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## Anti-diabetic activity of aqueous extract of *Cochlospermum planchonii* root in alloxan-induced diabetic rats

Musa Toyin YAKUBU\*, Musbau Adewumi AKANJI &amp; Mikhail Olugbemiro NAFIU

Phytomedicine, Toxicology, Reproductive and Developmental Biochemistry Research  
Laboratory, Department of Biochemistry, University of Ilorin,  
PMB 1515, Ilorin, Nigeria.\* Author to whom correspondence should be addressed: GSM: +2348037544437; Email: [tomuyak@yahoo.com](mailto:tomuyak@yahoo.com);  
[tomuyak@gmail.com](mailto:tomuyak@gmail.com)**ABSTRACT**

Aqueous extract of *Cochlospermum planchonii* root was investigated for antidiabetic activity in alloxan-induced diabetic rats. Thirty albino rats ( $110.33 \pm 8.69$  g) were randomized into six groups (A-F) such that group A (non-diabetic) received orally 0.5 ml of distilled water, thrice daily for 10 days. Animals in groups B, C, D, E and F which were all made diabetic with alloxan (150 mg/kg b. w., i.p.) also received 0.5 ml of glibenclamide (2.5 mg/kg b. w., p.o.), 25, 50 and 100 mg/kg b. w., p.o. of the extract respectively. The blood glucose of the alloxanized rats after 48 hours which ranged from 20.50-30.20 mmol/L were significantly ( $P < 0.05$ ) and progressively reduced in the glibenclamide and extract treated animals. Restlessness, respiratory distress, diarrhoea and convulsion in the untreated diabetic rats were reduced in the extract and glibenclamide treated animals. The trace amount of blood ketones and urine sugar in the untreated diabetic rats disappeared in the other treatment groups except in the 25 mg/kg b. w. where there was less than 0.25% of urine sugar. The significantly elevated levels of serum albumin, creatinine, urea, total cholesterol, triacylglycerol, liver malate dehydrogenase activity as well as reduced weight of pancreas and liver glycogen content in the untreated diabetic rats were reverted back to their respective values in distilled water control animals by the extract and glibenclamide. Overall, this study indicates that the aqueous extract of *Cochlospermum planchonii* root possesses anti-hyperglycemic activity similar to the reference drug. The extract of *Cochlospermum planchonii* root is also effective in controlling some of the disorders of metabolism associated with diabetes.

**Key words:** Alloxan, Cochlospermaceae, *Cochlospermum planchonii*, Diabetes, Metabolic disorders, Glibenclamide

**INTRODUCTION**

Diabetes mellitus is a clinical syndrome characterized by inappropriate hyperglycemia caused by a relative or absolute deficiency of insulin or resistance to the action of the hormone at the cellular level [1]. It is the most common endocrine disorder and the world's fastest growing metabolic disorder with an average annual growth of 1-2% [2]. Currently, the world diabetes prevalence in adults above 20 years of age is over 150 million and is expected to increase to 5.4 % (366 million) by 2030 [3]. In Nigeria, World Health Organization (WHO) [4] puts the incidence at 1995 as 576,000 while it is projected to rise to 685,000 by 2010. Chronic diabetes is associated with long term damage, dysfunction and failure of organs such as retinopathy, sexual inadequacies, nerve damage and loss of weight among others. Several drugs such as biguanides and sulfonylurea which are presently employed in the management of diabetes are not without side

effects such as worsening of hear diseases, increased body weight and hypoglycaemia [5]. However, since the introduction of these drugs in the last 50 years, no major lead with minimal side effects has been obtained in the direction of finding a proper anti-diabetic agent [1, 6]. Therefore, it is imperative to explore options in herbal medicine for the management of the disease. Notwithstanding the existence of scientific studies that have lend empirical evidence to the use of these botanicals as anti-diabetic and anti-hyperlipidemic remedies, the continued search for new drug for diabetes from herbs is still attractive because they are less expensive and safer. One plant claimed to be used in the management of diabetes mellitus in the folk medicine of Nigeria is *Cochlospermum planchonii*.

*Cochlospermum planchonii* Kunth (Cochlospermaceae), known as 'Gbehutu' or 'Feru' (Yoruba- Western Nigeria) is a low shrubby

plant commonly found in both Guinea and Sudan savannah zones [7]. It is also widespread from Senegal to East and West Cameroon up to Nigeria. It grows to about 2-4 m tall, with scarbid, trilobed leaves [8]. Various parts of the plant have been claimed to be used medicinally for managing a myriad of diseased conditions. For example, the rhizomes and leaves are separately used locally in the treatment of jaundice, malaria, diabetes and diarrhoea [9, 10]. The decoction of the root bark of the plant is used for treating hepatic fever, hepatobiliary affections (black toilet fever) and haemolytic anaemia in Burkina Faso [11]. In Mali, the powdered leaves and the concoction of the root as well as those of *Entada africans* and *Erythrina senegalensis* are used for the treatment of malaria fever and jaundice. Furthermore, the rhizomes have also been implicated in the treatment of stomach disorders, typhoid fever and urinary tract infections [12].

The leaf, stem bark and root bark of *C. planchonii* have been shown to have strong fungitoxicity against *Colletotrichum capsici* [13]. Again, the leaf oil of *C. planchonii* has been shown to possess a superior *in vitro* anti-plasmodial effect over chloroquine [14]. Other studies have also suggested trypanocidal properties for the petroleum extract of the stem bark of *C. planchonii* [10] while Anaga and Opara [15] have reported that the methanolic root extract of the plant possesses CNS depressing, analgesic, anti-inflammatory and anti-hyperglycemic activities with minimal toxicity using brine shrimps lethality model. Furthermore, Nafiu *et al* [16] have similarly reported that the aqueous extract of *C. planchonii* root at 50 mg/kg b. w. could adversely affect the normal functioning of the liver and kidney of albino rats.

Although, Anaga and Opara [15] have shown that the methanolic extract of *C. planchonii* root at 250, 500 and 1000 mg/kg b. w. reduced the blood glucose levels of alloxan-induced diabetic mice in a 360 minutes experimental period, there is still dearth of information in the open scientific literature on studies that evaluated the aqueous extract (as claimed to be used in the folk medicine of Nigeria) of *C. planchonii* root in both sexes of albino rats (since diabetes affect both males and females) and the impact of the extract on some metabolic disorders associated with diabetes. Therefore, we decided to provide information on the potentials of aqueous extract of *C. planchonii* root as an anti-diabetic agent at 25, 50 and 100

mg/kg b. w., thrice daily for 10 days in alloxan-induced diabetic rats as well as its potential effect on some metabolic disorders associated with diabetes mellitus.

## MATERIALS AND METHODS

### Plant material and authentication

The plant material obtained from the herbseller at 'Oja-oba' Market, Ilorin, Nigeria, was authenticated at the Forest Research Institute of Nigeria (FRIN), Jericho, Ibadan, Nigeria. A voucher specimen (FHI 99093) was deposited at the herbarium of the Institute.

### Glucometer and Assay Kit

Bayer Contour™ TS blood glucose meter kit was a product of Bayer Consumer Care AG, Postfach, Basel, Switzerland while keto-diastix reagent strips for urinalysis were products of Bayer Diagnostics India Ltd, Baroda, India. Assay kits for albumin, creatinine, urea, total cholesterol, triacylglycerol and glucose were products of Randox Laboratories, Co-Antrim, UK.

### Drug and Chemicals

Alloxan monohydrate was a product of May and Baker Ltd., Dagenham, England while Glibenclamide was a product of HOVID Bhd., Ipoh, Malaysia. All other chemicals were products of Sigma-Aldrich CHEME GmbH, Steinheim, Germany.

### Laboratory Animals

Male and female albino rats (*Rattus norvegicus*) of Wistar strain, weighing  $110.33 \pm 8.69$  g were obtained from the Animal Holding Unit of the Department of Biochemistry, University of Ilorin, Ilorin, Nigeria. The animals were housed in clean metabolic cages that provided free access to rat pellets (Bendel Feeds and Flour Mills Limited, Ewu, Nigeria) and tap water that was free of contaminants. The cages were contained in a well ventilated standard housing conditions (temperature: 28-31°C; photoperiod: 12 h natural light and 12 h dark; humidity: 50 – 55%).

## Methods

### Preparation of extract

Fresh roots of *Cochlospermum planchonii* were cut into very thin slices, air dried at room temperature for three weeks to a constant weight. The dried materials were pulverized using an electric blender (Philips Comfort Blender, Model HR 1727, Holland). A known weight of the powder (280 g) was extracted in 500 ml of distilled water for 12 h with intermittent shaking. The extract was

then filtered with Whatman No. 1 filter paper (Springfield, Maidstone, Kent, England) and thereafter evaporated on a steam bath to give a yield of 7.98 g. A calculated amount of the residue was weighed and constituted in distilled water to give the required doses of 25, 50 and 100 mg/kg b. w.. The doses used in this study were as obtained from the ethnobotanical survey carried out on the plant by the authors within our locality.

#### Animal grouping and extract administration

Thirty albino rats of both sexes were randomized into six groups (A-F) such that group A (non-diabetic) received orally 0.5 ml of distilled water, three times a day for 10 days (Preliminary studies revealed that the untreated diabetic rats could survive up till the 12<sup>th</sup> day; therefore, our experiment was terminated shortly before their death). Animals in groups B, C, D, E and F which were made diabetic with alloxan (150 mg/kg b. w., i.p.) received 0.5 ml of distilled water, p.o., same volume of glibenclamide (2.5 mg/kg b. w., p.o.), 25, 50 and 100 mg/kg b. w., p.o. of the extract respectively. The study was carried out after approval from the Departmental Ethical Committee on the Use and Care of Experimental Animals. The animals were handled humanely in accordance with the guidelines of European Convention for the Protection of Vertebrate Animals and Other Scientific Purposes- ETS-123 (17).

#### Induction of diabetes and determination of blood glucose

The animals were made diabetic by single intraperitoneal injection of 150 mg/kg b. w. of alloxan monohydrate in sterile physiological saline. After a six hours fast (without food, but water) on the second day (48 hr), blood samples (0.6 µL) were drawn from the tail vein and glucose levels were determined to confirm the induction of diabetes using the Bayer Contour™ test strips and blood glucose meter according to the instructions outlined in the User Guide. Only animals with blood glucose level higher than 7.0 mmol/L were used for the study. Furthermore, 1 hr after the administration of alloxan, the animals were equally given their pellet *ad libitum* and 5% dextrose saline in a feeding bottle to overcome the early hypoglycaemic phase (18). The blood glucose levels of the animals were also determined before the administration of alloxan using the same procedure.

#### Determination of blood ketones and urine glucose

For the determination of blood ketones, the tip of the tail of the animals was cut carefully by one stroke with a sharp sterile blade. The resultant blood was checked for ketones following the procedures outlined in the manufacturer's kits using keto-diax strips. Fresh urine, collected three times on the designated days by slightly pressing the tail and back of the rat, was centrifuged at 224 *g* x 10 min. The urine glucose was determined according to the procedures outlined in the assay kit adopting the principle of Trinder (19).

#### Preparation of serum and liver homogenate

Under ether anaesthesia, the neck areas of the animals were quickly cleared of fur and skin to expose the jugular veins. The animals were then made to bleed through their cut jugular vein into a clean, dry centrifuge tube which was allowed to clot for 30 min. The blood samples were centrifuged at 224 *g* x 10 min using Uniscope Laboratory Centrifuge (Model SM800B, Surgifriend Medicals, Essex, England). The sera were thereafter aspirated with Pasteur pipette into clean, dry, sample bottles and kept frozen overnight before being used for the assays. The animals were quickly dissected and the liver and pancreas removed. The organs were blotted in clean tissue paper and weighed. The liver was homogenized in 0.25 M sucrose solution (1:5 w/v) as described by Akanji and Yakubu (20). The homogenates were immediately transferred into specimen bottles and kept frozen for 24 hr before analyses.

#### Determination of biochemical parameters

The biochemical parameters were determined in the liver homogenate, serum and urine using standard methods described for albumin (21), creatinine (22), urea (23), total cholesterol (24), triacylglycerol (25), glycogen (26), protein (27), glucose (19) and malate dehydrogenase (EC 1.1.1.37) (28).

#### Statistical analysis

Data were expressed as mean of five determinations  $\pm$  SD. One-way analysis of variance and Duncan Multiple Range Test complemented with Student's t-test were used to account for the differences among the means as well as the interaction between the variables. Differences were considered statistically significant at  $P < 0.05$ .

## RESULTS

The results revealed that all the alloxanized rats became diabetic after 48 hr with blood glucose level ranging from 20.50 - 30.20 mmol/L (Table 1). The blood glucose levels were however, reduced significantly ( $P < 0.05$ ) and progressively in the glibenclamide- and extract-treated animals. By the end of the experimental period, the extract at the doses of 25, 50 and 100 mg/kg b. w. had reduced the blood glucose levels of the animals by 86.27%, 88.26% and 89.74% respectively. All the computed percentage reductions in the blood glucose level of the extract treated animals were similar to the 86.42% obtained for the glibenclamide-treated animals (Table 1).

Clinical signs of toxicity observed from the cage side in the untreated diabetic rats included restlessness, respiratory distress, diarrhoea and convulsion. The severity of these symptoms however, decreased progressively throughout the 10 days exposure period in the glibenclamide- and extract- treated animals.

The blood ketones (greater than 5 mg/ml) in the untreated diabetic rats was sustained throughout the experimental period whereas the same blood ketone which was detected in trace amount in the other treatment groups on Day 0 disappeared while the study lasted (Table 2).

The urine sugar which was greater than 2% in the untreated diabetic rats throughout the experimental period decreased to 0.25% and

eventually disappeared in the animals administered with 25 and 50 mg/kg b. w. of the extract. This trend was similar to the alloxanized animals treated with glibenclamide. In contrast however, urine sugar was not detected in the diabetic animals treated with 100 mg/kg b. w. of the extract (Table 3).

Compared with the control, the levels of serum albumin, creatinine, urea, total cholesterol, triacylglycerol and the activity of malate dehydrogenase in the liver of the animals were significantly ( $P < 0.05$ ) elevated in the untreated diabetic rats (Table 4). With the exception of total cholesterol, triacylglycerol and malate dehydrogenase, all other elevations were reverted back to their respective distilled water control values in the glibenclamide- and extract-treated animals. Although, there were significant reductions in the total cholesterol, triacylglycerol and malate dehydrogenase by the glibenclamide and 25 mg/kg b. w. of the extract, the 50 and 100 mg/kg b. w. produced serum lipid levels and enzyme activity that compared favourably ( $P > 0.05$ ) with their respective distilled water control values. Furthermore, the reductions in both the weight of the pancreas and liver glycogen content of the untreated diabetic rats were attenuated towards the distilled water control values in the extract- and glibenclamide- treated animals (Table 4).

Table 1: Effect of administration of aqueous extract of *Cochlospermum planchonii* root on the blood glucose level (mmol/L) of alloxanized diabetic rats

Treatment groups	Days after administration of alloxan		
	Day 0	Day 5	Day 10
Control	3.10±0.01 <sup>a</sup>	3.09±0.01 <sup>a</sup>	3.11±0.01 <sup>a</sup>
Diabetic rats + Distilled water	20.50±3.13 <sup>b</sup>	28.10±0.90 <sup>b</sup>	> 33.80±0.00 <sup>b</sup> (High)
Diabetic rats + Glibenclamide	23.20±1.08 <sup>b</sup>	5.10 ±0.00 <sup>c</sup> (78.02%)	3.15±0.05 <sup>a</sup> (86.42%)
Diabetic rats + 25 mg/kg body weight of the extract	22.80±0.55 <sup>b</sup>	9.60±0.018 <sup>d</sup> (57.89%)	3.13±0.11 <sup>a</sup> (86.27%)
Diabetic rats + 50 mg/kg body weight of the extract	26.40±1.02 <sup>c</sup>	5.10±0.04 <sup>c</sup> (80.68%)	3.10±0.08 <sup>a</sup> (88.26%)
Diabetic rats + 100 mg/kg body weight of the extract	30.20±2.07 <sup>d</sup>	3.20±0.05 <sup>a</sup> (89.40%)	3.10±0.04 <sup>a</sup> (89.74%)

n = 5 ± SD;

Values in parenthesis represent computed percent blood glucose level

<sup>a-d</sup>Values down the column carrying superscript different from their respective control for each day are significantly different ( $P < 0.05$ ).

Table 2: Effect of administration of aqueous extract of *Cochlospermum planchonii* root on the blood ketone (mg/dl) of alloxanized diabetic rats

Treatment groups	Days after administration of alloxan		
	Day 0	Day 5	Day 10
Control	ND	ND	ND
Diabetic rats + Distilled water	++	++	++
Diabetic rats + Glibenclamide	+	ND	ND
Diabetic rats + 25 mg/kg body weight of the extract	+	ND	ND
Diabetic rats + 50 mg/kg body weight of the extract	+	ND	ND
Diabetic rats + 100 mg/kg body weight of the extract	+	ND	ND

ND = Not detected (+) = Trace amount of 5 mg/dl of blood ketone (++) = Greater than 5 mg/dl of blood ketone

Table 3: Effect of administration of aqueous extract of *Cochlospermum planchonii* root on the urine glucose (mmol/L) of alloxanized diabetic rats

Treatment groups	Days after administration of alloxan		
	Day 0	Day 5	Day 10
Control	ND	ND	ND
Diabetic rats + Distilled water	+++	+++	+++
Diabetic rats + Glibenclamide	+++	+	ND
Diabetic rats + 25 mg/kg body weight of the extract	+++	+	ND
Diabetic rats + 50 mg/kg body weight of the extract	+++	+	ND
Diabetic rats + 100 mg/kg body weight of the extract	+++	ND	ND

ND = Not detected (+) = 0.25%, sugar (++) = More than 0.25% but not up to 1%, (+++) = More than 2% sugar

Table 4: Effect of administration of aqueous extract of *Cochlospermum planchonii* root on selected biomolecules of alloxanized diabetic rat serum

Treatment groups	Weight of pancreas (g)	Albumin (mmol/L)	Creatinine (mmol/L)	Urea (mmol/L)	Total cholesterol (mmol/L)	Triacylglycerol (mmol/L)	Liver glycogen (mg of glucose/g of wet tissue)	Liver Malate dehydrogenase (nM/min/mg protein)
Control	0.51±0.01 <sup>a</sup>	10.22±0.51 <sup>a</sup>	85.00±0.05 <sup>a</sup>	5.41±0.08 <sup>a</sup>	1.20±0.18 <sup>a</sup>	0.40±0.07 <sup>a</sup>	55.23±3.87 <sup>a</sup>	215.08±10.11 <sup>a</sup>
Diabetic rats + Distilled water	0.40±0.03 <sup>b</sup>	19.28±0.46 <sup>b</sup>	142.10±2.82 <sup>b</sup>	10.02±1.20 <sup>b</sup>	2.48±0.36 <sup>b</sup>	1.26±0.05 <sup>b</sup>	27.09±4.15 <sup>b</sup>	297.20±12.41 <sup>b</sup>
Diabetic rats + Glibenclamide	0.50±0.02 <sup>a</sup>	10.30±0.82 <sup>a</sup>	84.00±0.22 <sup>a</sup>	5.38±0.05 <sup>a</sup>	1.58±0.36 <sup>c</sup>	0.63±0.03 <sup>c</sup>	53.94±5.01 <sup>a</sup>	235.14±20.07 <sup>c</sup>
Diabetic rats + 25 mg/kg body weight of the extract	0.50±0.01 <sup>a</sup>	9.64±1.31 <sup>a</sup>	85.01±0.47 <sup>a</sup>	5.42±0.04 <sup>a</sup>	1.42±0.17 <sup>d</sup>	0.48±0.05 <sup>d</sup>	53.66±5.10 <sup>a</sup>	227.20±2.41 <sup>d</sup>
Diabetic rats + 50 mg/kg body weight of the extract	0.48±0.03 <sup>a</sup>	9.58±0.00 <sup>a</sup>	84.00±0.00 <sup>a</sup>	5.44±0.06 <sup>a</sup>	1.21±0.10 <sup>a</sup>	0.46±0.06 <sup>d</sup>	56.14±2.60 <sup>a</sup>	225.48±9.90 <sup>d</sup>
Diabetic rats + 100 mg/kg body weight of the extract	0.52±0.01 <sup>a</sup>	10.60±0.14 <sup>a</sup>	84.001±0.20 <sup>a</sup>	5.39±0.10 <sup>a</sup>	1.19±0.21 <sup>a</sup>	0.42±0.08 <sup>a</sup>	56.02±2.03 <sup>a</sup>	217.20±8.70 <sup>a</sup>

n = 5 ± SD; <sup>a-d</sup>Values down the column for each parameter carrying superscript different from their respective control are significantly different (P<0.05).

## DISCUSSION

Plants have always been an exemplary source of drugs and many currently available drugs have been directly or indirectly obtained from botanicals. Several studies have revealed that a wide variety of plant extracts effectively lowered the glucose level in alloxan-induced diabetic animals (15, 18). In the present study, aqueous extract of *C. planchonii* root significantly reduced the blood glucose level in alloxan-induced diabetic rats and effectively attenuated other biochemical parameters relating to diabetes with the 100 mg/kg b. w. exhibiting the most profound anti-diabetic activity, even better than the reference drug, glibenclamide, although, notwithstanding the disparity in the doses.

Alloxan induces "chemical diabetes" in a wide variety of animal species by damaging the insulin secreting pancreatic  $\beta$ -cell of the islets of Langerhans, resulting in reduced synthesis and release of endogenous insulin characteristically similar to type 1 diabetes in humans (29). *In vitro* studies have shown that alloxan is selectively toxic to pancreatic beta cells, leading to the induction of cell necrosis (30). The cytotoxic action of alloxan is mediated by reactive oxygen species, with a simultaneous massive increase in cytosolic calcium concentration, leading to a rapid destruction of the  $\beta$ -cells (29). Therefore, the determination of glucose concentration in the blood of animals among others is a useful, quantitative index of diabetes. Furthermore, glibenclamide, a reference anti-diabetic drug, commonly used in several studies to compare the efficacy of various hypoglycemic compounds acts by various mechanisms such as binding to the ATP-sensitive potassium channel and in the process, lowers glucose levels. Others include suppressing hepatic glucose production, increasing insulin sensitivity of extrapancreatic tissues and fatty acid oxidation, enhancing peripheral glucose uptake, decreasing hepatic glycogenolysis and gluconeogenesis as well as absorption of glucose from the gastrointestinal tract (1). Therefore, the reduction in the blood glucose levels of the animals as well as glucosuria, a common feature of diabetes, from the chronic state to normal and its subsequent attenuation by the extract of *C. planchonii* root in the present study suggests anti-hyperglycemic effect of the plant extract. The extract might have acted via several mechanisms such as slowing down the absorption of sugar from the guts,

increasing insulin production by the pancreas from possibly regenerated  $\beta$ -cells, decreasing the release of glucose from the liver or increasing glucose uptake by fat and muscle cells. These proposed mechanisms of action may however await further study. The reduction in blood glucose of the albino rats by aqueous extract of *C. planchonii* root at 25, 50 and 100 mg/kg b. w. in the present study, notwithstanding the one-tenth reduction in the doses, is similar to the findings by Anaga and Opara (15) that the methanolic extract of *C. planchonii* root at the doses of 250, 500 and 1000 mg/kg b. w. reduced the blood glucose of alloxanized diabetic mice in a 360 min experimental period.

The observed clinical signs of toxicity such as restlessness, respiratory distress, diarrhoea and convulsion displayed by the alloxanized diabetic rats further corroborate some of the known clinical signs of chronic diabetes. However, the progressive decrease in the episode of these symptoms in the diabetic rats treated with the extract indicates the effectiveness of the extract at alleviating these toxicities and further supports anti-hyperglycemic activity of the extract.

Elevated blood levels of ketones have been reported to be a common feature of diabetes mellitus (1, 6), and this has been further corroborated in the present study by the presence of significant trace amount of blood ketones in the alloxanized diabetic rats. Although, specific ketone bodies such as acetoacetic acid,  $\beta$ -hydroxyl butyric acid and acetone were not analyzed individually in the blood of the animals, the presence of blood ketones may be attributed to enhanced production of ketone bodies by the liver and/or incomplete utilization by the tissue leading to their eventual accumulation in the blood and subsequent elimination in the urine (1). The ability of the aqueous extract of *C. planchonii* root to attenuate the elevated blood ketone observed in the untreated, diabetic rats, in a manner similar to glibenclamide, did not only buttress the anti-diabetic potential of the extract, but also its effectiveness against this metabolic disorder that is characteristic of diabetes mellitus.

Hyperalbuminemia, hypercreatininemia and hyperuremia have also been reported to occur in alloxanized diabetic rats (31), and such elevated levels of the biomolecules in the present study did not only suggest disturbance in the metabolism of these substances, but also agrees with previously published reports. The levels of the molecules in

the serum of the animals were normalized by the extract back to the control in a manner similar to that of the reference drug, glibenclamide. These attenuations further indicate that aqueous extract of *C. planchonii* root could also aid in the recovery of animals from some metabolic disorders associated with diabetes mellitus.

Several studies have reported that diabetes is associated with increases in serum lipids such as total cholesterol and triacylglycerol, which is related to significant changes in lipid metabolism and structure in the diseased state (32, 33). The abnormalities in cellular cholesterol metabolism could be partly responsible for the changes in the serum cholesterol levels in diabetes as well as oxidative stress which have been reported to increase the accumulation of lipids in cells (33). Therefore, the normalization of the serum total cholesterol and triacylglycerol by the extract of *C. planchonii* root suggest that the extract is effective in reversing the abnormalities in lipid metabolism characteristic of diabetes.

Furthermore, Kumar *et al* (30) reported a decrease in the number of secretory granules of the  $\beta$ -cells of the pancreas in diabetic rats. Although, histological examination of the pancreas was not conducted in this study, the decreased secretory granules may as well account for the reduction in the weight of the pancreas. It is also possible that the normal architecture of these secretory granules were restored following the administration of the extract and glibenclamide since the weights of the pancreas in these groups of animals compared favourably with distilled water control animals. The findings on the weight of the pancreas in the present study are similar to that reported by Kumar *et al* (30) following the treatment of diabetic rats with *Terminalia chebula* extract.

The conversion of glucose to glycogen in the liver is dependent on the extracellular glucose concentration and the availability of insulin which in turn stimulates glycogen synthesis over a wide range of glucose concentration (34). This *in vivo* regulation of glycogen metabolism depends on the important roles played by the multifunctional enzymes, glycogen synthase and glycogen phosphorylase. Therefore, the reduced level of glycogen in the liver of alloxanized diabetic rats may be attributed to either a decrease in the activity of glycogen synthase and or increase in the activity of glycogen phosphorylase or both. However, the reversal of the reduction in liver

glycogen by the extract and glibenclamide in this study suggest that these compounds could effectively attenuate the altered level of glycogen in the diabetic animals by promoting the synthesis of glycogen through modulatory effect on the activities of glycogen synthase and glycogen phosphorylase.

Malate dehydrogenase, an enzyme requiring NAD<sup>+</sup> converts malate to oxaloacetate, which is continuously removed to form citrate, a substrate for gluconeogenesis. The enzyme has been reported to increase in diabetes (35). Therefore, the increase in the activity of malate dehydrogenase in the diabetic animals in the present study will further promote gluconeogenesis, hence, the elevated levels of glucose in the blood of the animals which was not mopped up due to deficiency of insulin. The activity of the enzyme was controlled by the extract to the values in the distilled water treated non-diabetic animals. The extract was also equi-effective in restoring the activity of the enzyme when compared to the reference drug, glibenclamide. The complete reversion of the activity of the enzyme by the extract is therefore, an indication that the production of glucose became normalized in the diabetic animals which thus confers beneficial and anti-hyperglycemic effect on the extract.

In conclusion, the significant reduction of the elevated blood glucose in the untreated, diabetic rats to the values of the distilled water control non-diabetic rats by the aqueous extract of *Cochlospermum planchonii* root in this study indicates anti-hyperglycemic activity of the extract. The anti-diabetic activity of the extract of *Cochlospermum planchonii* root was similar to the reference drug, glibenclamide, with the best activity at 100 mg/kg b. w. of the extract. This study has also revealed that aqueous extract of *Cochlospermum planchonii* root can effectively control some of the metabolic disorders that are associated with diabetes. The present study thus provides scientific evidence to support the acclaimed use of *Cochlospermum planchonii* root in the folk medicine of Nigeria. Work is in progress on isolating and characterizing the anti-diabetic bioactive principle(s) in the extract, the mechanism of action and the toxic implications in rats.



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