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Original Research

Antioxidant, lipid modulating and hypoglyceamic effects of the aqueous extract of *Anacardium occidentale* leave in streptozotocin-induced diabetic rats

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ABSTRACT

Background/Aim: *Anacardium occidentale* leaves are used traditionally for the management of diabetes. This study seeks to evaluate the efficacy and safety of its continuous intake for 4 weeks in streptozotocin-induced diabetic rat model in comparison with metformin a reference drug. **Materials and Methods:** Thirty-six male Wistar rats (130 -145 g) were randomly divided into 6 groups of six animals each. Diabetes was induced in rats by a single intraperitoneal injection of streptozotocin (STZ; 50 mg/kg bw); plant extract and metformin were given orally (60 and 125 mg/kg/ bw). **Results:** Diabetes induction caused a significant weight loss (23.65 %) associated with a marked rise in levels of fasting blood glucose (295 mg/dl), triglycerides, total cholesterol, low-density-lipoprotein cholesterol, lipid peroxidation and serum aminotransferase activities. Besides, glucose-6-phosphate dehydrogenase (G6PD) activities, total protein concentration, high-density-lipoprotein cholesterol and tissue antioxidants (reduced glutathione; GSH, superoxide dismutase; SOD, catalase; CAT, glutathione-S-transferase; GST, Glutathione peroxidase; GPx) were diminished in STZ-induced diabetic rats. Histopathological studies also revealed various degrees of alteration in the liver diabetic rats. The effects of *A. occidentale* extract were compared with metformin as a reference antidiabetic drug. Treatment with *A. occidentale* (60 mg/kg/ bw) extract showed a significant ($P<0.05$) reversal effect that ameliorated the deleterious effect of STZ in all the biochemical parameters evaluated. **Conclusion:** Aqueous extract of *A. occidentale* leaves exhibits excellent antioxidant, hypoglycemic and antidiabetic effects and may be used as a therapeutic agent in the management of diabetes and its associated complications with caution as observed in histopathological studies.

KEY WORDS: *A. occidentale*; Antihyperlipidemic; Antioxidant; Hypoglycaemic; Metformin; Streptozotocin.

INTRODUCTION

Diabetes mellitus (DM) is a fairly common metabolic disease characterized by high blood glucose levels and often about 70 % diabetic patients are hypertensive too [1, 2]. 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 [3]. Hyperlipidemia is common in DM [4], 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 DM [5, 6]. Uncontrolled elevated blood glucose in DM over time could lead to glycation of biomolecules in the body and might induce oxidative stress with disease progression [5]. Oxidative stress from increased generation of reactive oxygen species (ROS) and defective antioxidant defense system in the body are the main contributors to complications of DM and other diseases [5]. Thus oxidative stress, high blood lipid levels, and hypertension are therefore characteristics associated with DM progression [6].

Leaf, stem and root bark of *Anacardium occidentale* are included in anti-diabetic formulations and are sold commonly as food supplements by herb sellers and vendors in South Western Nigeria. However, there is need to evaluate efficacy, safety, standardization of such products as well as compare the efficacy, side effects with commonly available medications which have been in use for DM treatment. Some studies have shown anti-diabetic properties of different parts of A. *occidentalis* plant in the literature on fructose and alloxan induced diabetic rats [7-10] and emphasis was on phytochemical constituents and fasting blood glucose levels. Thus, the objectives of this work were to study the hypoglycemic potential of A. *occidentale*, tissue oxidative stress markers, lipids metabolism and peroxidation, serum markers of tissue toxicity as well as liver and kidney tissue histopathology in STZ-induced diabetic rats and to compare its efficacy with metformin, a drug known to not only modulate blood glucose but also cholesterol and triglyceride levels [11].

MATERIALS AND METHODS

Plant material

Fresh leaves of A. *occidentale* were collected during the month of February, 2015 in Ibadan, and were identified and authenticated by Mr D. Eseimukhaiin of the Botany Department, University of Ibadan prior to air drying at room temperature. Dried leaves were ground into coarse powder using Hammer mill grinder and 1.5 kg of the ground powder was extracted by cold maceration using 5 L of distilled water for 72h. Extract was filtered using suction and the filtrate was concentrated to dryness on Bucchi

Rotary evaporator R111 at 50 °C. A dark brown residue of 150.5 g (10.386 %) was obtained and was stored in air tight bottles in the refrigerator until used.

Experimental animals, grouping and treatment

Thirty-six adult male Wistar rats (130-145 g) were procured from the Animal house of the Physiology Department, College of Medicine, University of Ibadan. They were acclimatized for two weeks to the animal house conditions of Biochemistry Department before commencing the experiments; they were fed with standard rat feed supplied by Ladokun Feed Mill, Ibadan. The animals were randomly distributed into six groups of six rats each. Animal grouping was as follows:

Control (Group I): Normal control rats on distilled water only

STZ (Group II): Diabetic control administered with Streptozotocin (STZ; 50 mg/kg ip)

METND (Group III): Non-diabetic rats given metformin only (125 mg/kg bw)

AOND (Group IV): Non-diabetic rats given *A. occidentale* (60 mg/kg bw).

STZMET (Group V): Diabetic rats treated with metformin (125 mg/kg bw)

STZAO (Group VI): Diabetic rats treated with *A. occidentale* (60 mg/kg bw)

Diabetes induction was after an overnight fast by a single intraperitoneal dose of 50 mg/kg bw of streptozotocin (STZ) in 0.1 M pH 4.5 citrate buffer, while administration of *A. occidentale* and metformin were orally at 60 and 125 mg/kg bw respectively once daily for 28 days. Protocol approval, animal care and handling were according to the University of Ibadan Ethics board animal experiments.

Chemicals and drugs

All reagents used were from Sigma Chemical (St Louis, MO, USA), N, N'-dimethylimidodicarbonimidic diamide (metformin) was bought from a local pharmacy shop in Ibadan, Nigeria and Randox diagnostic kits were used for cholesterol, triglyceride, HDL-c, ALT, AST, ALP, G6PD.

Sample collection Biochemical parameters

At the termination of the 28 days treatment, animals were fasted overnight and the rats were euthanized by cervical dislocation. Serum, tissue homogenate and sections of liver and kidney for histology were as reported earlier [12]. Biochemical parameters such as ALT, AST and ALP as well as Triglyceride, Total cholesterol, HDL-c and LDL-c were quantified spectrophotometrically from serum separated from blood of each animal using Randox commercial assay kits specific for each test. Lipid peroxidation (LPO) were evaluated by measuring thiobarbituric acid reactive substances (TBARS) as described by Varshney and Kale [13], superoxide dismutase (SOD) activity was determined according to the method of Misra and Fridovich [14]. Catalase (CAT) activity was estimated by adopting the method described by Sinha[15]. Reduced glutathione (GSH) level was assayed by using the method described by Beutler *et al.*, at 412 nm [16].Glutathione peroxidase (GPx) was assayed by the method of Hafeman *et al.*, based on the degradation of H_2O_2 in the presence of GSH [17]. Glutathione-S-transferase (GST) activity was determined according to Habig and co-workers [18]. glucose-6-phosphate dehydrogenase (G6PD) was assayed according to the method of Robert [19].

Statistical analysis

Results were expressed as mean ± standard deviation and the difference between the groups were tested by one-way analysis of variance (ANOVA) followed by the student t-test using SPSS software package (17.0). Results were considered as significant at $\rho < 0.05$.

RESULTS

The alteration in the body weight was observed throughout the study in the experimental animals. Table 1 shows data obtained for changes in body weight (bw) and fasting blood sugar (FBS). Diabetes induction resulted in a significant increase in FBS with a concomitant decrease in body weight of diabetic rats. However, after treatment of diabetic rats with plant extract (60 mg/kg bw) or metformin (125 mg/kg bw) for 28 days, the FBS level significantly decreases and body weight increases compared with the levels of untreated diabetic rats. Table 2 has data on total protein concentration, G6PD, AST, ALT and ALP in STZ-induced diabetic rats. The diabetic rats showed a significant reduction in G6PD activity and serum level of total protein, this was associated with a significant elevation in serum ALT, AST, ALP compared to control rats. Treatment with *A. occidentale* or metformin reversed the alterations in G6PD activity, serum level of total protein, AST, ALT and ALP after 28 days of treatment.

Table 3 portrays the alteration in serum lipid profile. Diabetic rats exhibited significant increase in serum triglyceride, total cholesterol and LDL-c with a corresponding decrease in HDL-c. However, treatment with with *A. occidentale* or metformin was able to normalize the serum lipid profile compared to the control. Table 4 illustrates the assessment of oxidative stress in diabetic rats. Diabetic rats showed significant elevations in the LPO level and marked reduction in enzymatic and non-enzymatic antioxidants (GSH, SOD, CAT, GST and GPx) compared to control. Histopathological studies of liver and kidney tissues of diabetic rats displayed various morphological alterations and abnormalities compared with the control group showing normal tissue morphology for both organs (Fig. 1 and 2).

Table 1. Effects of *A. occidentale* body weights and FBS levels in streptozotocin-induced diabetic rats

Groups	Initial body weight (g)	Final body weight (g)	Weight gained / loss (g)	Percentage increase/ loss in weight (%)	Initial FBG (mg/dl)	Final FBG (mg/dl)
Control	150±0.78	177± 8.21$^{\Delta}$	+26.50	17.67	105$^{\Delta}$	115$^{\Delta}$
STZ	148±0.62	113±6.05$^{*\blacktriangle}$	-35.00	23.65	390$^{*\blacktriangle}$	426$^{*\blacktriangle}$
METND	155±0.66	178±4.39$^{\Delta}$	+23.00	11.61	100$^{\Delta}$	111$^{\Delta}$
AOND	155±0.78	188±5.86$^{\Delta}$	+33.00	21.00	85$^{*\Delta\blacktriangle}$	100$^{\Delta}$
STZMET	148±0.81	133±5.37$^{*\Delta\blacktriangle}$	-15.00	10.00	350$^{*\blacktriangle}$	222$^{*\Delta\blacktriangle}$
STZAO	150±0.52	135±7.19$^{*\Delta\blacktriangle}$	-15.00	10.00	405$^{*\blacktriangle}$	255$^{*\Delta\blacktriangle}$

Values are expressed as mean ± standard deviation of 6 animals. *The mean is significantly different compared to control at P < 0.05, $^{\Delta}$mean is significantly different compared to diabetic control (STZ; 50 mg/kg ip) group at P < 0.05, and $^{\blacktriangle}$mean is significantly different compared to diabetic rats treated with Metformin only (125 mg/kg bw). Fasting blood glucose (FBG).

Table 2. Effect of *A. occidentale* on serum aminotransferase activities G6PD and protein levels in streptozotocin-diabetic rats

Groups	AST(U/L)	ALT(U/L)	G6PD (units/min/ mg of protein)	ALP (U/L)	Total Protein (g/dl)
Control	133.63±9.29$^{\Delta}$	6.3±0.26$^{\Delta}$	41.90±7.62$^{\Delta\blacktriangle}$	8.28±0.02$^{\Delta}$	29.41±2.37$^{\Delta\blacktriangle}$
STZ	211.88±10.00$^{*\blacktriangle}$	35.50±3.71$^{*\blacktriangle}$	27.14±14.59$^{*\blacktriangle}$	46.92±28.24$^{*\blacktriangle}$	16.86±0.51$^{*\blacktriangle}$
METND	156.13±10.33$^{\Delta}$	5.00±7.49$^{\Delta}$	53.33±8.80$^{*\Delta}$	5.52±3.19$^{\Delta}$	45.98±3.53$^{*\Delta}$
AOND	136.63±31.47$^{\Delta}$	5.55±0.25$^{\Delta}$	72.38±22.86$^{*\Delta\blacktriangle}$	5.52±0.01$^{\Delta}$	42.60±1.34$^{*\Delta}$
STZMET	162.50±17.15$^{*\Delta\blacktriangle}$	12.85±7.86$^{*\Delta\blacktriangle}$	43.81±8.80$^{\Delta\blacktriangle}$	24.14±1.59$^{*\Delta\blacktriangle}$	28.63±4.21$^{\Delta\blacktriangle}$
STZAO	185.63±37.05$^{*\Delta\blacktriangle}$	16.20±0.82$^{*\Delta\blacktriangle}$	45.71±21.55$^{\Delta\blacktriangle}$	27.59±1.38$^{*\Delta\blacktriangle}$	26.13±2.49$^{\Delta\blacktriangle}$

Values are expressed as mean ± standard deviation of 6 animals. *The mean is significantly different compared to control at P < 0.05, $^{\Delta}$mean is significantly different compared to diabetic control (STZ; 50 mg/kg ip) group at P < 0.05, and $^{\blacktriangle}$mean is significantly different compared to diabetic rats treated with Metformin only (125 mg/kg bw). Aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatise (ALP), glucose-6-phosphate dehydrogenase (G6PD).

Table 3. Effect of *A. occidentale* on triglyceride, total cholesterol, HDL-c and LDL-c levels in streptozotocin-induced diabetic rats

Group	Triglyceride (mg/dl)	Total cholesterol (mg/dl)	HDL-c (mg/dl)	LDL-c (mg/dl)
Control	67.78±1.67$^{\Delta}$	71.12±1.62$^{\Delta}$	35.53±1.56$^{\Delta}$	15.35±1.52$^{\Delta}$
STZ	75.33±1.09$^{*\blacktriangle}$	174.94±0.94$^{*\blacktriangle}$	18.11±1.36$^{*\blacktriangle}$	94.31±9.96$^{*\blacktriangle}$
METND	66.77±1.01$^{\Delta}$	71.53±0.70$^{\Delta}$	32.81±2.11$^{\Delta}$	17.07±0.76$^{\Delta}$
AOND	67.56±2.01$^{\Delta}$	68.45±0.86$^{\Delta}$	31.71±0.76$^{\Delta}$	16.25±2.11$^{\Delta}$
STZMET	70.78±1.78$^{\Delta}$	128.66±0.70$^{*\Delta\blacktriangle}$	24.34±3.13$^{*\Delta\blacktriangle}$	43.15±4.63$^{*\Delta\blacktriangle}$
STZAO	70.88±1.04$^{\Delta}$	97.30±0.82$^{*\Delta\blacktriangle}$	36.02±4.12$^{\Delta\blacktriangle}$	31.80±0.43$^{*\Delta\blacktriangle}$

Values are expressed as mean ± standard deviation of 6 animals. *The mean is significantly different compared to control at P < 0.05, $^{\Delta}$mean is significantly different compared to diabetic control (STZ; 50 mg/kg ip) group at P < 0.05, and $^{\blacktriangle}$mean is significantly different compared to diabetic rats treated with Metformin only (125 mg/kg bw). High-density-lipoprotein cholesterol (HDL-c), low-density-lipoprotein cholesterol (LDL-c).

Table 4. Effect of *A. occidentale* on SOD, CAT, GST, GPx. GSH and MDA in streptozotocin-diabetic rats

Group	SOD (units/mg protein)	CAT (units/mg protein)	GST (µm/min/ mg protein)	GPX (nmol/min/ mg protein)	GSH (µg/ml)	LPO (unit/mg protein)
Control	24.55±0.77$^{\Delta}$	13.56±0.74$^{\Delta}$	15.27±3.97$^{\Delta}$	8.61±0.51$^{\Delta}$	47.48±0.36$^{\Delta}$	13.43±0.01$^{\Delta}$
STZ	16.89±0.28$^{*\blacktriangle}$	9.21±0.50$^{*\blacktriangle}$	12.13±4.01$^{*\blacktriangle}$	4.09±0.91$^{*\blacktriangle}$	12.13±1.49$^{*\blacktriangle}$	30.59±0.04$^{*\blacktriangle}$
METND	24.62±2.19$^{\Delta}$	14.20±1.69$^{\Delta}$	16.84±2.34$^{\Delta}$	8.86±1.06$^{\Delta}$	47.89±1.01$^{\Delta}$	10.54±0.02$^{\Delta}$
AOND	22.29±0.15$^{\Delta}$	19.65±0.40$^{*\Delta\blacktriangle}$	13.81±3.17$^{*\blacktriangle}$	7.21±0.32$^{\Delta}$	38.08±0.98$^{*\Delta\blacktriangle}$	14.44±0.21$^{\Delta\blacktriangle}$
STZMET	24.19±2.01$^{\Delta}$	12.76±1.64$^{\Delta}$	15.99±3.54$^{\Delta}$	8.22±1.18$^{\Delta}$	32.89±0.44$^{*\Delta\blacktriangle}$	18.45±0.02$^{*\Delta\blacktriangle}$
STZAO	25.41±1.43$^{\Delta}$	14.19±1.77$^{\Delta}$	13.46±0.21$^{*\blacktriangle}$	8.66±0.30$^{\Delta}$	36.35±0.79$^{*\Delta\blacktriangle}$	21.57±0.10$^{*\Delta\blacktriangle}$

Values are expressed as mean ± standard deviation of 6 animals. *The mean is significantly different compared to control at P < 0.05, $^{\Delta}$mean is significantly different compared to diabetic control (STZ; 50 mg/kg ip) group at P < 0.05, and $^{\blacktriangle}$mean is significantly different compared to diabetic rats treated with Metformin only (125 mg/kg bw). Superoxide dismutase (SOD), catalase (CAT), glutathione-S-transferase (GST), Glutathione peroxidase (GPx) reduced glutathione (GSH), lipid peroxidation (LPO).

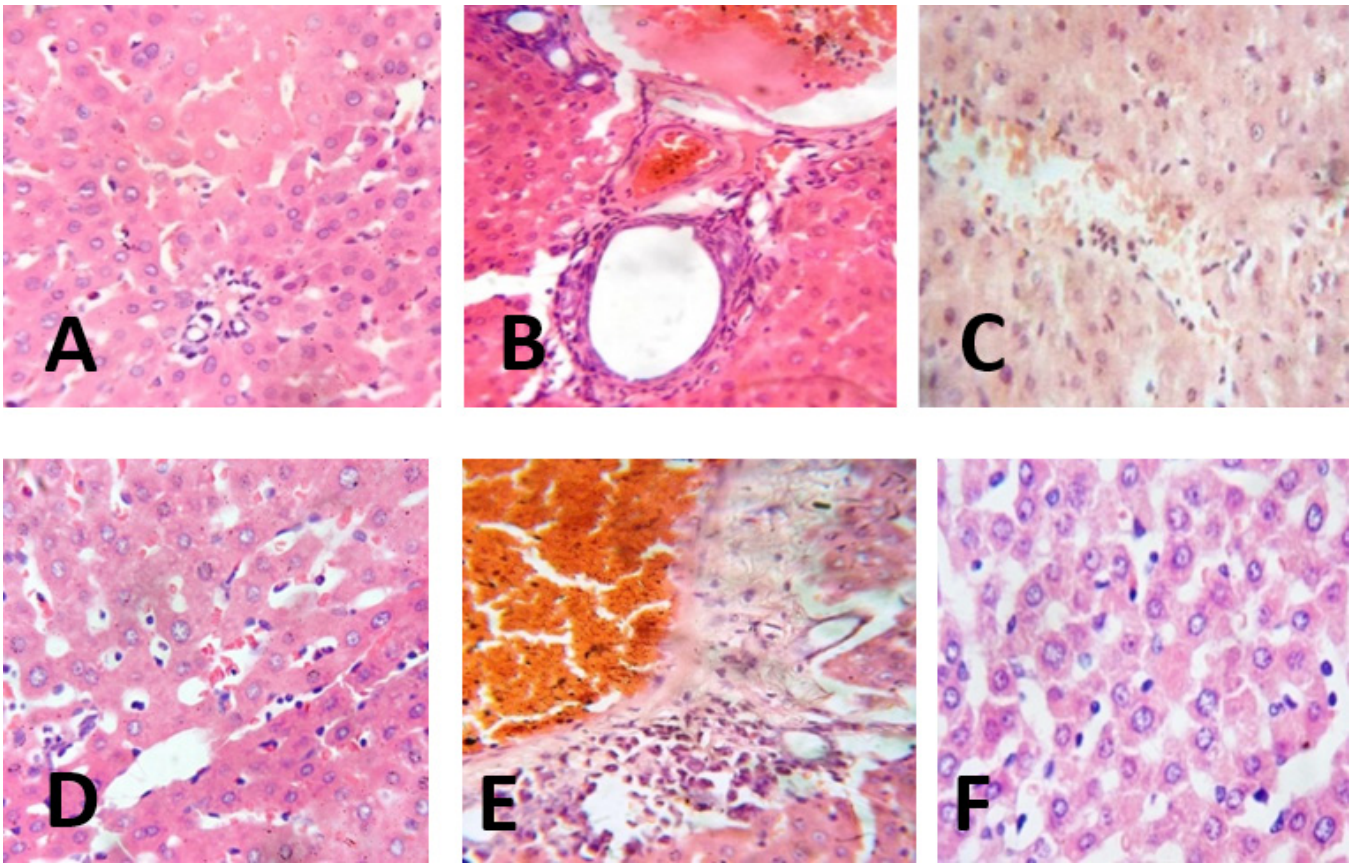

Fig. 1. Photomicrograph of liver sections stained with H and E, X400

A. Control (Group I): Normal control rats on distilled water only showing mild congestion of the central vein with inflammatory cell and necrosis.
B. STZ (Group II): Diabetic control administered with Streptozotocin (STZ; 50 mg/kg ip) showing moderate periportal inflammation with moderate congestion of both the portal and central veins.
C. METND (Group III): Non-diabetic rats given metformin only (125 mg/kg bw) showing moderate steatosis, congestion of sinusoids and blood vessels, with mild inflammation and high leucocyte concentration.
D. AOND (Group IV): Non-diabetic rats given *A. occidentale* (60 mg/kg bw) showing moderate inflammation and infiltration of fatty cells.
E. STZMET (Group V): Diabetic rats treated with metformin (125 mg/kg bw) showing severe congestion of the central and portal vein, moderate periportal inflammation and infiltration of focal areas by chronic inflammatory cells.
F. STZAO (Group VI): Diabetic rats treated with *A. occidentale* (60 mg/kg bw) showing acute inflammatory cells with focal necrosis associated with distortion in the hepatic tissue architecture.

DISCUSSION

The present study clearly indicate that aqueous extract of *A. occidentale* (60 mg/kg bw) considerable reversed all indices of alterations in all biochemical parameters evaluated in liver homogenates and serum of STZ-induced diabetic rats. This complemented previously identified protective roles of *A. occidentale* in the treatment and management of diabetes and its associated complications.

Previous experimental reports have identified polyuria, polydipsia, hyperglycemia and weight loss among others as symptoms of chronic Diabetes [20, 21]. In this study STZ-challenged rats had decreased body weight compared to the control groups. Reduction in body weight could be attributed to muscle wasting associated with degradation of structural proteins, probably due to their diabetic state [20, 21]. Administration of aqueous extract of *A. occidentale* (60 mg/kg bw) or metformin (125 mg/kg bw) for 28 days showed improvement in their body weight compared to the untreated diabetic group. This is an indication that *A. occidentale* have beneficial effect in preventing loss of body weight in diabetic rats, probably due the reversal of proteolysis, gluconeogenesis and glycogenolysis [21].

Fasting blood sugar (FBS) levels were greater than 350 mg/dL in all animals given STZ in this study, thus showing that the rats were diabetic. *A. occidentale* lowered FBS in the treated rats, the obtained results was comparable with that of metformin treated rats. *A. occidentale* may have exerted its hypoglycemic effect by stimulating enzymes involved in the carbohydrate metabolism, increasing glycogen storage in the liver, glucose uptake by the muscle, inhibit gluconeogenesis, favor triglyceride synthesis and storage in the adipose tissue, and inhibit protein synthesis; these synergetic effects may correct the altered carbohydrates and fatty acids metabolism associated with diabetes, leading to a postprandial glucose control [22].

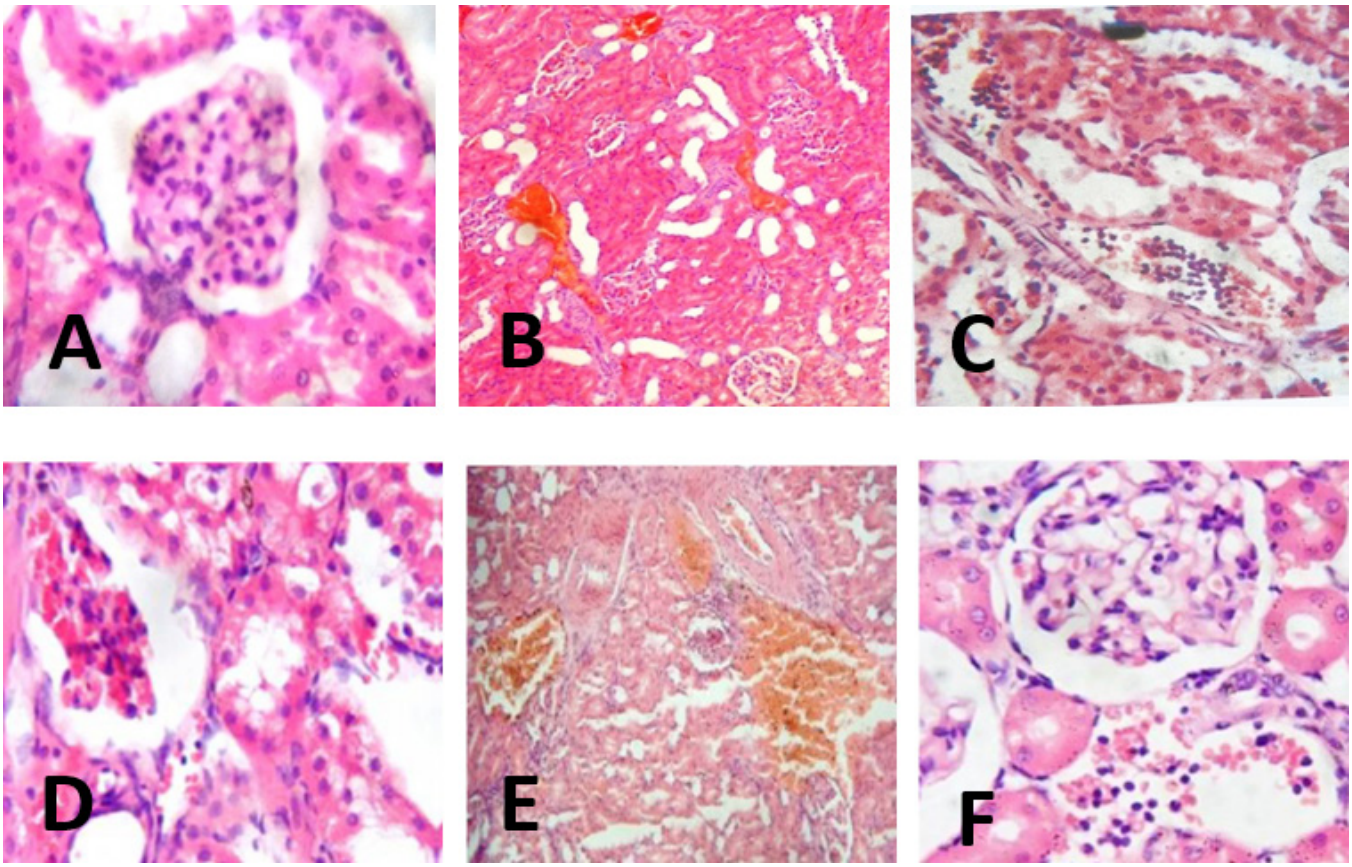

Fig. 1. Photomicrograph of liver sections stained with H and E, X400

A. Control (Group I): Normal control rats on distilled water only showing adequate amount of renal corpuscles in the cortex. No inflammation or necrosis seen.
B. STZ (Group II): Diabetic control administered with Streptozotocin (STZ; 50 mg/kg ip) showing moderate periportal inflammation and moderate congestion of the portal vein and central vein.
C. METND (Group III): Non-diabetic rats given metformin only (125 mg/kg bw) showing moderate inflammation, mild congestion.
D. AOND (Group IV): Non-diabetic rats given A. occidentale (60 mg/kg bw) showing moderate inflammatory cells of the tubules.
E. STZMET (Group V): Diabetic rats treated with metformin (125 mg/kg bw) showing chronic inflammation of the cortex and medulla.
F. STZAO (Group VI): Diabetic rats treated with A. occidentale (60 mg/kg bw) showing chronic inflammation, congestion and hemorrhage. The epithelium of the tubules shows vesicular nuclei and increase in the number of glomerulus in the cortex.

In this experiment, there was a significant reduction in Glucose-6-phosphate dehydrogenase (G6PD) activity in the liver of diabetic rats. Administration of our plant extract resulted in a significant restoration of G6PD activity compared with the diabetic rats treated with metformin. The reduction witnessed in G6PD activity may probably be due to insulin deficiency as this enzyme activity depends on insulin. G6PD is the key enzyme in pentose phosphate pathway which plays a pivotal role in maintaining normal blood glucose levels. Reduction in G6PD activity in liver is associated with obstruction in glucose utilization which results in hyperglycemia [23]. Our result shows that *A. occidentale* could improve the glycemic control by direct activation of glucose.

The present study found that *A. occidentale* significantly restored the decreased level of serum total protein (TP). In agreement with this finding, several studies have reported that the levels of serum total protein were declined in STZ diabetic animals. STZ-induced diabetes is associated with severe weight loss due to excessive breakdown of tissue proteins and an increased muscle wasting [24,25]. This result suggests that *A. occidentale* may inhibit protein catabolism and enhance protein production. Clinical and experimental evidence suggests that diabetes have profound effects on the liver [26]. Alteration in liver enzymes such as ALT, AST and ALP are important indicators of hepatocellular damage [27]. The results obtained in this study showed that STZ administration produced a certain degree of damage in the liver of diabetic rats as evidenced by the elevation of serum ALT, AST and ALP. The elevation in these enzymes could be attributed to damages in structural integrity of the liver. Interestingly, treatments with *A. occidentale* (60 mg/kg bw) or metformin (125 mg/kg bw) for 28 days significantly lowered the elevated levels of these enzymes in the treated rats, thus implying its protective effect on STZ-induced tissue damage.

Induction of diabetes caused a significant elevation in serum triglyceride, total cholesterol and LDL-c levels as well as a

corresponding reduction in HDL-c level. This observation complements earlier findings that diabetes is associated with abnormal lipid metabolism [28 - 30]. Lipid metabolism in type 2 diabetes is modulated by a series of factors among which, the degree of glycemic control and the presence of insulin resistance are the two most prominent players. Insulin resistance is at the basis of the pathophysiologic mechanisms of diabetic dyslipidemia, being closely linked to hypertriglyceridaemia and postprandial lipemia [30]. The increase in the total serum cholesterol, triglyceride and LDL-C levels in the diabetic rats is mainly due to increased mobilization of free fatty acids from peripheral deposits, as insulin inhibits the hormone-sensitive lipase [28]. This suggests that *A. occidentale* may inhibit the pathway of cholesterol synthesis and increased HDL/LDL ratio, may be due to the activation of LDL receptors in hepatocytes, which is responsible for taken up LDL into the liver and reduce the serum LDL level.

Increase in reactive oxygen species (ROS) generation and resultant oxidative stress not only contribute to the symptoms of diabetes but also induce some of the diabetic-related complications via oxidative damage. Various experimental evidences have shown link between diabetes and oxidative stress by measuring various biomarkers that include DNA damage biomarkers and lipid peroxidation products [31]. It is believed that free radicals are constantly produced in the body due to normal metabolic processes and interaction with environmental stimuli. A wide range of antioxidant defences protect against deleterious effects of free radical under normal physiological conditions. Elevation in lipid peroxidation (LPO) levels is an indication of severe damage to cell membranes, inhibition of several enzymes and cellular function. LPO levels within cell are controlled by different cellular defence mechanisms consisting of enzymatic and nonenzymatic antioxidant defence systems which are altered in diabetes [32].

In the present study, it was observed that administration of *A. occidentale* reversed the enhanced lipid peroxidation and the consequent decline in the level of enzymatic antioxidant (GSH) as well as the activities of nonenzymatic antioxidant (GST, GPx, SOD and CAT) in the liver of diabetic rats. The enhanced lipid peroxidation and various alterations in the endogenous antioxidants can be attributed to increased biomembrane lipid peroxidation due to the overwhelming effect of excessive ROS production on the cellular antioxidant status. The cell protects itself from oxidative damage by recruiting GSH and scavenging enzymes such as CAT, SOD, GPx, and GST as first-line cellular defense in response to oxidative challenges in order to protect cellular integrity [33]. These findings are in accordance with previous reports [34, 35]. Histopathological examination of the liver and kidney tissue in this study revealed the need for caution in continuous intake of the extract.

CONCLUSION

Based on the experimental findings, this study demonstrates that extracts from *A. occidentale* exert its beneficial metabolic effects in a way comparable to that of metformin. This ability could be attributed to the synergetic action of its bioactive constituents.

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