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Anti-ulcerogenic Effects and Anti-oxidative Properties of *Ceiba pentandra* Leaves on Alloxan-induced Diabetic Rats

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Authors' contributions

Author CAA designed the study and drafted the manuscript. Authors JCU and PCO carried out the animal studies. Author SCA did the literature searches and statistical analyses of the study. All authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Aims: To evaluate the protective effects of methanol extract of *Ceiba pentandra* leaves on indomethacin and ethanol induced gastric ulcer and on oxidative stress indices of alloxan-induced diabetic rats.
Study Design: Extraction and administration of graded doses of the extract
Place and Duration of Study: Department of Biochemistry, University of Nigeria, Nsukka. Enugu State, Nigeria, between May, 2011 and October, 2011.
Methodology: Extraction of *Ceiba pentandra* leaves was done using methanol. Twenty adult rats divided into five groups of four rats each were used for each of the ulcer studies. Gastric ulceration was induced in the rats by oral administration of indomethacin (50 mg/kg) and 95% ethanol (0.5 ml) thirty minutes after extract treatment, and the animals sacrificed 8 h later. For the diabetes study, thirty (30) albino rats divided into six (6) groups of five (5) rats each were used. Diabetes was induced by i.p injection of alloxan monohydrate (150 mg/kg) in overnight-fasted animals and the animals treated with varied doses (100, 200 and 400 mg/kg) of the extract for two weeks. Serum obtained from the diabetic rats was used for the determination of lipid profile and liver marker enzymes.
Results: Significant and dose dependent ulcer inhibition (70, 82 and 84 %; 19, 53, and 58 % for 100, 200 and 400mg/kg of the extract respectively) was produced in all the extract-treated groups for the ulcer models used. There were significant decreases ($p<0.05$) in fasting blood glucose levels, liver marker enzymes, total cholesterol, low density

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lipoprotein and triacylglycerides in the serum of extract-treated groups compared with that of the diabetes-untreated group.
Conclusion: The findings in this study show that methanol extract of *Ceiba pentandra* leaves possesses potent anti-ulcerogenic and anti-oxidative properties and has potential for use as an herbal remedy for the treatment of gastro-intestinal ulcer and management of diabetes.

Keywords: Ceiba pentandra; diabetes; liver enzymes; lipid profile; gastric ulcer; indomethacin.

1. INTRODUCTION

Plants have not only provided mankind with food, clothing, flavours and fragrances, but have also been an indispensable source of natural products for relief and treatment of different ailments [1]. Several natural products, mostly of plant origin have been shown to possess promising activities that could assist in the prevention and/or amelioration of diseases. Gastric ulcer is an ulceration of the gastrointestinal tract which results from persistent erosions and damage of the stomach wall that might become perforated and develop into peritonitis and massive haemorrhage [2-3]. This occurs as a result of imbalance between some endogenous aggressive factors such as hydrochloric acid, pepsin, reactive oxygen species (ROS) and cyto protective factors, which include the mucus bicarbonate barrier, surface active phospholipids, prostaglandins (PGs), mucosal blood flow, non-enzymatic and enzymatic antioxidants [4-6]. The success of commercially available antiulcer drugs such as H_2- receptor antagonists and proton-pump inhibitors in the treatment of gastric ulcer is usually overshadowed by various side effects. This has led to the search for new anti-ulcerogenic agents from plants with low toxicity and minimal side effects. Diabetes mellitus (DM) is a metabolic disorder of multiple aetiology; characterized by chronic hyperglycemia with alterations in carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both [7-9]. The major types of diabetes are Insulin-Dependent Diabetes Mellitus (IDDM) or type 1 diabetes, Non- Insulin Dependent Diabetes Mellitus (NIDDM) or type 2 diabetes and gestational diabetes [10]. The underlining causes of diabetic complications have been attributed to hyperglycemia which results in oxidative stress, alterations in enzyme activities, protein glycosylation and several structural changes [11-12]. The pathogenesis of diabetes mellitus and the possibility of its management by existing therapeutic agents without any side effects is still a challenge for the medical system and have stimulated great interests in recent years. This has led to increasing demand for natural products with anti-diabetic activity with fewer side effects. *Ceiba pentandra* (L) Gaertner, known as silk cotton tree belongs to the Bombacaceae family [13]. The plant is widely spread around the world and is reputed in the African traditional medicine [14]. Previous studies on various morphological parts of the plant have shown that the plant possesses hypoglycemic effects [15], anti ulcerogenic effects [16-17] and anti-diarrhoea properties [18]. The plant is also used as a diuretic and effective remedy against headache, dizziness, constipation and rheumatism [19-20]. This present study was undertaken to evaluate the protective effect of methanol extract of *Ceiba pentandra* leaves on indomethacin and ethanol induced ulcers and on oxidative stress indices of alloxan-induced diabetic rats.

2. MATERIALS AND METHODS

2.1 Materials

Fresh leaves of *Ceiba pentandra* were collected in the month of May, 2011 from the botanical garden of University of Nigeria, Nsukka. The leaves were identified and authenticated by Mr. Alfred O. Ozioko, a Botanist at the International Centre for Ethnomedicine and Drug Discovery, (InterCEED) Nsukka. A voucher specimen was deposited in the herbarium unit of the Department of Botany, University of Nigeria, Nsukka. The leaves were sun-dried for one week and milled to a coarse powder using a milling machine. The powdered leaves (1100 g) was macerated in methanol (5000 ml) for 48 h and filtered with Whatmann No. 1 filter paper. The filtrate obtained was dried in a rotary evaporator (IKA, Germany) at an optimum temperature of 50^{o}C and the dried crude extract of weight 52.6g that was obtained was stored in a sterile container until use.

2.2 Phytochemical and Proximate Analyses *Ceiba pentandra* Leaves

Qualitative phytochemical analyses of *Ceiba pentandra* leaves were carried out using the method of Harborne [21] and Trease and Evans [22]. The proximate analysis for moisture, ash and carbohydrate contents were determined as described by AOAC [23]. All determinations were done in triplicates and the results were expressed as averages of percent values on dry weight basis.

2.3 Animals

Swiss albino mice (22±10 g) of both sexes and adult male albino rats (150±10 g) obtained from the animal house of the Faculty of Biological Sciences, University of Nigeria, Nsukka were used for the studies. The animals were acclimatized for 7 days under standard environmental conditions, with a 12 h light/dark cycle and maintained on a regular feed (Vital feeds, Nigeria) and water *ad libitum*. The research was conducted in accordance with the ethical rules and recommendations of the University of Nigeria committee on the care and use of laboratory animals and the revised National Institute of Health Guide for Care and Use of Laboratory Animal (Pub No.85-23, revised 1985).

2.4 Acute Toxicity Study

The acute toxicity test of the plant extract was carried out by the method of Lorke [24]. Eighteen Swiss albino mice starved of food for 18 h but allowed access to water were used for the study. They were divided into six groups of three mice each and administered intraperitoneally (i.p.) with the plant extract at varied dose levels (10, 100, 1000, 1600, 2900 and 5000 mg/kg). The animals were then observed for nervousness, dullness, in-coordination and or mortality for 24 h.

2.5 Anti-ulcer Activity

Two experimental models of inducing gastric ulcer were used to assess the ulcer preventive properties of *Ceiba pentandra* leaves. Twenty adult rats randomly divided into five groups of four rats each were used for each model. They were deprived of food for 18 h and treated orally with normal saline and varying doses of methanol extract of *Ceiba pentandra* leaves. Group 1 (normal control) was administered orally with normal saline (5 ml/kg). Groups 2, 3

and 4 received the plant extract at varied dose levels: 100, 200 and 400 mg/kg respectively while group 5 (reference group) received the standard drug treatment of 100 mg/kg of ranitidine (Zantac®).

2.5.1 Effect of *Ceiba pentandra* leaves on indomethacin-induced ulcer

This assay was carried out using the method of Ubaka et al. [25] The animals were deprived of food for 18 h and treated orally with normal saline and varying doses of the plant extract as stated above. Thirty minutes later, 50 mg/kg of indomethacin was administered (p.o) to the rats. After 8 h, each animal in the groups was sacrificed by chloroform anaesthesia and the stomach removed and opened along the greater curvature, rinsed with normal saline and pinned flat on a board. Erosions formed on the glandular portions of the stomach were viewed with a hand lens (x10), counted and the ulcer scored using the following scale:

No ulcer	= 0 point
Superficial ulcer 1-2 mm in length	= 1 point
Elongated erosions 3-4 mm in length	= 2 points
Deep ulcer and perforations	= 3 points

The sum of all the lesions/ulcers in all the animals for each group (total ulcer score) was divided by 10 to obtain the mean ulcer index. The percent ulcer inhibition was calculated relative to control thus:

$$\% \text{ ulcer inhibition (\% U.I)} = \left(1 - {Ut}/{Uc}\right) \times 100$$

Where Ut and Uc represents the ulcer index of the treated and control groups respectively.

2.5.2 Effect of *Ceiba pentandra* leaves on ethanol–induced gastric ulcer

Ulcer was induced according to the method of Shokunbi and Odetola, [26]. Twenty rats were randomly divided into 5 groups of 4 rats each and pre-treated orally with the extract as stated above before ulcer induction. Ulcer lesion was established with 0.5 ml of 95% ethanol (p.o.). After 4 h, the animals were killed by cervical dislocation. The stomachs were removed and opened along the greater curvature and macroscopic examination carried out with a hand lens (x10).

2.6 Induction of Diabetes

Thirty (30) albino rats divided into six (6) groups of five (5) rats each were used for the study. Diabetes was induced by i.p injection of alloxan monohydrate (Sigma St. Louis, USA) (150mg/kg) in overnight-fasted animals. Diabetes was confirmed seven (7) days later in the alloxan-induced animals showing Fasting Blood Glucose, (FBG) level≥200 mg/dl (11.1mmol/L) and was monitored on blood obtained from tail vein puncture using an automated glucose sensor machine – Glucometer (AccuChek Active).

2.6.1 Treatment of animals

Rats in group 1 (normal control) were administered normal saline for 2 wks. Groups 3, 4 and 5 were diabetes-induced rats treated p.o. with 100, 200 and 400 mg/kg of the extract respectively while groups 2 (diabetes-untreated control) and 6 (standard drug control) were diabetes-induced rats administered with normal saline (5 ml/kg) and 5 mg/kg of

glibenclamide (standard anti-diabetic drug) respectively for 2 wks. Blood samples (20 µl) were obtained from the tail tip of fasted rats and the blood glucose level determined using a glucometer (AccuChek Active).

2.6.2 Preparation of serum

At the end of the experiment, blood was collected from the rats by carotid bleeding into centrifuge tubes. The blood samples were centrifuged and the clear serum supernatant was used freshly for the assessment of some biochemical and liver function tests.

2.6.3 Assessment of liver marker enzymes and other biochemical parameters

The activities of alanine amino transferase (ALT) and aspartate amino transferase (AST) were estimated by the Reitman-Frankel colorimetric method [27] using Quimica Clinica Applicada QCA test kits. Alkaline phosphatase (ALP) was measured by the method of Klein et al. [28] (Serum cholesterol and triacylglycerides were determined by the method of Allain et al. [29] and low density lipoprotein (LDL) was by the method of Assmann et al. [30].

2.7 Statistical Analysis of Data

Data obtained were analyzed by one-way ANOVA using SPSS version 17.0 (SPSS Inc. Chicago, IL. USA). All values were expressed as mean±SEM. Differences between means were assessed by Duncan's Multiple Range Test (DMRT). Differences were considered statistically significant when $P \leq 0.05$.

3. RESULTS

3.1 Acute Toxicity Test of the Extract

Result of acute toxicity test of the extract show no mortality in all the groups of mice administered with methanol extract of *C*. *Pentandra* leaves up to the dose of 5000 mg/kg body weight Table 1.

Table 1. Acute toxicity test of the extract

Group	No of mice used	Dose (mg/kg)	Dead (%)
1	3	10	0
2	3	100	0
3	3	1000	0
4	3	1600	0
5	3	2900	0
6	3	5000	0

3.2 Phytochemical Analysis of the Methanol Extract of *Ceiba pentandra* Leaves

Phytochemical analysis of the methanol extract of *C*. *pentandra* leaves showed the presence of bioactive compounds such as flavonoids, tannins glycosides, phenols, alkaloids, saponnins, steroids and terpernoids Table 2.

Table 2. Phytochemical constituents of methanol extract of *Ceiba pentandra* leaves

Constituents	Bioavailability
Alkaloid	++
Flavonoid	+++
Glycosides	+++
Saponnins	++
Tannins	+++
Resins	-
Steroids	++
Terpenoids	++
Acidic compounds	_
Phenols	++

++++ - Abundantly Present
+++ - Present in very high concentration
++ - Present in moderately high concentration
+ - Present in small concentration
- - Absent

3.3 Proximate Analysis of *Ceiba pentandra* Leaves

Proximate analysis of *Ceiba pentandra* leaves for moisture, ash and carbohydrate showed 53, 2.5 and 24% respectively while that of fats and protein showed 12 and 8.5% respectively Table 3.

Table 3. Proximate analysis of *Ceiba pentandra* leaves

Constituents	Quantity (%)
Ash	2.5 ± 0.08
Moisture	53 ± 0.16
Fats	12 ± 0.10
Protein	8.5 ± 0.05
Carbohydrate	24 ± 0.08

3.4 Indomethac in Induced Ulcer

Indomethacin produced ulcers in all the rats of the groups. Ulcers produced in this model were seen as large black sores (Fig. 1a). Potent and dose dependent ulcer inhibition was observed in all the groups treated with *Ceiba pentandra* leaf extract (Fig. 1b). This was also evidenced by the significantly ($P \leq 0.01$) reduced ulcer indices of the groups, which at 200 (0.45±0.02) and 400mg/kg (0.40±0.01) were comparable to that obtained for ranitidine (0.42 ±0.20), the standard anti-ulcer drug used. The percent ulcer inhibitions exerted by the extracts were 70, 82 and 84 % for 100, 200 and 400mg/kg of the extract respectively Table 4.

Fig. 1a. Black ulcer sores induced by indomethacin (control group)

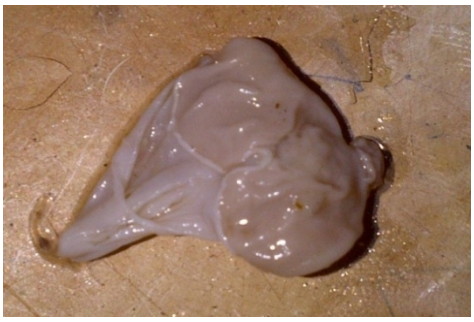

Fig. 1b. Reduced ulcer sores (400mg/kg extract)

Table 4. Effect of *Ceiba pentandra* leaves on indomethacin-induced ulcer in rats

Treatment	Dose (mg/kg)	No of rats	Mean Ulcer index	% ulcer inhibition
Normal saline	5 ml/kg	4	2.50 ± 0. 52	-
Extract	100	4	0.75 ± 0.02*	70
	200	4	0.45 ± 0.02*	82
	400	4	0.40 ± 0.01*	84
Ranitidine	100	4	0.42 ± 0.20*	83

*Values shown are mean ± SEM (n = 4). Level of significance * = P < 0.05*

3.5 Ethanol-induced Ulcer

Ethanol produced gastric ulceration in all the animals in the groups. Ulcers produced in this model were seen as reddish sores on the gastric epithelial walls (Fig. 2a). Treatment with the extract reduced ulcer formation in the gastric mucosa of the rats (Fig. 2b). There was significant ($P \leq 0.05$) reduction in the ulcer index of the groups treated with 200 (1.33±0.057) and 400mg/kg (1.20±0.087) of the extract when compared with that of the control group (2.86±0.430). The percent (%) ulcer inhibitions exerted by the extracts were 19, 53, and 58 % for the 100, 200 and 400mg/kg respectively Table 5.

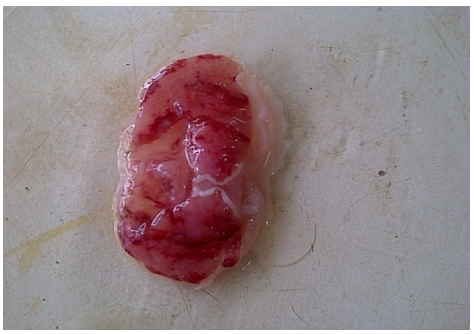

Fig. 2a. Reddish ulcer sores on the gastric walls induced by aspirin (Control group)

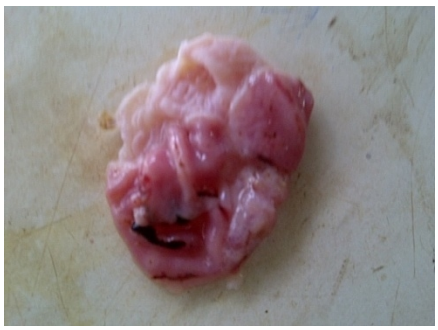

Fig. 2b. Reduced ulcerative sores on the gastric walls of rats (100mg/kg extract)

Table 5. Effect of *Ceiba pentandra* stem bark extract on ethanol-induced ulcer in rats

Treatment	Dose (mg/kg)	No of rats	Mean Ulcer index	% ulcer inhibition
Normal saline	5ml/kg	4	2.86 ± 0.430	-
Extract	100	4	2.33 ± 0.386	19
	200	4	1.33 ± 0.057*	53
	400	4	1.20 ± 0.087*	58
Ranitidine	100	4	1.23 ± 0.082*	57

*Values shown are mean ± SEM (n = 4). Level of significance *= P < 0.05*

3.6 Effect of *Ceiba pentandra* Leaves on Blood Glucose and Oxidative Stress Markers in Alloxan-induced Diabetic Rats

Data in Table 6 show that the diabetes-induced rats had significantly increased (P<0.01) levels of blood glucose before extract administration when compared to that of the non-diabetic (normal) control rats. Treatment of the animals with methanol extract of *Ceiba pentandra* leaves produced significant dose-dependent decreases (P<0.05) in the glucose level when compared with the diabetes-untreated rats. The reduced glucose levels obtained with extract treatment was comparable to that obtained with the treatment with glibenclamide. Result in Table 7 show significantly increased (P<0.01) activities of the liver enzymes (ALP, ALT, AST) in the diabetes-untreated rats when compared to that of the non-diabetic (normal) control rats. Treatment of the animals with 200 and 400 mg/kg of the methanol extract of *Ceiba pentandra* leaves produced significant dose-dependent decreases (P<0.05) in the liver enzymes with values comparable to those of glibenclamide-treated and normal control groups. Serum levels of cholesterol, TAG and LDL were significantly increased (P<0.05) while HDL significantly decreased (P<0.01) in the diabetes-untreated rats when compared to the normal rats. Treatment with the extract significantly reduced (P<0.05) the cholesterol, TAG and LDL levels and significantly increased (P<0.05) HDL of all the extract-treated groups with values comparable to those of glibenclamide treated and normal control groups.

Table 6. Blood glucose of alloxan induced-diabetic rats before and after treatment with methanol extract of *Ceiba pentandra* leaves and glibenclamide

Treatment groups Parameters	Normal control	Diabetes-untreated	Diabetes + 100mg/kg	Diabetes + 200mg/kg	Diabetes + 400mg/kg	Diabetes + glibenclamide
Glucose conc. (mg/dl) before extract administration	134 ± 8.58 [a]	168 ± 8.02 [b]	169 ± 10.57 [b]	170 ± 6.87 [b]	167 ± 12.32 [b]	171 ± 9.89 [b]
Glucose conc. (mg/dl) after 14 days extract administration	132 ± 12.24 [a]	166 ± 9.54 [b]	136 ± 8.51 [a]	133 ± 10.05 [a]	126 ± 6.68 [a]	129 ± 8.68 [a]

Means with different lower case superscripts ([a, b, c]) across the row i.e. between groups are significantly different at P<0.05

Table 7. Effect of methanol extract of *Ceiba pentandra* leaves on oxidative stress markers in alloxan induced-diabetic rats

Treatment groups Parameters	Normal control	Diabetes-untreated	Diabetes + 100mg/kg	Diabetes + 200mg/kg	Diabetes + 400mg/kg	Diabetes + glibenclamide
Alkaline phosphatase (U/L)	60 ± 8.48 [a]	112 ± 12.5 [b]	93 ± 4.24 [b]	56 ± 14.14 [a]	44.5 ± 3.54 [a]	57 ± 8.48 [a]
Alanine amino transferase (U/L)	33 ± 4.3 [a]	78 ± 2.83 [c]	81 ± 7.07 [c]	45.5 ± 4.95 [a, b]	45.5 ± 1.71 [a]	55.5 ± 1.96 [b]
Aspartate amino transferase (U/L)	52.5 ± 9.19 [a]	71 ± 5.66 [b]	54 ± 2.12 [a]	45 ± 3.4 [a]	44.5 ± 6.36 [a]	46 ± 4.24 [a]
Total cholesterol (mg/dl)	24.5 ± 6.4 [a]	62.5 ± 7.8 [b]	34 ± 1.4 [a]	30.5 ± 6.4 [a]	29 ± 8.5 [a]	31.5 ± 7.8 [a]
Triacylglyceride (mg/dl)	7.5 ± 2.1 [a]	40 ± 7.1 [c]	22 ± 2.8 [b]	17 ± 0.7 [a, b]	13.5 ± 0.7 [a, b]	25.5 ± 2.1 [b]
Low Density Lipoprotein (mg/dl)	19.5 ± 4.9 [a]	37 ± 1.4 [b]	22 ± 0.3 [a]	19 ± 4.2 [a]	21 ± 0.7 [a]	25.5 ± 4.9 [a]
High Density Lipoprotein (mg/dl)	40.0 ± 1.4 [a]	2.5 ± 0.3 [c]	7.5 ± 2.8 [c]	15 ± 5.6 [b]	33 ± 0.7 [a]	16.5 ± 1.4 [b]

Means with different lower case superscripts ([a, b, c]) across the row i.e. between groups are significantly different at P<0.05

4. DISCUSSION

Natural products derived from plant sources have always been the main sources of new drugs for the treatment of various diseases [31]. *Ceiba pentandra*, a multi- purpose and herbaceous plant native to Mexico, Central America and tropical West Africa has been reported to have diverse medicinal and pharmacological uses. In this work, an attempt was made to determine the effect of the methanol extract of *Ceiba pentandra* leaves on indomethacin and ethanol-induced ulcers and on oxidative stress markers of alloxan-induced diabetic rats. Result of the acute toxicity study showed that the plant leaves were non-toxic and relatively safe to the experimental animals. Pretreatment of rats with methanol extracts of *Ceiba pentandra* leaves before induction with indomethacin/ethanol significantly decreased the ulceration in the gastric linings of the animals when compared to the control group. Indomethacin induces ulcer in rats either by direct mucosal injury which involves the breaking of the mucosal barrier and exposure of the underlying tissue to the corrosive action of acid and pepsin or by a decrease in endogenous gastric prostaglandin production and release through COX-1 and COX- 2 inhibition [3,32]. The naturally occurring prostaglandins are important for the production of gastric bicarbonate and mucous which are the key components of the stomach protective barrier [5]. They inhibit acid secretion, maintain gastric microcirculation and increase mucosal blood flow. Thus, continuous generation of prostaglandins by the mucosa is crucial for the maintenance of mucosal integrity and protection against ulcerogenic and necrotizing agents and its inhibition triggers damage to the mucosal lining [3,33]. Pre-treatment with *Ceiba pentandra* extract in this study, reduced the indomethacin-induced ulcer in the rats perhaps by the mechanism of increased endogenous prostaglandin synthesis which in turn promoted mucus secretion and enhanced the mucosal barrier against the action of the ulcerogenic agent. Ethanol administration to experimental rats damages the gastrointestinal mucosa by micro-vascular injury leading to increased vascular permeability, gastric mucus depletion and edema formation. It is metabolized in the body to release superoxide anion and hydroperoxyl free radicals which are involved in the mechanism of acute and chronic ulceration of the gastric mucosa [34-35]. The inhibition of the ethanol-induced ulcer by the *Ceiba pentandra* leaves could be due to the plant's antioxidant property and ability to chelate free radicals and reactive oxygen species, thus reducing oxidative damage to the mucosal membrane and epithelial cells. This activity could be linked to the presence of some antioxidant constituents; flavonoids, saponnins and tannins, in the plant. These substances characterized by their polyphenolic nature, have been reported to have cytoprotective and antiulcer activities in other plants [36-37]. Ulcer preventive effect of the plant could also be attributed to the presence of alkaloids in the plant leaves. Reports have shown that plant derived alkaloids have significant activity in acute and chronic gastric ulcers in rats. These alkaloids increase free mucus and prostaglandin production and show a reduction in hemorrhages and blood cell infiltration in the gastric mucosa [38-39]. The report of ulcer reduction by *Ceiba pentandra* leaves in this study corroborates earlier reports of the anti-ulcerogenic activity of *Ceiba pentandra* against indomethacin-induced ulcer [16-17].

In the diabetes study, there were significant elevations in the activities of the liver enzymes (ALP, ALT and AST) and lipid profiles (cholesterol, TAG and LDL) in the diabetes-untreated rats when compared to those of the non-diabetic (normal) control rats. Mild chronic elevations of transaminases are frequently found in type 2 diabetic patients and often reflect underlying insulin resistance. Potential explanations for elevated transaminases in insulin-resistant states include oxidant stress from reactive lipid peroxidation, peroxisomal beta-oxidation, and recruited inflammatory cells [11,40]. The insulin-resistant state is also characterized by an increase in proinflammatory cytokines such as tumor necrosis factor-α

(TNF-α), which may also contribute to hepatocellular injury. The liver helps maintain normal blood glucose concentration in the fasting and postprandial states. Loss of insulin effect on the liver leads to glycogenolysis and an increase in hepatic glucose production [41-42]. In contrast, anti-diabetic agents decrease the aminotransferase levels as tighter blood glucose levels are achieved. Treatment of the animals with 200 and 400 mg/kg of the methanol extract of *Ceiba pentandra* leaves produced significant dose-dependent decreases ($P<0.05$) in the liver enzymes with values comparable to those of glibenclamide-treated and normal control groups. Diabetes mellitus is also characterized by chronic hyperglycaemia and lipoprotein abnormalities. This is as a result of altered intermediary regulation of major food substrates. Deficiency of a polypeptide hormone, insulin, which plays a role in the metabolism of carbohydrate, is a predisposing factor leading to hypercholesterolaemia and hypertriglyceridaemia [43]. Abnormalities of triglyceride storage and lipolysis in insulin-sensitive tissue such as the liver are also an early manifestation of diabetes characterized by insulin resistance [44]. Insulin deficiency or resistance could be responsible for dyslipidaemia because it increases fatty acid as well as triglyceride synthesis in adipose tissue and liver [45]. In severe and uncontrolled diabetes, the resultant increases in LDL, triglycerides and total cholesterol are associated with increased morbidity and mortality from coronary artery disease [46]. Treatment with methanol extract of *Ceiba pentandra* leaves in this study significantly decreased the elevated levels of blood glucose, serum cholesterol, triacylglycerides, and LDL and increased the level of HDL in the alloxan-induced diabetic rats. Earlier studies have reported the hypoglycaemic activity of *Ceiba pentandra* stem bark and leaves on alloxan and Streptozotocin -induced diabetic rats [15,47]. Effective control of blood glucose is a key step in preventing diabetic complications and improving the quality of life in both Type I and Type II diabetic patients [48-49]. Reports have shown that most plants used in the treatment and management of diabetes possess both hypoglycaemic and anti-oxidative properties [50-52]. Numerous mechanism of action have been proposed for these plant extracts. Some hypotheses relate their effect to the activity of pancreatic β cells (synthesis, release, cell regeneration) [53] the increase in the protective/inhibitory effect against insulinase and increase of insulin sensitivity or the insulin-like activity of the plant extracts [54], inhibition of renal glucose reabsorption [53] and inhibition of endogenous glucose production [55]. These actions may be responsible for the reduction or abolition of the diabetic complications. Reduction of blood glucose by *Ceiba pentandra* leaves in this study could perhaps be related to stimulation of beta cells of Islet of Langerhans to enhance insulin secretion or increase of the body's sensitivity for insulin. Significant elevation of HDL in the *Ceiba pentandra* extract treated groups suggests that the plant has protective effect on the heart. The phytochemical results of *Ceiba pentandra* leaves showed the presence of flavonoids, glycosides, alkaloids, saponnins and tannins. Some of these plant components, particularly flavonoids and tannins, have been reported to have hypoglycaemic activity [56]. It is therefore speculated that the hypoglycaemic effect exhibited by methanol extract of *Ceiba pentandra* leaves in the present study may partly be due to some of these bioactive components. The result from this study showed that the methanol extract of *Ceiba pentandra* leaves decreased the activities of the liver enzymes, fasting blood glucose and lipid profile levels in diabetic rats and thus, could be effective in the management of diabetes and its complications.

5. CONCLUSION

The results shown in this work suggest that the methanol extract of *Ceiba pentandra* leaves has potential for use in the treatment of stomach ulcers and management of diabetes mellitus and its associated complications.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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