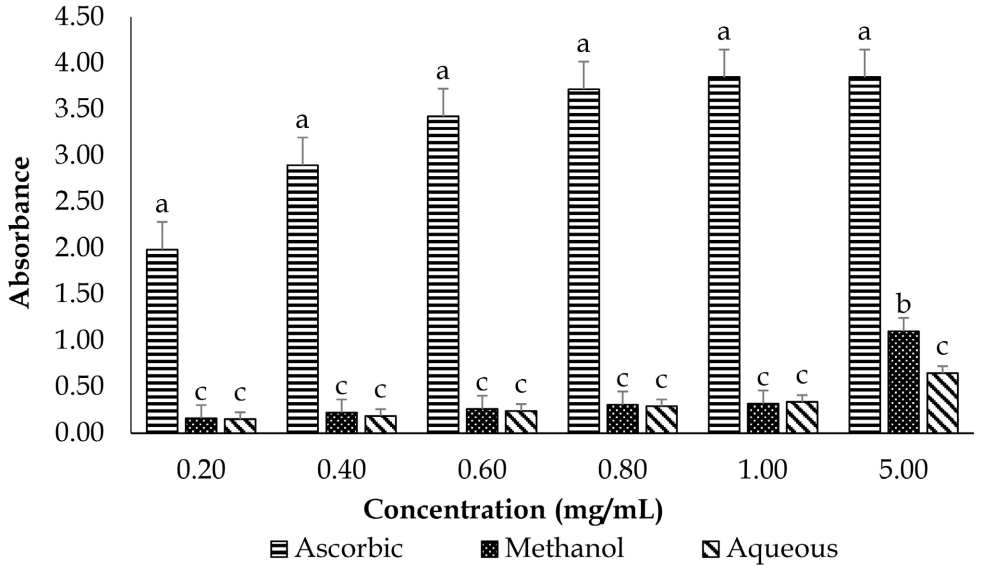

Figure 2. Ferric ions reducing power of *Mondia whitei* root extracts. Values are expressed as mean ± SEM; n = 3. Bars with different letters are significantly different ($p < 0.05$, ANOVA).

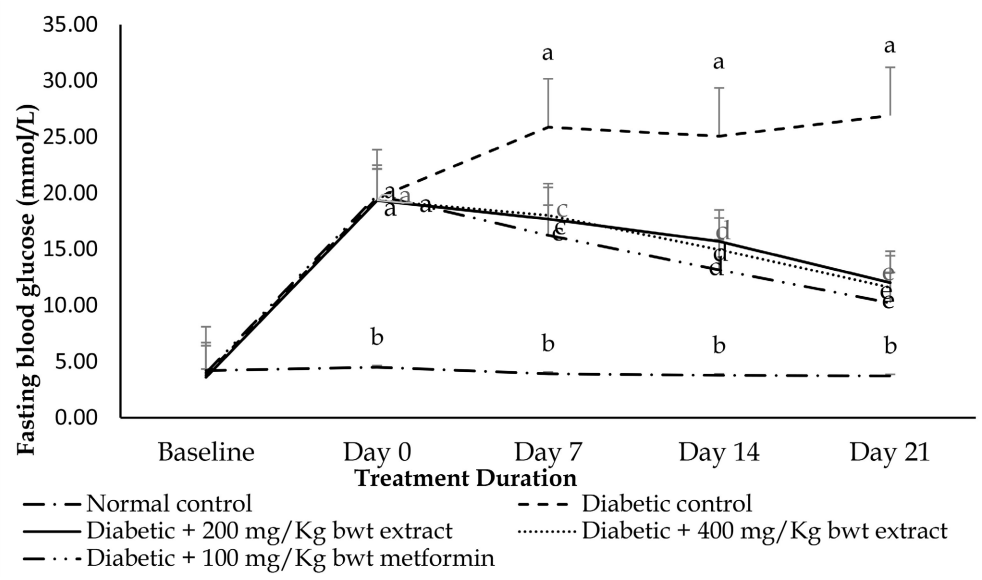

Figure 3. Effects of *Mondia whitei* crude root extract on fasting blood sugar levels in STZ-induced diabetic rats. Values are expressed as mean ± SEM, n = 6. Values with superscript c, d & e are significantly different compared to diabetic control while values with superscript a, c, d & e are significantly different compared to normal control ($p < 0.05$, ANOVA). Baseline values represent the mean values before induction of diabetes.

Table 2. Effects of *M. whitei* crude root extract on body weights (g).

Treatment group	Day 0_FBW (g)	Day 7_FBW (g)	Day 14_FBW (g)	Day 21_FBW (g)	% Change in body weight on 21st day (from day 0)
Normal control	153.50 ± 4.63	153.50 ± 2.99	154.00 ± 2.94	164.00 ± 5.49	+7
Diabetic control	147.67 ± 2.67	141.33 ± 2.03	135.00 ± 4.04	125.33 ± 3.76[a]	−15
Diabetic + 200 mg/Kg bwt extract	155.67 ± 7.86	159.00 ± 7.23	145.67 ± 6.89	133.67 ± 4.81[a]	−14
Diabetic + 400 mg/Kg bwt extract	144.00 ± 4.03	135.00 ± 7.09	135.50 ± 7.09	124.25 ± 6.17[a]	−13
Diabetic + 100 mg/Kg bwt metformin	145.00 ± 2.89[a]	138.00 ± 1.73[a]	134.33 ± 4.10[a]	126.33 ± 1.76[a]	−13

Values are expressed as mean ± SEM, n = 6. Values with superscript are significantly different compared to diabetic and normal control. ($p < 0.05$, ANOVA). FBW; Fasting body weight.

3.4. Effects of Crude *M. whitei* Root Extract on Liver and Kidney Function Serum Indices

The normal control also had significantly lower levels of GGT, ALT, and ALP than the diabetic control. Treatment with 200 mg/kg bwt of *M. whitei* root extract and 100 mg/kg bwt of metformin significantly reduced GGT levels. ALP and ALT levels were significantly reduced by 200 mg/kg and 400 mg/kg bwt of *M. whitei* root extract and 100 mg/kg bwt of metformin compared to the diabetic control. AST levels were significantly lower in the normal control compared to the diabetic control, with no significant differences between the treatment groups and diabetic control. Total and direct bilirubin levels showed no significant difference between the normal and diabetic control groups. However, 200 mg/kg bwt of *M. whitei* root extract significantly reduced direct bilirubin levels. In contrast, treatment with 400 mg/kg bwt of *M. whitei* root extract resulted in a significant increase in total bilirubin compared to the diabetic control. No significant difference in TP was observed between normal and diabetic control groups, with all treatment groups showing a non-significant increase in TP. The normal control had significantly higher albumin levels than the diabetic control, but all treatment groups showed only a non-significant increase in albumin. The normal control had significantly lower urea levels and significantly higher creatinine levels than the diabetic control. All treatment groups led to a non-significant reduction in both urea and creatinine compared to the diabetic control. These results are summarized in Table 3.

3.5. Effects of *M. whitei* Crude Root Extract on Serum Lipid Profile Parameters

TG levels in the normal control were insignificantly lower than in the diabetic control (Figure 4). Also, treatment with 400 mg/kg bwt of *M. whitei* root extract led to a significant reduction in triglycerides compared to the diabetic control

(Figure 4). The normal control had significantly lower total cholesterol than the diabetic control. Treatment with 200 mg/kg bwt of *M. whitei* root extract significantly increased total cholesterol, while 400 mg/kg bwt of *Mondia whitei* root extract significantly decreased it compared to the diabetic control. The normal control had significantly higher HDL-C levels than the diabetic control. Treatment with 200 mg/kg bwt of *M. whitei* root extract significantly increased HDL-C, while 400 mg/kg bwt of *M. whitei* root extract and 100 mg/kg bwt of metformin led to a non-significant increase. The normal control had an insignificantly lower LDL-C level than the diabetic control. All treatment groups showed a non-significant reduction in LDL-C, with the greatest reduction observed in the 100 mg/kg bwt of metformin group.

Table 3. Effects of crude *M. whitei* root extract on liver and kidney function serum indices.

Biochemical parameters	Normal control	Diabetic control	Diabetic + 200 mg/Kg bwt extract	Diabetic + 400 mg/Kg bwt extract	Diabetic + 100 mg/Kg bwt metformin
Total bilirubin (mmol/L)	1.20 ± 0.15	1.50 ± 0.15	1.40 ± 0.06	2.13 ± 0.06^{a}	1.65 ± 0.06^{b}
Bilirubin direct (mmol/L)	0.58 ± 0.10	1.17 ± 0.12	0.63 ± 0.03^{c}	1.38 ± 0.05^{b}	0.68 ± 0.05
GGT (u/L)	2.75 ± 1.11	11.33 ±0 .88^{a}	4.00 ± 0.58^{d}	7.00 ± 0.41^{b}	5.75 ± 0.48^{d}
AST (u/L)	181.43 ± 8.24	253.20 ± 14.75^{b}	245.70 ± 4.65^{b}	338.60 ± 14.36^{b}	252.60 ± 8.34^{b}
ALT (u/L)	66.13 ± 3.12	192.60 ± 15.13^{a}	106.80 ± 6.30^{c}	148.93 ± 5.13^{a}	131.88 ± 4.96^{a}
ALP (u/L)	94.50 ± 5.30	388.33 ± 12.39^{a}	192.67 ± 13.86^{c}	260.25 ± 7.70^{c}	280.00 ± 8.71^{c}
Total protein (g/L)	73.58 ± 3.28	59.57 ± 5.77	66.37 ± 3.35	59.60 ± 2.51	63.13 ± 3.67
Albumin (g/L)	41.93 ± 1.67	28.50 ± 1.25^{b}	34.13 ± 1.63	31.90 ± 0.66^{b}	33.95 ± 3.42
Urea (mmol/L)	8.13 ± 0.46	23.60 ± 2.51^{b}	19.47 ± 0.56^{b}	22.60 ± 1.16^{b}	18.90 ± 1.35^{b}
Creatinine (mmol/L)	30.50 ± 1.76	22.00 ± 2.52^{b}	22.67 ± 1.45^{b}	20.25 ± 0.63^{b}	23.50 ± 1.04^{b}

Values represent mean ± SEM; n = 6. Mean values with letters a, c, d, e are significantly different compared to diabetic control while those with letter a, b & e are significantly different compared to normal control. ($p < 0.05$, Student's t test). GGT; Gamma-glutamyl transferase, AST; Aspartate transaminase, ALT; Alanine transaminase, ALP; Alkaline phosphatase.

3.6. Effects of *M. whitei* Crude Root Extract on Liver Tissue and Blood Plasma Capacity to Reduce Ferric Ions

The impact of *M. whitei* crude root extract on *in vivo* antioxidant capacity was evaluated by measuring the ferric ions reduction capacity of liver tissue and blood plasma using the Ferric Reducing Antioxidant Power (FRAP) assay and the results are as shown in Figure 5. Absorbance at 700 nm was not significantly different between normal control and diabetic control. Treatment with 400 mg/kg bwt of *M. whitei* root extract and 100 mg/kg bwt of metformin led to a significant increase of absorbance compared to normal control and diabetic control. 200 mg/kg bwt of *M. whitei* root extract also led to an increase compared to normal control and diabetic control though not significant.

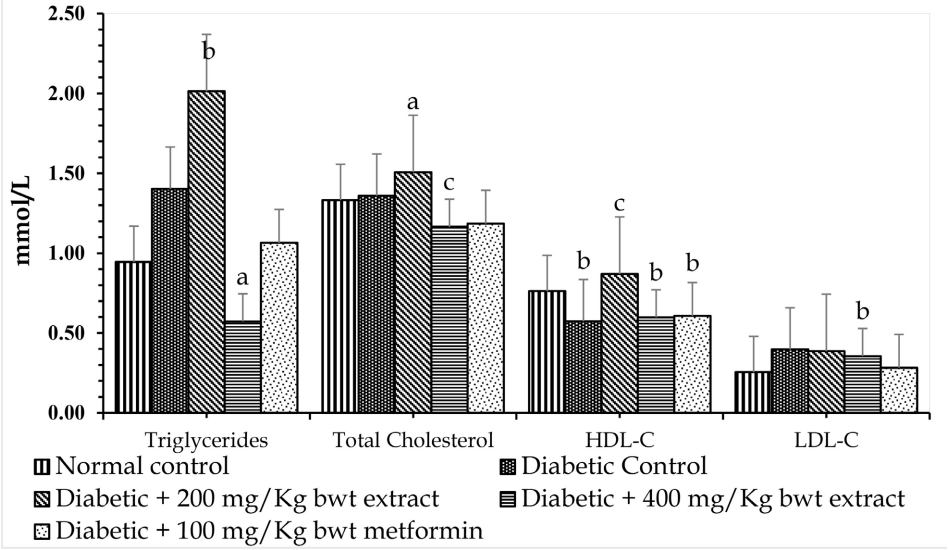

Figure 4. Effects of *Mondia whitei* crude root extract on serum lipid profile parameters in STZ-induced diabetic rats. Values represent mean ± SEM; n = 6. Mean values with letter a, c on bar graphs are statistically significant compared to diabetic control & while those with letter a & b, are significantly different compared to normal control ($p < 0.05$, Student's t-test). HDL-C; High-density lipoprotein-cholesterol, LDL-C; Low-density lipoprotein-cholesterol.

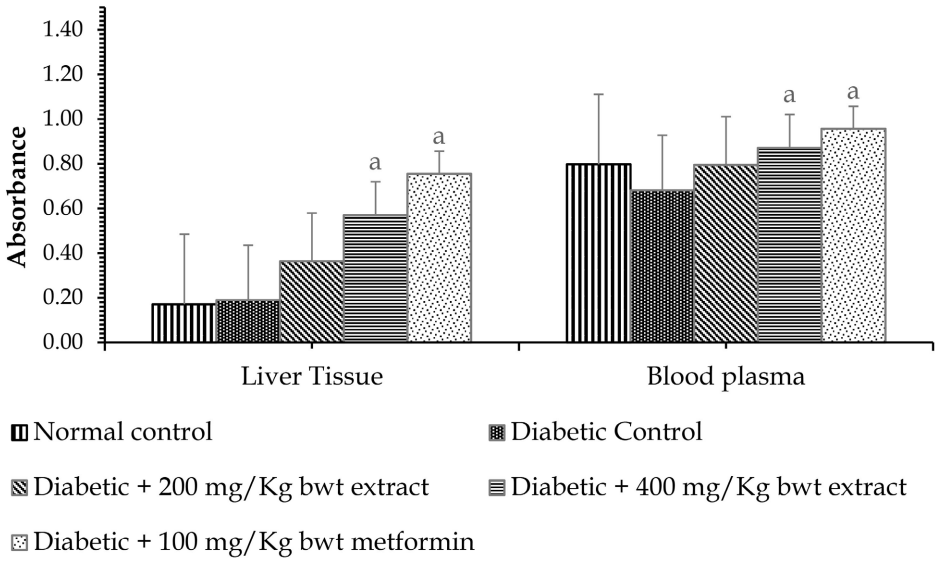

Figure 5. Effects of *M. whitei* crude root extract on liver tissue and blood plasma capacity to reduce ferric ions. Values are expressed as mean ± SEM, with n = 6. Bar graphs with letter a are statistically significant compared to diabetic and normal control ($p < 0.05$, Student's t-test).

3.7. Effects of *M. whitei* Crude Root Extract on Lipid Peroxidation in Liver Tissues

Lipid peroxidation in liver tissues was assessed by measuring malondialdehyde (MDA) levels whose absorbance was measured at 532 nm, as shown in **Figure 6**. Normal control had significantly lower MDA levels compared to diabetic control. Treatment with *M. whitei* root extract at 400 mg/kg bwt and metformin at 100

mg/kg bwt resulted in a significant reduction in MDA levels compared to the diabetic control. Although the 200 mg/kg bwt dose of *M. whitei* extract also reduced MDA levels, the decrease was not statistically significant.

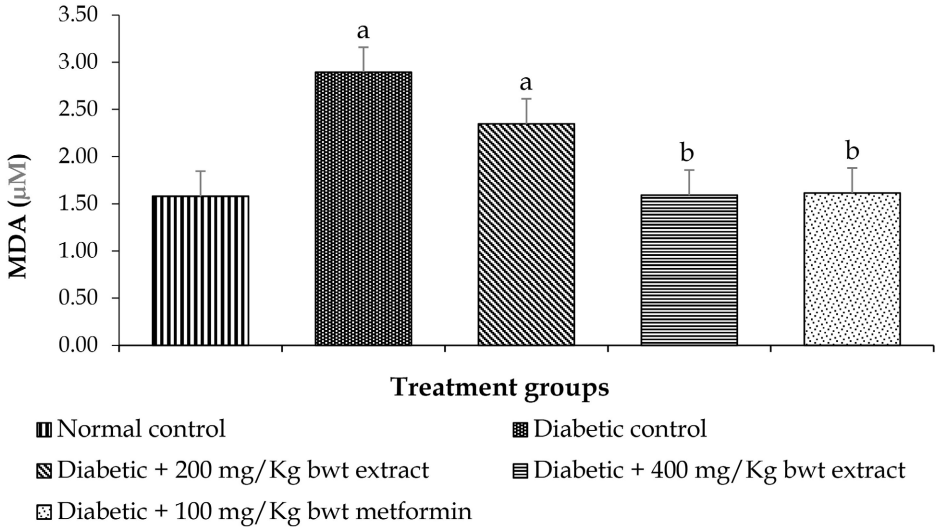

Figure 6. Effects of crude *M. whitei* root extract on lipid peroxidation in liver tissues. Values represent mean ± SEM; n = 6. Mean values with b letters on bar graphs are statistically significant compared to diabetic control while those with letter a are significantly different compared to normal control ($p < 0.05$, Student's t test). MDA; Malondialdehyde.

4. Discussion

This study aimed to qualitatively determine the phytochemical composition of *Mondia whitei* (*M. whitei*) crude root extract, evaluate its antioxidant properties, and investigate its effects on fasting blood sugar (FBS), body weight, serum liver and kidney function markers, lipid profile, and liver lipid peroxidation in streptozotocin (STZ)-induced diabetic Wistar rats.

The variation in phytochemical constituents across different solvent extracts highlights the importance of solvent polarity in phytochemical extraction. Methanol and aqueous extracts yielded a broader range of phytochemicals due to their ability to solubilize both polar and semi-polar compounds, whereas hexane, being non-polar, extracted fewer compounds. These findings align with those of [29], who reported that methanol and aqueous extracts of *Beilschmiedia roxburghiana* extracted more diverse phytochemicals than hexane.

The antioxidant activity of *M. whitei* root extracts was confirmed *in vitro* using DPPH and ferric reducing assays. Both methanol and aqueous extracts demonstrated concentration-dependent free radical scavenging ability. This activity is likely due to the presence of phytochemicals such as flavonoids, phenols, tannins, saponins, alkaloids, and terpenoids, which are known to donate hydrogen atoms or electrons and neutralize reactive species [30] [31].

STZ-induced diabetes is a well-established model for studying hyperglycemia due to its specific cytotoxic effects on pancreatic β-cells via GLUT2-mediated up-

take and nitrosourea-induced oxidative damage [32] [33]. In this study, treatment with *M. whitei* root extract significantly reduced FBS in a dose-dependent manner over 21 days. The 400 mg/kg dose produced hypoglycemic effects comparable to metformin, the standard control. These findings suggest that *M. whitei* possesses antihyperglycemic properties, potentially through mechanisms involving both pancreatic and extrapancreatic pathways. The hypoglycemic effect can be attributed to the presence of flavonoids, saponins, and phenols, which have documented anti-inflammatory, antioxidant, and insulin-sensitizing properties [34]. These secondary metabolites modulate key molecular targets involved in metabolism of glucose, insulin signaling, and development of oxidative stress, thereby improving glycemic control and lowering the risk of complications [6]. These bioactives can inhibit carbohydrate digesting enzymes, enhance insulin secretion and sensitivity, regulate glucose transporters, and suppress pathways with inflammatory responses and formation of advanced glycation end products [6]. Flavonoids in particular are known to enhance insulin secretion, promote peripheral glucose uptake, inhibit intestinal glucose absorption, and suppress hepatic glucose production [35] [36]. Furthermore, they support antioxidant enzyme activity (e.g., SOD, CAT, GPx) and reduce reactive oxygen species, thus protecting β-cells from oxidative damage. Phytosterols, also found in *M. whitei*, contribute to glucose and lipid metabolism regulation [35].

Weight loss is a hallmark of uncontrolled diabetes, often driven by increased proteolysis and lipid catabolism. Treatment with *M. whitei* extract mitigated body weight loss in diabetic rats. Although not statistically significant compared to the non-diabetic control, the attenuation in weight loss suggests improved glucose utilization and potential muscle preservation [37] [38].

M. whitei extracts also modulated lipid profiles in diabetic rats, reducing triglycerides (TG), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C), while increasing high-density lipoprotein cholesterol (HDL-C). These improvements reflect the extract's potential in managing diabetes-associated dyslipidemia, likely due to the action of flavonoids and saponins that regulate lipid metabolism enzymes and reduce intestinal lipid absorption [39]. The 200 mg/kg dose unexpectedly increased TG and TC levels, suggesting a possible threshold effect, consistent with reports that subtherapeutic doses may not effectively trigger lipid-regulating pathways [40] [41].

The cholesterol-lowering effects may also be attributed to saponins' ability to bind bile acids and enhance cholesterol excretion, while flavonoids modulate bile acid metabolism and inhibit cholesterol absorption [42] [43]. Notably, the 200 mg/kg dose produced a 52.6% increase in HDL-C, possibly via flavonoid-induced upregulation of liver X receptors (LXRs), which stimulate reverse cholesterol transport [36]. The lack of further increase at the 400 mg/kg dose suggests a potential saturation effect, emphasizing the need to determine optimal therapeutic doses [40].

Hepatoprotective activity was demonstrated by reduced levels of liver enzymes

(ALT, ALP, GGT) in treated groups, indicating a protective effect against STZ-induced liver damage. Although reductions in AST and bilirubin were not statistically significant, trends were favorable. Similarly, increases in total protein and albumin, though not significant, point toward a restorative effect on hepatic synthetic function. Although the decreases in AST and bilirubin did not achieve statistical significance, they nevertheless imply a degree of hepatoprotective effect. This is supported by favorable shifts in liver enzymes and corroborates improvements observed in antioxidant capacity and reduced lipid peroxidation in this study. Kidney function markers (urea and creatinine) also decreased modestly with treatment, suggesting nephroprotective potential.

In vivo antioxidant assessments revealed that *M. whitei* restored antioxidant capacity in liver tissue and plasma in a dose-dependent manner. Although metformin exhibited a stronger effect, the extract significantly increased antioxidant enzyme activity and reduced malondialdehyde (MDA) levels, a marker of lipid peroxidation. This indicates reduced oxidative stress and protection against cellular damage. The antioxidant effects are attributed to the synergistic action of terpenoids, flavonoids, phenols, and tannins, all known to scavenge free radicals, chelate metal ions, and enhance endogenous antioxidant defenses [44]-[46].

The observed decrease in liver lipid peroxidation supports the antioxidant role of *M. whitei*, corroborated by both *in vitro* and *in vivo* assays. These findings affirm the extract's potential to counteract oxidative damage associated with diabetes. However, no adverse clinical effects were investigated in this to justify the biosafety and dosage tolerability of this extract and this is research that can be further explored. Future work should involve quantitative phytochemical analysis, isolation of active constituents, and mechanistic studies—such as histological evaluation of pancreatic and liver tissues—to elucidate the exact pathways through which *M. whitei* exerts its effects. Additionally, dose optimization and toxicity profiling will be crucial for potential clinical applications.

5. Conclusion

The phytochemical-rich crude root extract of *Mondia whitei* exhibited notable antidiabetic, antioxidant, lipid-modulating, and hepatoprotective effects in STZ-induced diabetic Wistar rats. These findings highlight *Mondia whitei's* therapeutic potential as a complementary treatment for managing diabetes mellitus and its associated complications. The extract's multifaceted actions on glycemic control, lipid regulation, and tissue protection position *M. whitei* as a promising candidate for alternative or adjunctive diabetes therapy.

Ethics Approval

Ethical clearance for the animal protocols of this study was approved by the Research Ethics Committee of University of Eastern Africa, Baraton, Kenya (Reference; UEAB/ISERC/09/06/2023). Research license was obtained from National Commission for Science, Technology & Innovation (License No; NACOSTI/P/24/333020).

Availability of Data

Data will be available from the corresponding author upon reasonable request.

Authors' Contribution

KKG was involved in conceptualization, experimentation, data analysis & interpretation, writing original manuscript draft and reviewing. JKK was involved in animal study, experimentation and reviewing. NB was involved in conceptualization, supervision, data interpretation and reviewing. VCT was involved in conceptualization, supervision, data interpretation and reviewing.

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Conflicts of Interest

The authors declare no conflicts of interest.

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Abbreviations

DM: Diabetes mellitus;
STZ: Streptozotocin;
Bwt: Body weight;
FBS: Fasting blood sugar;
FBW: Fasting body weight;
MDA: Malondialdehyde;
LDL-C: Low density lipoprotein cholesterol;
TG: Triglycerides;
TC: Total cholesterol;
HDL-C: High density lipoprotein cholesterol;
GGT: Gamma-glutamyl transferase;
ALP: Alkaline phosphatase;
AST: Aspartate transaminase;
ALT: Alanine transaminase;
TP: Total protein;
ALB: Albumin;
DPPH: 2,2-diphenyl-1-picrylhydrazyl;
EDTA: Ethylene diamine tetra acetic acid;
FRAP: Ferric reducing antioxidant power.