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The Hypoglycaemic, Antihyperlipidemic and Antioxidative Effects of *Anacardium occidentale* Methanolic Nut Extract in Streptozotocin-Induced Diabetic Rats

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Abstract: This research work investigated the anti-diabetic, anti-hyperlipidemic, and anti-oxidative effects of *Anacardium occidentale* methanolic nut extract in Streptozotocin-induced diabetic Wistar rats. Forty (40) Wistar rats weighing 250±30g were randomly divided into five groups of 8rats each. Group1served as the control; Group2-5were induced with diabetes with a single dose of 50mg/kgbw of streptozotocin intraperitoneally. After diabetes induction, Group2 served as the streptozotocin only group, Group3and4 were administered 100mg/kgbw and 200mg/kgbwp.o of *Anacardium occidentale* nut extract, respectively, while Group5 was administered 2mg/kgbw of glimepiride as a reference drug for a period of 4weeks. Food and water intake were monitored daily, bodyweight, and blood glucose levels weekly throughout the experiment. On day29, the animals were sacrificed, and blood samples were collected through cardiac puncture for biochemical studies. Administration of *Anacardium occidentale* nut extract significantly decreased ($p<0.05$) the fasting blood glucose level, oral glucose tolerance test (OGTT), triglyceride (TG), total cholesterol (TC), low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL) concentrations and significantly increase ($p<0.05$) the high-density lipoprotein (HDL) in diabetic treated rats. Superoxide dismutase (SOD), Glutathione peroxidase (GPx), Reduced glutathione (GSH), and Catalase (CAT) levels significantly ($p<0.05$) increases with a decrease Malondialdehyde (MDA) level in diabetic treated rats. Food intake and bodyweight of diabetic treated rats significantly increases ($p<0.05$). Markers of liver and kidney functions were also improved in diabetic treated rats. The results from this study suggest that *Anacardium occidentale* nut may be useful in the therapeutic management of diabetes and its related complications.

Keywords: *Anacardium occidentale*, Diabetes, Dyslipidemia, Oxidative Stress, Liver

1. Background

Diabetes mellitus is a cluster of metabolic diseases characterized by hyperglycemia as a result of abnormal secretion and action of insulin or both. Globally the incidence of the disease is escalating. In 2017, about 451million individuals suffered from diabetes worldwide, with a projection that about 693million people will be affected by the disease by the year 2045 according to International Diabetes Federation [1]. Approximately 14.7million Adults suffer from diabetes in Africa, with Nigeria having the highest and a consistent rise in mortality rate [2].

Chronic hyperglycemia leads to long-term diabetic complications such as macrovascular and microvascular disease, dyslipidemia, and oxidative stress [3]. Diabetes-specific micro-vascular disease is a leading cause of blindness, renal failure, and nerve damage [4]. Long-term hyperglycemia in diabetes mellitus also generates reactive oxygen species (ROS), and a decline in antioxidant status which destroys the cells with resultant secondary complications [5]. This elevation in the ROS level could be due to a decrease in destruction and/or increase in catalase

(CAT), superoxide dismutase (SOD), and glutathione peroxidase (GSH–Px) antioxidants production. The altered levels of these enzymes make the tissues susceptible to oxidative stress leading to the development of diabetic complications [6]. According to epidemiological studies, diabetic mortalities can be explained notably by an increase in vascular diseases other than hyperglycemia [7].

The uptake of glucose by cells and metabolic utilization is disrupted, and the conversion of excess glucose to either glycogen in the liver or as fat for storage is usually decreased compared to non-diabetic persons. Hyperlipidemia is common in diabetes mellitus [8] especially elevated triglyceride and cholesterol levels. Hypercholesterolemia is one of the risk factors responsible for the onset of the development of atherosclerosis during the course of diabetes mellitus [9].

Oral hypoglycemic drugs used in management of these diseases have side effects such as gastrointestinal discomfort, weight gain, and hepatic dysfunction [10]. Therefore, there is an increasing need to find more safe and efficient therapies for prevent diabetes mellitus and its related complications. Plants are known to possess a wide variety of pharmacological effects and extraordinary therapeutic possibilities.

The Cashew tree, also known as *Anacardium occidentale* (Latinname), is a member of the Anacardiaceae family. *Anacardium occidentale* is grown widely in tropical countries like Malaysia, India, Brazil, Nigeria, and occurs widely in Senegal and is known as Darkassou [11].

The stem, bark, fruits, and leaf extract, have pharmaceutical properties and extensively used as anti-inflammatory, anti-oxidant, anti-bacterial, and anti-diarrheal [12-15]. The anti-diabetic and anti-inflammatory properties have also been reported [16]. Phytochemicals study of the methanolic leave extract revealed the presence of phenolic, flavonoids, steroids and triterpenes [17]. The hypoglycemic effect of the administration of methanol plant extract at a single dose of 800.0mg/kgb.w was found to be more pronounced than that of the aqueous extract in both the normal and streptozotocin-diabetic rats [18]. Thus, the current study was aimed at investigating the anti-diabetic, anti-hyperlipidemic, and anti-oxidative effects of *Anacardium occidentale* methanolic nut extract in Streptozotocin (STZ)-induced diabetic rats.

2. Methods

Chemicals: Steptozotocin, Ketamine, Xylazine, Methanol.

2.1. Animals

Healthy male Wistar rats (180g±20g) were used. The animals were received from the Animal House of Physiology Department, Ladoke Akintola University of Technology, Ogbomoso, Oyo State, Nigeria. Rats were housed in a plastic cage (8rats per cage) under controlled conditions of temperature (25±2°C), humidity (45%+5%) and light (12h light/dark cycles). The animals were fed with rat pellets (Premier Feed Ltd. Ibadan) and water *adlibitum* and were acclimatized for 1week prior to the initiation of the experiment. All procedures were approved by the Animal Care Committee of Ladoke Akintola University of Technology. All experimental protocols and handling of the animals were following the Guide for the Care and Use of Laboratory Animals [19].

2.2. Plant Materials

Anacardium occidentale nuts were obtained from plants grown at Ladoke Akintola University of Technology (LAUTECH) farm, Ogbomoso, Oyo state. The plant was identified and authenticated by Dr. A. T. J. Ogunkunle, Biology Department, Ladoke Akintola University of Technology, Ogbomoso, Oyo state, and a voucher specimen number of LH0533 was given.

2.3. Plant Extraction

The nut of *Anacardium occidentale* plant was sun-dried at room temperature in the laboratory, powdered and stored in air tight container. The powdered nut of *Anacardium occidentale* was extracted with 95% ethanol in the Soxhlet apparatus [20].

2.4. Phytochemicals Analysis

Anacardium occidentale nut extracts were subjected to preliminary phytochemicals screening for the presence of alkaloids, quinines, resins, tannins, fixed oils, flavonoids, fats, saponins, phenolic compounds, Proteins and carboxylic acids using the procedures outlined by Sofowora; Trease and Evans [21, 22].

2.5. Acute Toxicity Test

Acute toxicity test was carried out according to the modified Lorke's method [23] using a total of 12rats. At the initial phase, the rats were assigned randomly into three groups of 3rats each. The rats in each group were administered an intraperitoneal injection of extract at 10, 100, and 1000mg/kg. Their body weight was observed for signs of toxicity and death in the first 24hours. In the second phase, another set of rats were randomly assigned into four groups of one rat each and administered the *Anacardium occidentale* methanolic nut extract intraperitoneally, at 1600, 2900, and 5000mg/kg based on the result of the first phase. The LD_{50} was then calculated as the square root of the product of the maximum dose for all surviving and minimum dose for all mortality using the formula;

$$LD_{50}=(D_oXD_{100})$$

2.6. Experimental Induction of Diabetes

Diabetes was induced through a single intraperitoneal injection of (50mg/kgb.w.) freshly prepared streptozotocin (STZ) in 0.1M citrate buffer (pH=4.5) to overnight fasted rats [24]. To prevent the initial drug induced hypoglycemic death, diabetic rats were permitted to drink a 20% glucose solution

overnight. The blood glucose level was measured after three days, and rats with glucose levels >200mg/dL were considered as diabetic. Control rats however injected with 0.2mL of the vehicle (0.1M citrate buffer, pH4.5) alone.

2.7. Experimental Design

A total of 40 experimental rats were used to assess the effect of the nut extracts on the experimental rats: 32STZ induced diabetic rats plus 8normal control rats. Animals were divided into five (5) major groups and housed under controlled environmental conditions. Rats were divided into the following groups:

Group1: Control (CON)

Group2: STZ induced diabetic rats (STZ)

Group3: STZ induced diabetic rats + nut extract *Anacardium occidentale* (100mg/kgb.w.)

Group4: STZ induced diabetic rats + nut extract *Anacardium occidentale* (200mg/kgb.w.)

Group5: STZ induced diabetic rats + 2mg/kgb.w. Glimepiramide (GMP)

2.8. Assessment of Fasting Plasma Glucose Levels and Body Weight Measurement

The body weight measurement and fasting plasma glucose levels were assessed before and during the administration of the extracts weekly, till the end of the study. The glucose level in plasma was determined by glucose oxidase /peroxidase method as described by Lorke [25] using a digital glucometer and tests trips (Accu-Chek Advantage, Roche Diagnostic, Germany)

2.9. Biochemical Parameters

At the end of the experimental treatment, after 12h fasting, the animals were anaesthetized with ketamine-75mg/kg and xylazine-20mg/kg intraperitoneal injection. The unconscious animals were sacrificed by cervical dislocation and the hearts were exposed by thoracotomy. The fasting blood was collected via cardiac punctured into heparinized tubes, centrifuged at 13000 rpm for 5mins, and the plasma was then retrieved. The plasma determination of plasma total cholesterol (TC), triglycerides (TG) and HDL-cholesterol, was done using a commercial Diagnostic Kit (Genzyme Diagnostics, MA. USA).

Antioxidant enzyme activities in the plasma were assayed using commercial kits: Serum GSH was measured based on the method described by Gupta and Gupta [26]. Serum MDA, SOD, and GPx levels were measured by enzyme linked immunosorbent assay (ELISA) methods using Rat MDA, SOD, and GPx Elisa Kit (Elabscince, China).

Markers of kidney function (blood urea nitrogen (BUN), plasma creatinine, and uric acid) were determined by using the commercially kits from Siemens Health Care Diagnostics. The liver biomarkers such as Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP), Totalprotein (TP), and Albumin were assayed in plasma spectrophotometrically by standard automated techniques according to the procedures described by the manufacturers.

2.10. Statistical Analysis

Data statistical analysis was carried out using SPSS, Version 21 software. The results were expressed as mean±SEM, and the statistical difference was evaluated using one-way analysis of variance (ANOVA) followed by Bonferroni post hoc test. Data were considered statistically significant at p less than 0.05 ($p<0.05$).

3. Results

3.1. Preliminary Phytochemicals Screening of Methanolic Extract of Anacardium occidentale Nut

The *Anacardium occidentale* nut extract was screened for the different classes of secondary metabolites. Tests for saponins, tannins, steroid, terpenoid, cardiacglycosides, phlobatanins, flavonoids, anthraquinones, alkaloids and carbohydrates were carried out. Tannins, terpenoids, and reducing sugar all tested positive while Saponins, phlobatamins, cardiacglycosides, anthraquinones, alkaloids, flavonoids and steroids tested negative (Table 1).

Table 1. *Preliminary phytochemicals analysis of Anacardium occidentale nut extract.*

S/N	METABOLITES	NUT
1	Saponin	-
2	Flavonoids	-
3	Tannin	+
4	Phlobatannin	-
5	Steroids	-
6	Terpenoids	+
7	CardiacGlycosides	-
8	Anthraquinones	-
9	Alkaloids	-
10	ReducingSugar	+

Key
(-) means not present
(+) means present

3.2. Effects of Anacardium occidetale Nut Extract on Water Intake in Streptozotocin-Induced Diabetic Rats

Figure 1 shows the water intake of control and treated rats after administration of *Anacardium occidentale* nut extract. There was a significant increase ($p<0.05$) in the water intake of diabetic rats when compared with the control. Administration of 100mg/kgb.w and 200mg/kgb.w of *Anacardium occidentale* nut extract and glimepiride significantly decrease water intake in groups 3, 4 and 5 compared to the diabetic group.

3.3. Effects of Anacardium occidetale nut Extract on Food Intake in Streptozotocin-Induced Diabetic Rats

Figure 2 shows the food intake of control and treated rats after administration of *Anacardium occidentale* nut extract. There was a significant decrease ($p<0.05$) in the food intake

of diabetic rats when compared with the control. Administration of 100mg/kgb.w and 200mg/kgb.w of *Anacardium occidentale* nut extract and glimepiride significantly increase food intake in groups 3, 4 and 5 compared to the diabetic group.

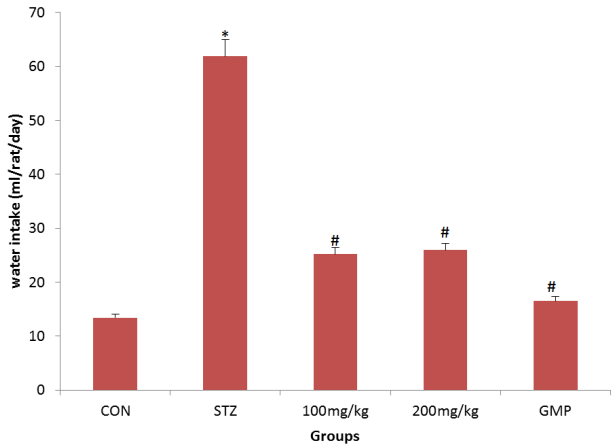

Figure 1. *Values are expressed as mean±SEM (n=8).*significant at p<0.05 compared with control, #significant at p<0.05 compared with STZ group.*

Key:
CON-Control group
STZ-Streptozotocin-induced untreated group
GMP-Glimepiride treated group

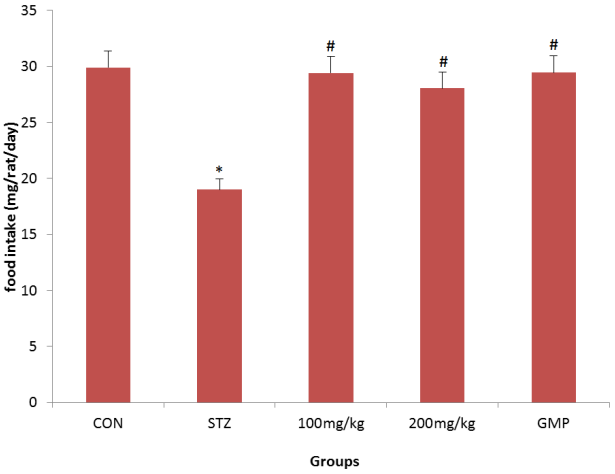

Figure 2. *Values are expressed as mean±SEM (n=8). *significant at p<0.05 compared with control, #significant at p<0.05 compared with STZ group.*

Key:
CON-Control group
STZ-Streptozotocin-induced untreated group
GMP-Glimepiride treated group

3.4. Effects of Anacardium occidentale Nut Extract on Fasting Blood Glucose in Streptozotocin-Induced Diabetic Rats

Figure 3 shows the fasting blood glucose of control and treated rats after administration of *Anacardium occidentale* nut extract. There was a significant increase (p<0.05) in the fasting blood glucose of diabetic rats when compared with the control. Administrationof 100mg/kgb.w and 200mg/kgb.w of *Anarcadium occidentale* nut extract and glimepiride ameliorates the increase in fasting blood glucose in groups 3, 4 and 5 compared to the diabetic group.

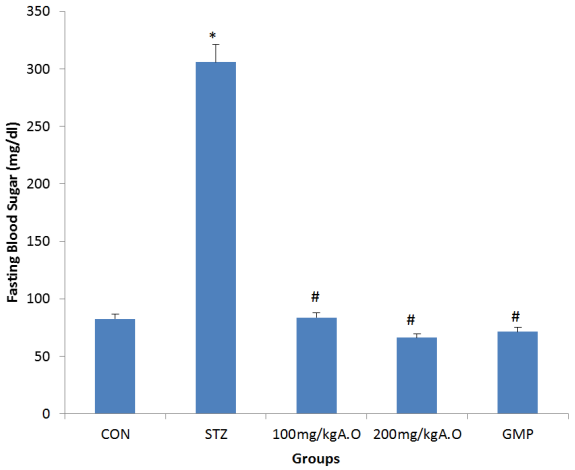

Figure 3. *Values are expressed as mean±SEM (n=8). *significant at p<0.05 compared with control, #significant at p<0.05 compared with STZ group.*

Key:
CON-Control group
STZ-Streptozotocin-induced untreated group
GMP-Glimepiride treated group

3.5. Effects of Anarcardium occidetale Nut Extract on Body Weight in Streptozotocin-Induced Diabetic Rats

Figure 4 shows the body weight of control and treated rats after administration of *Anacardium occidentale* nut extract. There was a significant decrease (p<0.05) in the body weight of diabetic rats when compared with the control. Administration of 100mg/kgb.w and 200mg/kgb.w of *Anacardium occidentale* nut extract and glimepiride attenuate the decreased bodyweight in groups 3, 4 and 5 compared to the diabetic group.

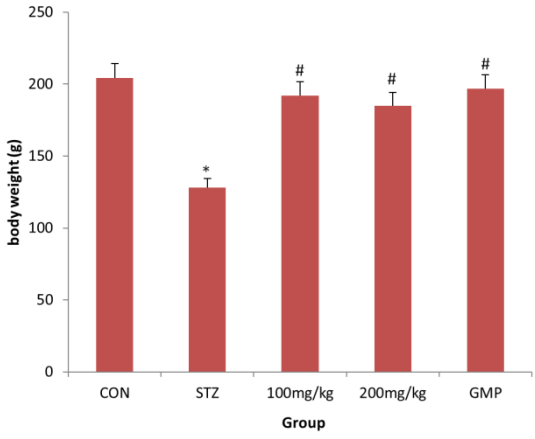

Figure 4. *Values are expressed as mean±SEM (n=8). *significant at p<0.05 compared with control, #significant at p<0.05 compared with STZ group.*

Key:
CON-Control group
STZ-Streptozotocin-induced untreated group
GMP-Glimepiride treated group

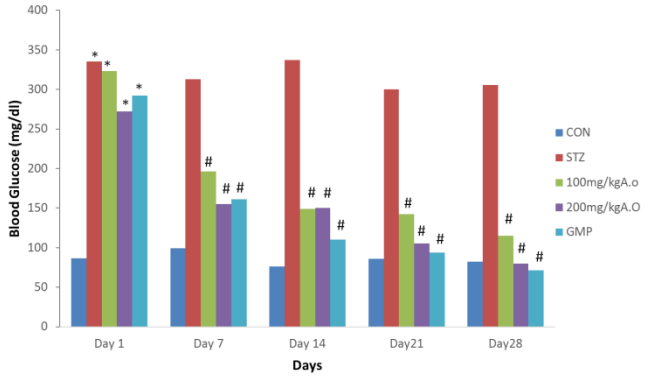

Figure 5. *Values are expressed as mean±SEM (n=8). *significant at p<0.05 compared with control, #significant at p<0.05 compared with STZ group.*

Key:
CON-Control group
STZ-Streptozotocin-induced untreated group
GMP-Glimepiride treated group

3.6. Assessment of Weekly Blood Glucose Level in Streptozotocin-Induced diabetic Rats

In figure 5, blood glucose level of control group was 86.5±4.5mg/dL while that of the diabetic groups increased significantly when compared with control induction of diabetes (Day1). Blood glucose in the diabetic rats treated with 100mg/kg and 200mg/kg of *Anacardium occidentale* nut extract and 2mg/kg Glimepiride (GMP) respectively decreased when compared with diabetic non-treated rats on Days 7, 14, 21 and 28 of the experiment.

3.7. Effect of Anacardium occidentale Nut Extract on Antioxidant Enzymes and Oxidative Stress Parameters in Streptozotocin-Induced Diabetic Rats

Table 2 illustrates the oxidative stress indices assessed in experimental rats. The superoxide dismutase activity (SOD), catalase level (CAT), glutathione peroxidase (GPx) and reduced glutathione (GSH) activity in the STZ group decreased significantly while malondialdehyde (MDA) level was increased significantly when compared to control. After treatment, there was significant increase in enzyme activity of glutathione peroxidase in the extract ($p<0.05$) and GMP ($p<0.01$) treated groups. Superoxide dismutase, catalase and reduced glutathione levels also increased significantly ($p<0.01$) in the extract and GMP treated groups compared to STZ group. The MDA activity however reduced significantly in the extract treated groups comparable to the GMP group.

Table 2. *Effects of Anacardium occidentale nut extract on Antioxidant Enzymes and Oxidative Stress Parameters in Streptozotocin-Induced Diabetic Rats.*

PARAMETERS	CON	STZ	100mg/kg	200mg/kg	GMP
SOD (µ/ml)	1.83±0.02	0.79±0.01*	1.62±0.05#	1.55±0.02#	1.67±0.01#
GPx (U/L)	51.01±1.91	24.00±2.07*	59.27±.1.40#	55.14±2.43#	66.02±2.27#
MDA (µM)	6.74±0.80	11.75±0.57*	6.73±0.60#	6.63±0.78#	3.37±0.06#
GSH (mM)	2.62±0.13	1.52±0.03*	2.49±0.28#	3.35±0.18#	2.30±0.17
CAT (mol/ml/min)	24.67±0.63	12.40±0.32**	27.18±1.79#	34.04±1.84#	31.13±0.85#

Values are expressed as mean±SEM (n=8).*-significant at p<0.05 compared with control, #-significant at p<0.05compared with STZ group
LEGEND: CON-Control, STZ-Streptozotocin, GMP-glimepiride, SOD-Superoxidedismutase, GPx-Glutathione peroxidase, MDA-Malondialdehyde, GSH-Glutathione, CAT-Catalase.

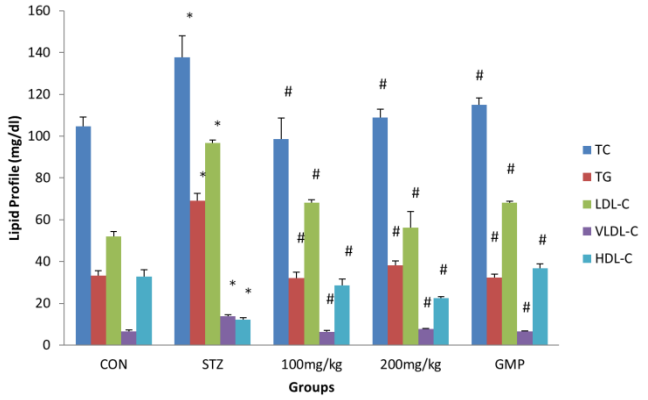

Figure 6. *Values are expressed as mean±SEM (n=8). *significant at p<0.05 compared with control, #significant at p<0.05 compared with STZ group.*

Key:
CON-Control group
STZ-Streptozotocin-induced untreated group
GMP-Glimepiride treated group

3.8. Effect of Anacardium occidentale Nut Extract on Lipid Profile in Streptozotocin-Induced Diabetic Rats

The lipid profile result (Figure 6) showed significant increases in total cholesterol, triglyceride, low density lipoprotein and very low density lipoprotein concentrations in the STZ group when compared to control. The high density lipoprotein concentration however decreased significantly. After treatment of diabetic rats with both doses of the extract, the high density lipoprotein concentration increased significantly while the total cholesterol, triglyceride, low density lipoprotein and very low density lipoprotein concentrations were significantly reduced comparable to the GMP group.

3.9. Effects of Anacardium occidentale Nut Extract on Markers of Liver Function in Diabetic Wistar Rats

There were significant ($p<0.01$) increases in aspartate aminotransferase (AST), alkaline phosphatase (ALP) and alanine transaminase (ALT) in the STZ group compared to control (Table 3). However, in administration of

Anacardium occidentale nut extracts to STZ-induced diabetic rats, apartate aminotransferase, alkaline phosphatase and alanine transaminase activities reduced Significantly ($p<0.05$) comparable to the GMP group.

Table 3. *Effects of Anacardium occidentale nut extract on Markers of Liver function in Streptozotocin-Induced Diabetic Rats.*

PARAMETERS	CON	STZ	100mg/kg	200mg/kg	GMP
AST (U/L)	117.9±11.27	300.7±19.52*	122.3±6.83#	123.3±13.1#	1.67±0.01#
ALP (U/L)	326.8±15.65	584.6±52.37*	245.4±.17.29#	288.9±18.18#	135.7±24.55#
ALT (U/L)	43.75±3.88	95.67±1.61*	37.55±1.28#	45.71±2.66#	34.60±5.37#

Values are expressed as mean±SEM (n=8).*-significant at $p<0.05$ compared with control, #-significant at $p<0.05$ compared with STZ group
LEGEND: CON-Control, STZ-Streptozotocin, GMP-glimepiride, AST-apartate aminotransferase, ALP-Alkaline phosphatase, ALT-Alanine transaminase.

3.10. Effects of Anacardium occidentale Nut Extract on Some Markers of Kidney Function in Streptozotocin Induced Diabetic Rats

The markers of kidney function assessed in this study were presented in Table 4. The urea, uric acid and creatinine levels in the STZ group increased significantly ($p<0.05$) compared to control. However, there were significant ($p<0.01$) reductions in levels of urea, uric acid, and creatinine in the extract and GMP groups compared to STZ group after treatment.

Table 4. *Effects of Anacardium occidentale nut extract on Markers of Kidney function in Streptozotocin-Induced Diabetic Rats.*

PARAMETERS	CON	STZ	100mg/kg	200mg/kg	GMP
UREA (mg/dl)	20.76±0.24	66.68±5.30*	30.62±0.48#	23.46±2.77#	23.03±0.29#
URICACID (mg/dl)	326.8±15.65	584.6±52.37*	245.4±.17.29#	288.9±18.18#	135.7±24.55#
CREATININE (umol/l)	43.75±3.88	95.67±1.61*	37.55±1.28#	45.71±2.66#	34.60±5.37#

Values are expressed as mean±SEM (n=8).*-significant at $p<0.05$ compared with control, #-significant at $p<0.05$ compared with STZ group
LEGEND: CON-Control, STZ-Streptozotocin, GMP-glimepiride.

4. Discussion

Diabetes mellitus can be characterized as exposure to hyperglycemia and increase in total lipids, total cholesterol and LDL-cholesterol in diabetic rats which is now recognized as the primary causal factor in the pathogenesis of diabetic complications as well as induce a large number of alterations in vascular tissue that potentially promotes or accelerates atherosclerosis [27]. Hyperglycemia generates reactive oxygen species (ROS), which in turn causes cellular damage in many ways. Damage to the cells ultimately results in secondary complications in diabetes mellitus [28]. The elevations of total lipids are due to the decrease in lipoprotein lipase (LPL) activity secondary to insulin deficiency [29].

In the study of Locke et al. [30], it has been stated that acute oral toxicity studies are performed in animals to evaluate the safety of plant-based products and other formulations for humans [31]. In this study, the non toxic nature of the methanolic nut extract of *Anacardium occidentale* was observed by the acute oral toxicity test. The safe doses in animals were extrapolated to human doses, and at the dose level of 100mg/kg and 200mg/kg of the extract, no mortality or any toxic reactions were found at any of the doses; thus they are used as the low (100mg/kg) and high (200mg/kg) doses in this study respectively.

The phytochemicals constituents available in the methanolic nut extract of *Anacardium occidentale* in this research work revealed the presence of tannins, terpenoids, and reducing sugar while saponins, phlobotannins, cardiacglycosides, anthraquinones, alkaloids, flavonoids and steroids tested were all absent which correlates with the previous research [32].

In the present investigation, weight loss was one of the symptoms noticed after the induction of diabetes with STZ, which showed a significant decrease in bodyweight, which may be due to increased muscle wasting. STZ, by causing hyperglycemia and hyperinsulinemia causes a decrease in bodyweight of diabetic rats as reported by Swanston-Flatt et al [33]. Treatment with *Anacardium occidentale* nut extract at low (100mg/kg) and high (200mg/kg) doses for 28days increase their bodyweight compared to the levels of untreated diabetic rats.

Fasting blood sugar (FBS) is an important and necessary basal parameter among DM patients [34]. This study showed that *Anacardium occidentale* nut extract decreased FBS levels and reversed its value in STZ-induced diabetic rats. STZ can damage pancreatic β-cells and decrease endogenous insulin secretion, thereby reducing glucose utilization of tissues. Therefore, the possible mechanism for decreased lipid levels could either be an insulin-releasing effect of *Anacardium occidentale* nut extract or insulin-sensitizing activity, because insulin has been proved to inhibit the activity of the hormone sensitive lipases in adipose tissue and suppresses the release of lipids. The HDL cholesterol is involved in transport of cholesterol from peripheral tissues to the liver and thereby, it acts as a protective factor. In the present study, the level of HDL-cholesterol was also found to be reduced in diabetic rats. The level of HDL-cholesterol was increased in STZ-induced diabetic rats when treated with *Anacardium occidentale* methanolic nut extract. This indicates that *Anacardium occidentale* methanolic nut extract may help to increase transport of peripheral tissue cholesterol to the liver and thereby decrease blood cholesterol levels [35].

The food intake decreased while water intake increased in STZ-induced diabetic rats compared to normal control. Treatment with *Anacardium occidentale* methanolic nut extract showed increased food intake and decreased water intake in extract-treated rats compared to diabetic control. This is similar to the findings of Al-Awwadi et al. [36], who reported that the classical clinical manifestations of diabetes type I, including weight loss, increased food, and water intakes and reduced insulin concentrations in rats administered STZ. This may be due to *Anacardium occidentale* alleviating the symptoms of type I diabetes mellitus.

The effect of Glimepiride and *Anacardium occidentale* on FBS was evaluated after the 28days study period. Both treatments showed ($p<0.05$) hypoglycemic activity compared to diabetic control. Experimental animals treated with *Anacardium occidentale* methanolic nut extract showed a decrease in FBS level but not as much as those treated with standard drugs. Improved blood glucose in the treated animals suggests either increased insulin release or improved insulin activity, both of which could be attributed to improvement in the integrity of β–endocrinocytes [37].

GSH, SOD, GPx, and CAT concentration all showed significant ($p<0.05$) increase in all treated groups as compared with the STZ untreated group. Increase in the level of GSH, SOD, GPx, and CAT concentration may protect the tissues against diabetic associated injury, by reducing the susceptibility to toxic radicals (Inove *et al.,* 1987) [38]. This research work hence showed that *Anacardium occidentale* methanolic nut extract contains some components, especially antioxidants capable of suppressing oxidative stress.

5. Conclusion

Administration of *Anacardium occidentale* methanolic nut extract exert significant anti-diabetic, anti-oxidative, and anti-hyperlipidemic effects as well as improvement in liver and kidney functions in STZ-induced diabetic rats. *Anacardiumo ccidentale* methanolic nut extract can therefore be a therapeutic application for diabetes mellitus. There is a need for further studies to confirm the mechanism of actions and isolate the active ingredients of this extract so as to develop it as a potent anti-diabetic formulation.

Abbreviations

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; TP: Total protein; SOD: Superoxide dismutase; CAT: Catalase; GPx: Glutathione peroxidase; GSH: Reduced glutathione; MDA: Malondialdehyde; CON: Control; STZ: Streptozotocin; GMP: Glimepiride; ROS: Reactive oxygen species; TC: Total cholesterol; TG: Triglycerides; HDL-c: High density lipoprotein-cholesterol; LDL-c: Low density lipoprotein-cholesterol; VLDL-c: Very low density lipoprotein-cholesterol.

Declarations

Ethics Approval

All procedures were approved by the Animal care committee of the Ladoke Akintola University of Technology and conducted according to the "Principles of Laboratory Animal Care" and specific national laws where applicable.

Consent to Participate

Not applicable.

Consent for Publication

All authors agreed to publish the article.

Availability of Data and Materials

The data sets used and / or analysed during this current study are included in this manuscripts.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

All authors have made considerable contribution to the work and approved the final version of the publication. FO, MA, and MO carried out the experiment. MO wrote the manuscript with the support of FO. FO supervised the project. MA conceived the original idea.

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