

Pharmacotherapeutic Effect of Methanolic Extract of *Telfairia* occidentalis Leaves on Glycemic and Lipidemic Indexes of Alloxan-Induced Diabetic Rats

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ABSTRACT

Diabetes is a major health challenge globally and it is on the increase as carbohydrate is the main food consumed by an average human. Up till now, no synthetic drug has been able to provide permanent cure to diabetes. This study sought to investigate the pharmacotherapeutic effect of methanolic extract of Telfairia occidentalis leaves on glycemic and lipidemic indexes of alloxan-induced diabetic rats. Thirty adult male albino rats were induced intraperitoneally with alloxan. The rats were grouped into six groups of five animals per group: Group A rats are not induced with alloxan, Group B animals serve as the negative control, Group C animals serve as positive control and were treated with glibenclaimide, Group D, E and F animals were treated with 200, 400 and 600 mg/kg body weight of methanolic *leaf extract of* T. occidentalis respectively. The extracts were administered to the animals orally for 14 days. The animal's blood sugar levels were assayed using glucometer. The lipid profiles parameters were assayed using standard methods. The animals administered with 200, 400 and 600 mg/Kg B.W of extract showed significant decrease (P<0.05) in blood sugar level compared to the untreated animals. The decrease in the blood glucose level of the animals following the administration of the plant extract suggested that the plant extract possesses hypoglycemic effects in alloxan-induced diabetic rats. The extract of T.

occidentalis produces hypolipidaemic effect and this is evident as there are significant decrease in plasma total cholesterol, triglycerides, low density lipoprotein-cholesterol and an increase in plasma high density lipoprotein-cholesterol in the treated groups compared to the untreated group. This implies that T. occidentalis leaves could replace glibenclamide in the treatment of diabetes as it has no side effect. The leaves could also be exceedingly helpful in the control of obesity and hypertension. This pharmacological study is a useful tool for further drug development from the natural plant products.

Keywords: *Telfairia occidentalis* leaves; fasting blood sugar; lipid profile; alloxan-induced diabetes.

1. INTRODUCTION

Diabetes is a complex metabolic disorder associated with developing insulin resistance, impaired insulin signaling and β -cell dysfunction, abnormal glucose and lipid metabolism, sub-clinical inflammation and increased oxidative stress. These metabolic disorders lead to long-term pathogenic conditions including microand macro-vascular complications, neuropathy, retinopathy, nephropathy, and а consequent decrease in quality of life and an increase in the rate of mortality [1]. Among the multiple risk factors underlining the incidence and progression of diabetes, diet is the main modifiable factor. Both



experimental and epidemiological evidences have shown that consumption of vegetables rich in phenolic compounds and possess high antioxidant capacity may have inverse relationship with the incidence and prevalence of diabetes [2]. Dietary control remains one of the most desirable avenues for the prevention and management of chronic degenerative diseases such as diabetes and cardiovascular diseases.

Although various plants have been employed in traditional medicine in Nigeria to treat diabetes, a lot still remains to be done scientifically to confirm the efficacy of these herbal drugs. *Telfairia occidentalis* is a tropical vine grown in West Africa as a leaf vegetable and for its edible seeds. It is also known as fluted pumpkin, fluted gourd, or Ugu in Ibo Language in Eastern Part of Nigeria. Its scientific classification is as follows: Kingdom: Plantae, Division: Magnoliophyta, Class: Magnoliopsida, Order: Cucurbitales, Family: Cucurbitaceae, Genus: Telfairia, Species: T. occidentalis.

T. occidentalis (Cucurbitaceae), is cultivated mainly in West Africa, especially in Nigeria, Ghana, and Sierra Leone [3, 4]. T. occidentalis is a creeping vegetative shrub that spreads low across the ground with large lobed leaves and long twisting tendrils [5]. Harvesting of fluted pumpkin takes place between 120–150 days after sowing. It is grown for its leafy and its oily seed. The plant is a drought-tolerant; dioeciously perennial that is usually grown trellised. The young shoots and leaves of the female plant are the main ingredients of a Nigerian soup, edikangikong. The large (up to 5 cm), dark red seed is rich in fat and protein, and can be eaten whole, ground into powder for another kind of soup, or made into a fermented porridge. The fruit of the plant is large, weighing up to 13 kg, but inedible. The leaves are cooked and eaten while the seeds which contain about 30% protein can be boiled and eaten, or ground into powder for soup. The seed can also be fermented for several days and eaten as slurry [6-9]. The medicinal importance of the plant is being gradually investigated.

T. occidentalis has been reported to possess antiinflammatory effect [10], anti-bacterial activity [11], erythropoietic value [12], anticholesterolemic and

immune building properties [13], and hypoglycemic effect [14-17]. The seed of T. occidentalis is a rich source of minerals such as calcium, phosphorous, iron, zinc, and copper. The seed contains 47% oil. The oil obtained from the seed contains 61% unsaturated fatty acids which offer protective role against atherosclerosis and cardiovascular disease [18]. The phospholipids, glycolipids, and neutral lipid contents of the seed are 58%, 26%, and 15%, respectively [19]. The root of T. occidentalis has been screened for hypoglycemia activity [11]. Leaves from this plant constitute an important ingredient in soup making since they are good sources of proteins, vitamins (B-complex), minerals, fatty acids (linoleic and oleic acids), and fibers. The seed is used for marmalade manufacturing [20] and cookie formulations [21]. This darkish-green leafy vegetable is popularly used in soup and in herbal preparations for the management of many diseases in Nigeria. Studies have shown that the leaf of T. occidentalis is very rich in antioxidants and phytochemicals [22], and has been found to possess antimicrobial and free radical scavenging abilities [23, 24]. Airaodion et al. [25] has reported its therapeutic effect against acute ethanol-induced oxidative stress in Wistar rats. However, there is a dearth of information on the beneficial effect of T. occidentalis on the lipid profile of alloxan-induced diabetic animals. Based on the different health benefits associated with Τ. occidentalis leaves and their widespread acceptability, this study was carried out to investigate its hypoglycemic and hypolipidemic effects in diabetic rats.

2. MATERIALS AND METHODS

2.1 Collection and Extraction of Plant Material

Fresh plants of *T. occidentalis* were purchased from Oja-Oba market in Ibadan, Nigeria and were identified by a botanist. The leaves were carefully removed from the stem and washed in running water to remove contaminants. They were air dried at room temperature in an open laboratory space for 14 days and milled into powder using an electronic blender (Moulinex). The extraction was done using soxhlet apparatus and methanol as the solvent according to the method described by Airaodion et al. [26]. About



25 g of the powder was packed into the thimble of the soxhlet extractor and 250 mL of methanol was added to a round bottom flask, which was attached to the soxhlet extractor and condenser on a heating mantle. The solvent was heated using the heating mantle and began to evaporate moving through the apparatus to the condenser. The condensate dripped into the reservoir housing the thimble containing the sample. Once the level of the solvent reached the siphon, it poured back into the round bottom flask and the cycle began again. The process was allowed to run for a total of 18 hours. Once the process was completed, the methanol was evaporated in a rotary evaporator at 35 °C with a yield of 2.31 g representing a percentage yield of 9.24%. The extract was preserved in the refrigerator for further analysis.

2.2. Experimental Animals

A total of 30 male albino rats with body weight ranging from 160 to 180 g were obtained from the Federal College of Animal Health and Production Technology, Moor Plantation, Ibadan, Nigeria. They were acclimatized for seven days to Laboratory condition. They were kept in plastic cages and fed with commercial rat chow and supplied with water ad libitum. The rats were used in accordance with NIH Guide for the care and use of laboratory animals; NIPRD Standard Operation Procedures (SOPs). After the acclimatization period, the rats were injected with alloxan monohydrate dissolved in sterile normal saline in a dose of 150 mg/kg body weight intraperitoneally [27]. After 72 hours of the injection, rats with fasting blood glucose (FBG) at or above 126 mg/dL. (7.0 mmol/L) were considered diabetic.

2.3. Grouping of Animals

The animals were randomly divided into six groups of five animals each. They were grouped as follows:

Group A:	Normal control (non-diabetic rats)
Group B:	Negative control (diabetic without
	treatment)
Group C:	Positive control (diabetic +
	Glibenclamide)
Group D:	Diabetic + 200mg/Kg B.WT of T.
	occidentalis leaves
Group E:	Diabetic + 400mg/Kg B.WT of T.
	occidentalis leaves

N.B: Glibenclamide is the standard drug use for diabetes management

After fourteen days treatment, the animals were fasted overnight and anaesthetized using diethyl ether. Blood samples were collected by cardiac puncture into heparinized bottles.

2.4. Determination of Fasting Blood Sugar

Fasting blood sugar was determined three times in the course of this study. Firstly, after the induction of diabetes by alloxan administration; secondly, after seven days treatment and lastly, after fourteen (14) days treatment. The blood glucose level were taken by sterilizing the tails of the animals with 10% alcohol, and cutting the tails using scissors then allowing the blood to touch the test strip which was inserted into a calibrated glucose meter (One touch Glucometer, Acon Laboratory INC. San Diego, USA) according to the methods described by Airaodion et al. [28]. This gave direct reading after 5 seconds in mg/dL.

2.5 Determination of Lipids

Lipids were extracted and determined according to previously described methods [29, 30].

2.6 Statistical Analysis

Data were subjected to analysis of variance using Graph Pad Prism. Results were presented as Mean \pm Standard Error of the Mean (SEM). One way analysis of variance (ANOVA) was used for comparison of the means. Differences between means were considered to be significant at p<0.05.

3. RESULTS AND DISCUSSION

The growing number of diabetes coupled with the harsh side effects of some synthetic drugs has led to the increasing search for alternatives which are relatively cheap with minimal side effects. Various in vivo models (e.g., diazoxide. alloxan. or streptozotocin-induced diabetic rats) are used in evaluating medicinal plants with suspected hypoglycemic potentials [31]. In this study, diabetes



mellitus was induced using intraperitoneal injection of alloxan at a dose of 140 mg/kg of body weight. This dose induced diabetes mellitus in the treated rats 72 hours after administration. Alloxan induces diabetes mellitus by selectively destroying the pancreatic beta cells which are involved in the synthesis, storage, and release of insulin which is a peptide hormone that regulate carbohydrate, protein, and lipid metabolism [31]. Green leafy vegetables and fruits have been reported to have some health benefits [32-34]. Consequently, T. occidentalis leaf is a green leafy vegetable popularly used as food and in traditional medicine for the management of some diseases. However, there is dearth of information on the possible mechanisms of action by which these vegetables exert their health benefits. Therefore, this study sought to investigate the possible mechanisms

of action of this vegetable in blood glucose and lipid profile in alloxan-induced diabetes.

In this study, no significant difference was observed in the fasting blood sugar of all the animals before induction of diabetes (Figure 1). After the induction of diabetes by alloxan administration, a significant increase was observed in the fasting blood sugar of all the treatment groups when compared with the normal control group at p< 0.05 (Figure 2). In the normal control group, the beta cells of the pancreas which produce insulin are intact. But alloxan might have destroyed these beta cells in animals in groups B to F. Alloxan-induced diabetic rats, therefore, no longer have functional pancreatic beta cells and have lost the capacity to secrete insulin which is required for glucose absorption [35].

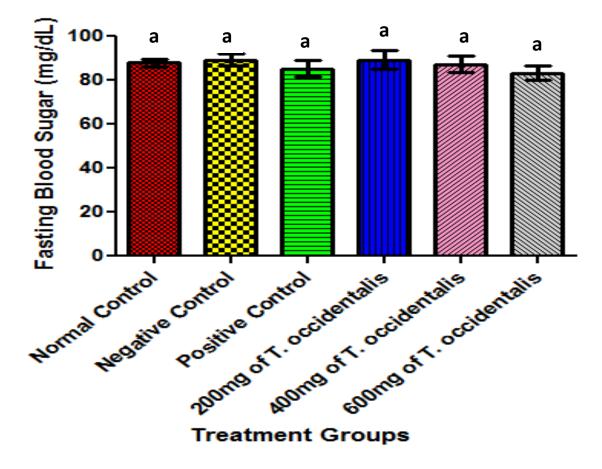


Figure 1: Fasting Blood Sugar of Animals before Diabetes Induction

Results are presented as mean \pm SEM with n = 5. Bars with different letters are significantly different at p<0.05.

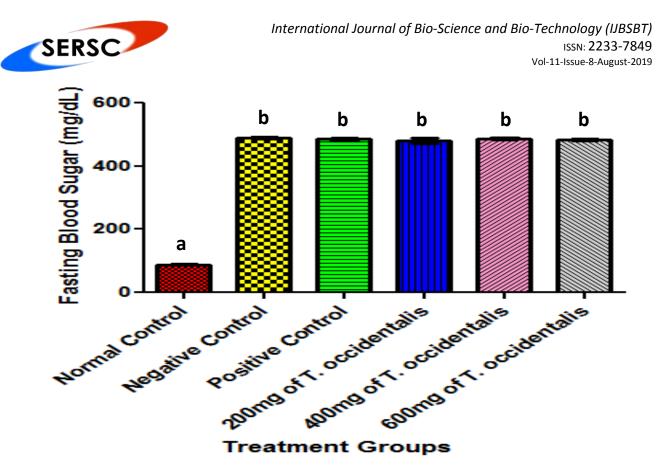


Figure 2: Fasting Blood Sugar of Animals after Diabetes Induction by Alloxan

After treatment for seven days, the fasting blood sugar of animals treated with glibenclamide, the reference diabetes drug (group C) and different doses of *T. occidentalis* leaf extract (groups D, E and F) was significantly lower when compared with diabetic untreated group (negative control group) but significantly higher than those of the undiabetic group (normal control group). This might imply that the reference drug and *T. occidentalis* leaf extract has hypoglycemic properties which help to reduce the blood sugar. The elevation in the fasting blood sugar of treated diabetic animals when compared with undiabetic animals after seven days could mean that seven days period of treatment is not sufficient to reverse the effect of alloxan-induced hyperglycemia.

After fourteen days of treatment, animals treated with varying dosage of extract of *T. occidentalis* leaves had significantly lowered fasting blood sugar when compared with diabetic untreated group (negative control group) as presented in figure 2. This suggests

that Т. occidentalis leaves may have an extrapancreatic antihyperglycemic mechanism of action. This is in agreement with the study of Airaodion et al. [28] on the effect of oral intake of African locust bean on fasting blood sugar and lipid profile of albino rats. It also corresponds to the report of Airaodion et al. [36] who studied the effect of methanolic extract of Corchorus olitorius leaves on hypoglycemic and hypolipidaemic activities in albino rats. A number of other plants and extracts have also been reported to have an antihyperglycemic and an insulin-stimulatory effect [37, 38, 39]. Most of the plants with hypoglycemic properties have been found to contain metabolites such as glycosides, alkaloid and flavonoids [32, 33, 40]. One interesting finding of this study is that 600 mg/kg body weight of T. occidentalis leaf extract reduced blood glucose as much as glibenclamide, the standard drug used in the treatment of diabetes. This is an indication that 600 mg/kg body weight of T. occidentalis leaf extract will



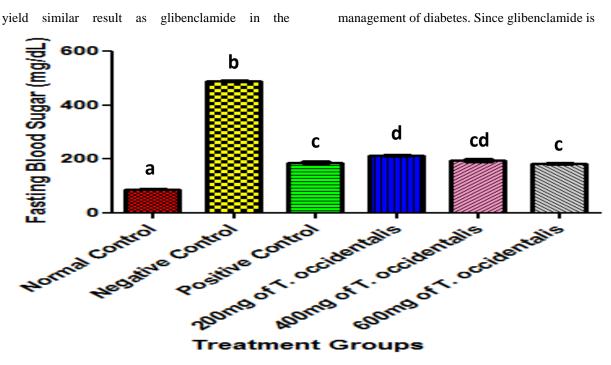


Figure 3: Effect of different Doses of *T. occidentalis* leaf extract administration on the Fasting Blood Sugar of Animals after 7 Days Treatment

made of chemicals with adverse health effect, it is advisable to use *T. occidentalis* to yield the same result with little or no side effect instead of glibenclamide. Similarly, the extract was able to restore the effect of alloxan-induced diabetes as no significant different was observed when the fasting blood sugar of animals treated with 600 mg/kg body weight of *T. occidentalis* leaf extract when compared with the undiabetic animals (normal control) after fourteen days treatment at p<0.05.

Chemical investigation of *T. occidentalis* leaves has shown that they contain flavonoids, alkaloids, glycoside, and phenolic compounds [22]. It has also been proved to possess remarkable antioxidant activity [22]. These chemical substances may then be responsible for the hypoglycemic effect of *T. occidentalis* leaves observed in this study. The fasting blood sugar lowering effect of *T. occidentalis* leaves may also indicate that it possesses antidiabetic agents which could control hyperglycemia. This is in consonance with earlier reports that green leafy vegetables possess antidiabetic properties [41, 42]. One therapeutic approach for treating early stage of diabetes is to decrease post-prandial hyperglycemia. This is done by retarding the absorption of glucose through the inhibition of the carbohydratehydrolyzing enzymes, α -amylase and α -glucosidase, in the digestive tract. Consequently, inhibitors of these enzymes determine a reduction in the rate of glucose absorption and consequently blunting the post-prandial plasma glucose rise [43]. Based on these findings, it could be suggested that T. occidentalis leaves may inhibit platelet aggregation and promote vasodilatation, exerting an important protective role in the prevention of the development and progression of vascular complications caused by the hyperglycemic state. In fact, studies have shown that polyphenolic compounds present in some plant foods can inhibit the process of thrombus formation [44, 45].

Apart from the regulation of carbohydrate metabolism, insulin plays an important role in lipid metabolism. Insulin insufficiency, as in diabetes mellitus, is associated with hypercholesterolemia and hypertriglyceridemia, which have been reported to occur in experimental diabetic rats [46-48]. Hypercholesterolemia could result in a relative molecular ordering of the residual phospholipids,



resulting in a decrease in membrane fluidity [49]. Accumulation of triglycerides is one of the leading risk factors in coronary heart disease (CHD). Lipid and lipoprotein abnormalities have been shown to

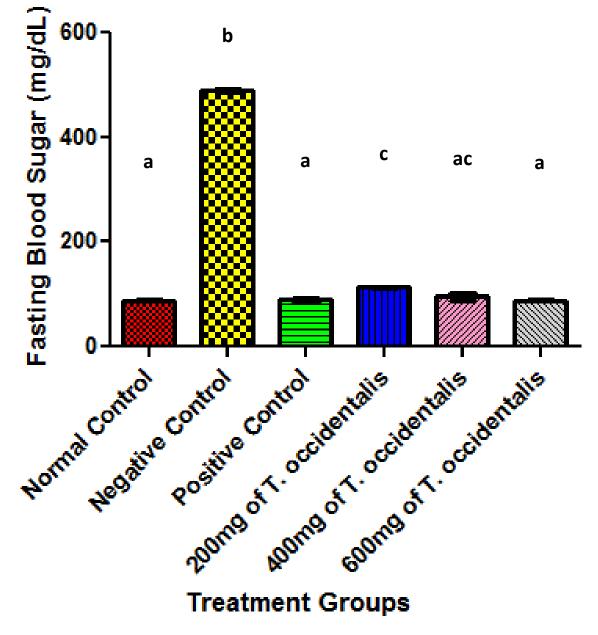


Figure 4: Effect of different Doses of *T. occidentalis* leaf extract administration on the Fasting Blood Sugar of Animals after 14 Days Treatment Results are presented as mean ± SEM with n = 5. Bars with different letters are significantly different at p<0.05.



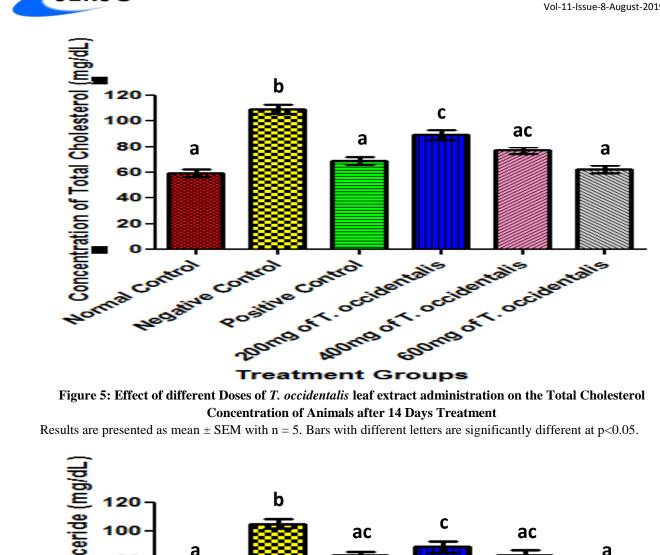


Figure 5: Effect of different Doses of T. occidentalis leaf extract administration on the Total Cholesterol

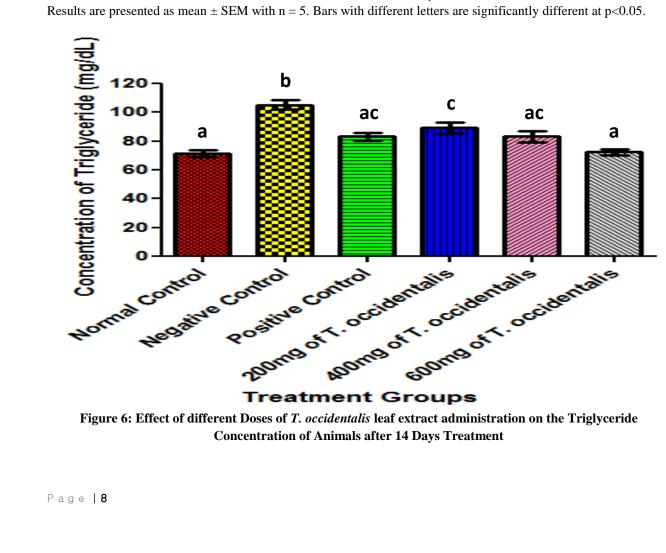


Figure 6: Effect of different Doses of T. occidentalis leaf extract administration on the Triglyceride



play a major role in the pathogenesis and progression of several disease conditions [50].

In this study, total cholesterol and triglycerides concentrations were observed to decrease significantly when diabetic animals treated with glibenclamide and varying doses of T. occidentalis leaf extract were compared with those of the negative control group (diabetic but untreated animals) at p < 0.05 (Figures 5 and 6 respectively). The similar result obtained for glibenclamide and T. occidentalis leaves could mean that T. occidentalis leaves may prevent the progression of CHD. Despite the availability of known anti-diabetic medications, remedies from medicinal plants are used with increasing success to treat this disease and manage its complications better [51]. Furthermore, it has been suggested that plant drugs and herbal formulations are less toxic and are free from side-effects compared with synthetic drugs, leading to an increasing

preference for traditional plants over synthetic drugs Increased evidence of [52-56]. therapeutic effectiveness of herbal medicines may have influenced the interest of world health organization (WHO) in hypoglycemic agents of plant origin used in the traditional treatment of diabetes [57]. Hypertriglyceridaemia has been reported in diabetic animals [58]. This was reported to be due to increased absorption and formation of triglycerides in the form of chylomicrons following exogenous consumption of diet rich in fat or through increased endogenous production of triglyceride-enriched hepatic VLDL-cholesterol and decreased triglyceride uptake in peripheral tissues [58]. The effect of T. occidentalis leaves observed in this study might suggest that T. occidentalis leaves have the ability to inhibit the absorption and formation of triglycerides in the form of chylomicrons. Hypercholesterolaemia has also been reported in diabetic animals [58]. This was attributed to the increased dietary cholesterol

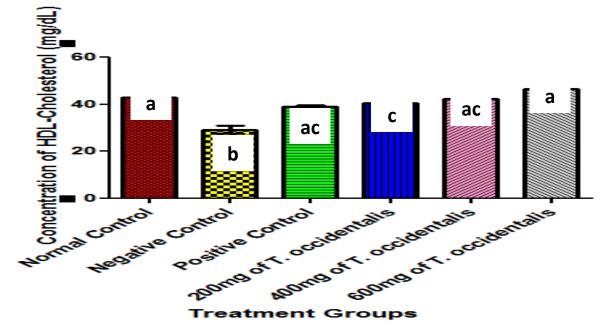


Figure 7: Effect of different Doses of *T. occidentalis* leaf extract administration on the HDL-Cholesterol of Animals after 14 Days Treatment

Results are presented as mean \pm SEM with n = 5. Bars with different letters are significantly different at p<0.05.



absorption from the small intestine following the intake of high fat diet in a diabetic condition [59].

However, the levels of serum triglyceride, VLDLcholesterol and total cholesterol were significantly reduced in animals treated with varying doses of extracts of T. occidentalis leaves when compared with those of the negative control group (diabetic but untreated animals) in the present study. Moreover, it can be conjectured that the lipid lowering effects of T. occidentalis leaves could be due to the inhibition of hepatic cholesterol, triglyceride and possibly fatty acid synthesis by the phenolic constituents of T. occidentalis leaves [42].

Hypertriglyceridaemia has also been reported to be a predictor of hypertension [60]. In the peripheral vascular system, endothelial cells rely on lipoproteins

for the transfer of neutral sterols at this site. Although free cholesterol is transferred to HDL-cholesterol particles through the functioning of a designated HDL-cholesterol receptor, lecithin cholesterol acyl transferase (LCAT) serves to maintain the concentration toward the HDL core and preserve the hydrophobic nature that facilitates the transfer. Esterification of cholesterol produces cholesterol ester (CE), which is concentrated in HDL core, and may be transferred by cholesterol ester transfer protein (CETP) in the plasma compartment to apo-B containing lipoproteins in exchange for triglyceride. Increased CETP activity would suggest an enrichment of apo-B lipoproteins in plasma, while simultaneously decreasing HDL-cholesterol, and has generally been considered pro-atherogenic [61]. This probably explains why T. occidentalis leaves may

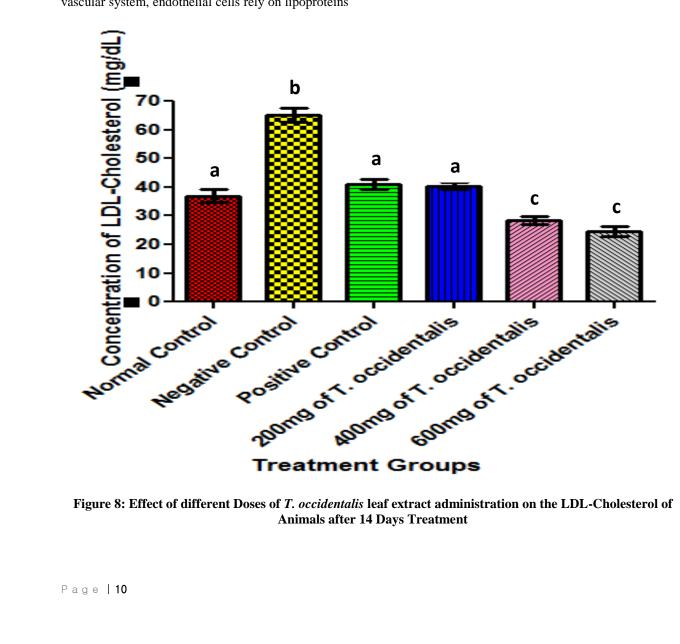


Figure 8: Effect of different Doses of T. occidentalis leaf extract administration on the LDL-Cholesterol of



lead to a reduction in the risk of developing heart since a high HDL-cholesterol/LDLdiseases cholesterol ratio has been shown to be beneficial and is indicative of a lower risk of cardiovascular diseases [62].

HDL-cholesterol and LDL-cholesterol are two of the four main groups of plasma lipoproteins that are involved in lipid metabolism and the exchange of cholesterol, cholesterol ester and triglycerides between tissues [63, 64]. Numerous population studies have shown an inverse correlation between plasma HDL-cholesterol levels and risk of cardiovascular disease, implying that factors associated with HDL-cholesterol protects against atherosclerosis. Some of these factors appear to have antioxidant and anti-inflammatory effects which may obviate processes that initiate atherogenesis [65, 66].

Epidemiological studies have also shown that elevated concentrations of total cholesterol and/or LDL-cholesterol in the blood are powerful risk factors for coronary heart disease [67]. Most extrahepatic tissues, although having a requirement for cholesterol, have low activity of the cholesterol biosynthetic pathway. Their cholesterol requirements are supplied by LDL, which is internalized by receptor-mediated endocytosis. A major function of HDL-cholesterol is to enhance reverse cholesterol transport by scavenging excess cholesterol from peripheral tissues followed by esterification through

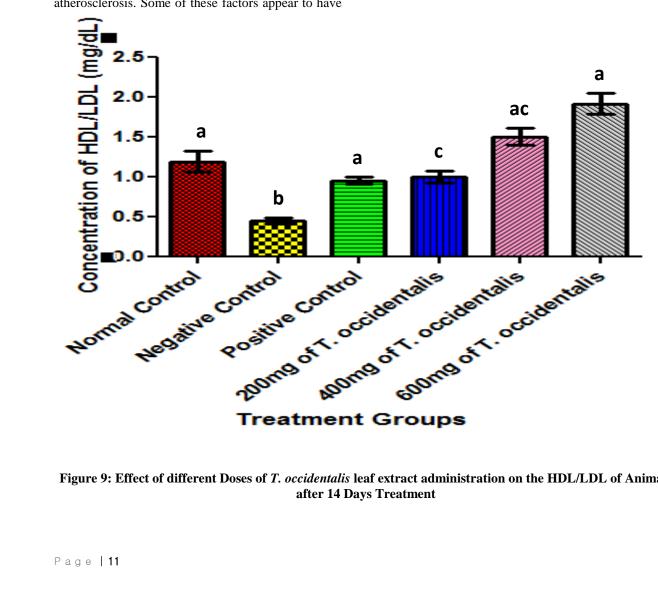


Figure 9: Effect of different Doses of T. occidentalis leaf extract administration on the HDL/LDL of Animals



lecithin: cholesterolacyltransferase and delivering it to the liver and steroidogenic organs for subsequent synthesis of bile acids and lipoproteins and eventual elimination from the body [68, 69]. This role of HDL-cholesterol has been shown to be responsible for its atheroprotective properties. HDL-cholesterol also regulates the exchange of proteins and lipids between various lipoproteins.

In addition, HDL-cholesterol provides the protein components required to activate lipoprotein lipase which releases fatty acids that can be oxidized by the ß-oxidation pathway to release energy [63, 64]. Most importantly, HDL-cholesterol can inhibit oxidation of LDL-cholesterol as well as the atherogenic effects of oxidized LDL-cholesterol by virtue of its antioxidant property [69]. LDL is a lipoprotein that transports cholesterol and triglyceride from the liver to peripheral tissues. It enables fat and cholesterol to move within the water-blood solution of the blood stream. LDL is often called bad cholesterol; hence low levels are beneficial [70].

Interestingly, the administration of *T. occidentalis* leaves in varying dosage in this study caused a significant increase in the serum level of HDL-cholesterol when compared with the negative control animals (diabetic but untreated animals) (Figure 7) at p<0.05. HDL-cholesterol is usually referred to as the 'good cholesterol' [29]. Again, *T. occidentalis* leaves administration significantly decreased the



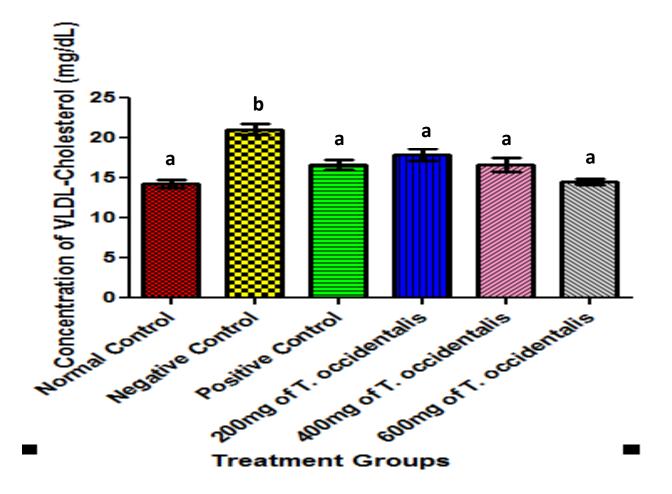


Figure 10: Effect of different Doses of *T. occidentalis* leaf extract administration on the VLDL-Cholesterol of Animals after 14 Days Treatment

concentration of LDL-cholesterol (bad cholesterol) when compared with that of the negative control group (diabetic but untreated animals) at p<0.05 (Figure 8). This result is in agreement with the findings of Airaodion et al. [40] who studied the hypoglycemic and hypolipidaemic activities of methanolic extract of *Talinum triangulare* leaves in Wistar rats but contradicts the findings of Airaodion et al. [28] who reported a non-significant difference in the LDL-cholesterol concentration when animals were treated with African locust bean for 14 days. The combined effect of increased HDL-cholesterol

(good cholesterol) and decreased LDL-cholesterol (bad cholesterol) in the present study resulted in an increased HDL-cholesterol/LDL-cholesterol ratio in animals treated with varying dose of *T. occidentalis* leaves when compared with the negative control group (Figure 9). This strongly supports the notion that dietary supplementation with the extract of *T. occidentalis* leaves may lead to a reduction in the risk of developing heart diseases, because a high HDLcholesterol/LDL-cholesterol ratio has been shown to be beneficial and is indicative of a lower risk of CHD [71]. Although, the activities of enzymes were not



investigated in this study, but it is possible that *T*. *occidentalis* leaves decreased the activity of 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase (the rate-limiting enzyme in cholesterol biosynthesis) [30]. This implies that *T. occidentalis* leaves are of significant health importance as far as hyperlipidaemia is concern. It could also be exceedingly helpful in the control of obesity.

5. Conclusion

The extract of *T. occidentalis* leaves at varying doses especially at 600mg/kg body weight restored the diabetic effect of alloxan in animals by regulating the glycemic and lipidemic indexes similar to that of glibenclamide, the standard diabetes drug. This implies that *T. occidentalis* leaves could replace glibenclamide in the treatment of diabetes as it has no side effect. The leaves could also be exceedingly helpful in the control of obesity and hypertension. This pharmacological study is a useful tool for further drug development from the natural plant products.

6. Conflict of Interest

Authors declare that no conflict of interest exist in this paper.

7. Acknowledgement

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