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Antidiabetic property of *Chrysophyllum albidum* extract in Streptozotocin- induced diabetic rats

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ABSTRACT

This study is aimed at evaluating the anti-diabetes property of *Chrysophyllum albidum* on Streptozotocin-induced *Diabetic mellitus* in rats. *Diabetic mellitus* induced intraperitoneally with streptozotocin (STZ) using standard dose of 40 mg/kg after fasted for 12 hours as protocol implies. Blood glucose levels were determined using Accu-check glucometer before and during treatment of 10 and 30 mg/kg *C. albidum* when compared with Metformin and diabetic control groups. Animals whose blood glucose level was above 200 mg/dL were considered diabetic. After 28 days of treatment, blood and tissue samples were isolated for fasting blood sugar, haematological, bioassay and histopathological study using standard procedures. Result revealed a significant decrease ($p < 0.05$) in the treated groups specifically at 30 mg/kg body *C. albidum* ethanol extract when compared with metformin and diabetic control group from weeks 0 to 5. The haematological result showed slight significant difference ($p > 0.05$) now some parameters across treated groups excluding 10 mg/kg of *C. albidum* of MCH that showed a significant difference when compared with metformin and control group. Result showed a significant increase in the level of CAT, SOD, MDA and GST across the treated groups (10 and 30 mg/kg *C. albidum*) ethanol extract when compared with standard (10 mg/kg metformin) and diabetic control. The histopathological alteration observed in this study include; severe interlobular oedema and fatty droplets in the interlobular ducts and connective tissues. These alterations were prominent in the diabetic control group while 30 mg/kg of *C. albidum* showed prominent reduction in damage done by an anti-diabetonic agent (streptozotocin). This study showed that *C. albidum* is effective in the management of diabetes, which concord with its ethnomedicinal reports.

Keywords: *Chrysophyllum albidum*, Diabetes mellitus, Streptozotocin, Metformin.

INTRODUCTION

Diabetes mellitus comprises of heterogeneous diseases presented with the occurrence of glucose intolerance and hyperglycaemia owing to deficiency in insulin, malfunctioning in insulin potential, or the two defects [1]. Such problems occur due to the imbalances of the regulatory structures for metabolic fuels utilization and storage such as anabolism and catabolism of lipids, proteins and carbohydrates derived from insulin secretory defect, insulin potentials, or the two defects [2]. Reduction in glucose narrowness, *Diabetes mellitus* and mainly impairment of glucose tolerance are being originated in virtually every populace in the globe with epidemiological proof recommended without active deterrence and regulatory programmes, diabetes drives apparently continue with global increase [3]. In 2010, approximately 285 million individuals in age bracket 20 to 79 were visualized to acquire diabetes globally of 70 % in developing countries. The evaluated values are projected to incline to approximately 438 million by the year 2030. More so, the number of individuals having compromised glucose tolerance (IGT) by the year 2030, is estimated to escalate to about 472 million whiles, 8.4 % of adult in the population will be prone to this disorder [1]. Incapacitating *Diabetes mellitus* effects on several organ associated problems, advanced metabolic problems include nephropathy, neuropathy and/or retinopathy [4]. *Diabetics' mellitus* displayed several risks of peripheral vascular, cerebrovascular and cardiovascular diseases. Numerous pathogenetic procedures are convoluted in the progress of diabetes, such as pancreatic damage of β -cells progressing to reduced insulin sensitivity action [2].

Medicinal plants are rich with therapeutic properties, yet untapped prospective sources as anti-diabetic agents, though utilized since times of antiquity for the management of Diabetes mellitus. Several synthetic agents were obtained directly or incidentally from plant source. Medicinal plants are made up of varieties of natural occurring antioxidants potential employed in the management and treatment of diverse diseases globally [1]. Recently, due to beneficial effects of antioxidants, particularly natural antioxidants, in the treatment and prevention of diseases, there has been a considerable interest in finding natural antioxidants

from plant sources. The studies on medicinal plants show that most of them possess significant antioxidant activity.

Chrysophyllum albidum (Sapotaceae) is a popular forest tree, widely distributed in the low and rain forest zones and frequently found in villages in Nigeria and across the whole of Africa [5]. The roots, barks and leaves of *Chrysophyllum albidum* have been employed in folk medicine for the treatment of diseases. The bark is used for the treatment of yellow fever and malaria, while the leaf is used as an emollient for the treatment of skin eruption, stomach ache and diarrhea [6]. *Chrysophyllum albidum* occurs on ferallitic soils. It is a lowland rain forest tree species which can reach 25 to 37 m height at maturity with a girth varying from 1.5 to 2 m. The seed-coats are hard, bony, shiny, and dark brown, and when broken reveals white-colored cotyledons. The fruit is seasonal, usually from the months of December to March. *C. albidum* is highly used and appreciated in Southern Benin, where it is called Azongogwe or Azonbobwe in local language "Fon, Goun" and Azonvivo, Azonvovwe or Azonbebi in local language "Aïzo". It is called Agbalumo among the Yoruba in Western Nigeria while it is called Udara in the Eastern and Southern part of Nigeria [6].

MATERIALS AND METHODS

Plant material

Chrysophyllum albidum stem bark was obtained from Adekunle Ajasin University, Akungba-Akoko, Ondo State. It was identified and authenticated by Dr. Obembein the Department of Plant Science and Biotechnology, Adekunle Ajasin University, Akungba Akoko.

Preparation of extract

The procedure described by [7] was adopted. The stem bark was shade dried at room temperature for three weeks. Briefly, the shade dried stem bark was crushed with a grinder into fine powder. Five hundred grams (500g) of the ground stem-bark were extracted with 1500 ml of ethanol. The extract was evaporated via rotatory evaporator with the temperature at 40°C presented with 50 g yield of the sample. It was kept in a clean and dry McCartney bottle and was stored in a desiccator to maintain dryness and to prevent from moisture until needed use.

Experimental Animals

Twenty (20) healthy and active male and female wistar albino rats weighing between 40 and 100 g were obtained from Ikare-Akoko, Ondo State, Nigeria; and housed in animal house of the Centre for Bio-computing and Drug Development, Adekunle Ajasin University, Akungba-Akoko, Ondo State, Nigeria. They were acclimatized for 3 weeks before the commencement of the experiment and were kept in a cage under controlled environmental conditions of temperature, relative humidity with 12 hours light/dark cycle. The animals were fed *ad libitum* using standard pelleted diet and water and were handled in compliance with National Institute of Health guidance [8]. Animals were divided into four groups based on their body weight which was used to calculate the amount of the treatment administered.

Induction of the experimental animals

Streptozotocin (STZ) was prepared based on the animals' average weight. It was dissolved in 0.1M citrate buffer (pH 4.5) and administered across the rats intraperitoneally at a dose of 30 mg/kg after twelve (12 h) hours fast to make them more susceptible to developing diabetes. The animals were given feed and sucrose water after induction for forty eight (48 h) hours, fasting blood glucose level of the animals were determined after twelve (12 h) hours of fasting using glucometer and compatible test strips, with blood obtained from the rats tail tip. Rat with a blood glucose level rise to ≥ 200 mg/dl were confirmed diabetic.

Experimental design and treatment administration

Twenty (20) Wistar rats were randomly selected into five groups (= 4). Group one animals, the basal control, were given feed and water only with no treatment; group two (the diabetic control), was given feed and water only without treatment, group three was treated with 10 mg/kg metformin, group four was treated with *C. albidum* ethanol extract (10 mg/kg) and group five was treated with *C. albidum* ethanol extract (30mg/kg). Treatment was administered orally using oral cannula and was done once daily for a period of 28days, blood glucose level was monitored every 5th day after twelve (12 h) hours fast using glucometer and test strips. The animals were also weighed using weighing balance. The experiment lasted for 28 days. Animals were subsequently anaesthetized in mild di-ethyl-ether and blood and tissue samples were isolated for various hematological parameters, bioassay such as; superoxide dismutase (SOD), lipid peroxidation [malondialdehyde determination (MOD)], glutathione-s-transferase (GST), catalase (CAT), total protein, assays and histopathological study.

Blood sample collection

The rats in their respective groups were anaesthetized in mild di-ethyl-ether proceeding to dissection. Blood samples were collected via cardiac puncture in EDTA bottle. Plasma samples were gotten after centrifuging the whole blood at 10,000 revolutions per minute for 15 minutes into clean eppendoff tubes. The serum was then stored at 4°C in the freezer and placed on ice when in use.

Haematological Assay

Hematological assay was done on Packed Cell Volume (PCV), Red Blood Cell count (RBC), Haemoglobin (Hb), Lymphocytes (LYM), Platelets (PLT), and Mean Corpuscular Haemoglobin Concentration (MCHC), Granulocytes (GRAN), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Volume (MCV) and White Blood Cell count (WBC).

Analysis of enzyme assays parameters

Commercial test kits obtained from the biochemistry laboratory, Adekunle Ajasin University Akungba Akoko, Ondo state, was used in the biochemical parameter's measurement. Standard procedures were used to evaluate superoxide dismutase (SOD) [9], lipid peroxidation, malondialdehyde determination (MDA), catalase (CAT), glutathione-s-transferase determination (GST), and Total protein [10].

Tissue collection and processing

At the end of the 28th days of treatment, animals were subjected to fasting overnight and then sacrificed; tissues of interest (pancreas) were excised from all the subjects (animals), washed in normal saline solution before preserved in sample bottles containing formalin for further analysis.

Histological Analysis

Samples preserved were subjected to routine histology using haematoxylin and eosin staining method. Tissues were dehydrated in ethyl alcohol sequence of ascending concentrations; cleared with xylene and embedded in paraffin. Then the sagittal sections (5 μ thickness) were cut using a rotary microtome and mounted on glass slides. Sections were deparaffinized in xylene, hydrated in ethanol and stained with haematoxylin and alcoholic eosin (H&E) for general histological evaluation. Photomicrographs of control groups were compared with treatments groups under the guidance of a pathologist.

Statistical Analysis

Values were analyzed as mean \pm S.E.M, ANNOVA and Dunette's Test to show the level of significant across the groups using graph pad prism 6. Values with $p < 0.05$ were considered as significant.

RESULTS

Table 1: Blood Glucose of diabetic rats treated with *Chrysophyllum albidum* stem-bark

Weeks	Treatments				
	Normal Control (10 mg/kg b.w)	Diabetic Control (10 mg/kg b.w)	Metformin (30 mg/kg b.w)	<i>C. albidum</i>	<i>C. albidum</i>
0	61.33±2.19 ^a	342.33±1.20 ^b	342.00±1.53 ^b	338.98±0.45 ^b	343.67±0.88 ^b
1	64.33±6.39 ^a	347.00±1.53 ^c	319.00±1.15 ^b	344.78±1.78 ^c	341.00±0.58 ^c
2	75.33±2.85 ^a	424.33±7.54 ^c	300.33±4.41 ^b	389.56±5.89 ^c	290.33±8.11 ^b
3	75.33±2.85 ^a	466.67±10.40 ^d	261.67±10.65 ^b	365.34±10.56 ^c	254.00±8.74 ^b
4	67.33±1.76 ^a	494.00±3.51 ^d	213.33±9.49 ^b	332.87±4.56 ^c	209.67±5.55 ^b
5	74.67±4.26 ^a	537.33±25.09 ^d	166.67±6.12 ^b	308.34±3.78 ^c	145.00±5.03 ^b

Mean values with the same superscript alphabets in the rows are not significantly different at (P>0.05)

Table 2: Haematological parameters of diabetic rats treated with *Chrysophyllum albidum* stem-bark

Parameters	Treatments				
	Normal Control	Diabetic Control (30 mg/kg)	Metformin (10 mg/kg)	<i>C. albidum</i> (10 mg/kg)	<i>C. albidum</i> (30 mg/kg)
PCV (%)	42.50±0.31 ^b	34.58±7.81 ^a	40.00±2.81 ^b	35.28±5.67 ^a	36.42±6.39 ^a
WBC	8.80±1.19 ^a	24.86±4.47 ^b	7.82±0.54 ^a	14.56±4.78 ^a	12.66±4.65 ^a
RBC	7.49±0.18 ^b	4.89±1.78 ^a	5.82±0.56 ^a	5.23±0.34 ^a	5.89±1.34 ^a
Hb (g/dl)	14.85±0.16 ^b	9.50±3.05 ^a	12.03±0.91 ^b	10.35±2.89 ^a	11.76±2.34 ^b
LYM (%)	64.56±1.19 ^a	69.65±8.28 ^a	60.75±0.86 ^a	61.56±7.67 ^a	53.87±10.63 ^a
GRAN (%)	24.59±0.75 ^a	28.86±7.18 ^a	28.62±1.14 ^a	28.56±6.89 ^a	29.72±8.23 ^a
PLT	406.63±6.68 ^a	596.33±23.09 ^b	403.32±17.90 ^a	378.67±9.45 ^a	332.30±8.35 ^a
MCV (fl)	56.13±0.88 ^a	58.19±3.71 ^a	64.02±0.77 ^b	60.67±3.98 ^a	64.46±4.70 ^b
MCH	19.62±0.41 ^b	17.53±0.38 ^a	20.54±0.59 ^b	18.56±0.45 ^a	21.03±0.79 ^b
MCHC	34.89±0.21 ^a	30.63±2.11 ^a	31.75±0.83 ^a	30.97±1.19 ^a	31.43±1.20 ^a

Mean values with the same superscript alphabets in the rows are not significantly different at (P>0.05)

Table 3: Enzymes activities in diabetic rats treated with *Chrysophyllum albidum* stem-bark ethanol extract

Parameters	Treatments				
	Normal Control	Diabetic Control (10 mg/kg b.w)	Metformin (10 mg/kg b.w)	<i>C. albidum</i> (10 mg/kg b.w)	<i>C. Albidum</i> (30 mg/kg b.w)
CAT	19.14±2.38 ^{ab}	8.67±5.34 ^a	15.18±1.10 ^{ab}	16.13±3.46 ^{ab}	22.39±0.97 ^b
SOD	0.40±0.04 ^{ab}	0.28±0.04 ^a	0.51±0.02 ^b	0.40±0.04 ^{ab}	0.52±1.20 ^b
MDA	0.22±0.04 ^c	0.09±0.00 ^a	0.09±0.00 ^a	0.11±0.00 ^{ab}	0.17±0.01 ^{bc}
GST	20.83±10.42 ^{ab}	10.42±0.00 ^a	34.11±1.23 ^c	21.44±1.46 ^{ab}	41.67±41.67 ^c

Mean values with the same superscript alphabets in the rows are not significantly different at (P>0.05).

KEY; CAT = Catalase, SOD = Superoxide dismutase, MDA = Malondialdehyde and GST = glutathione-S-transferase, b.w = Body weight.

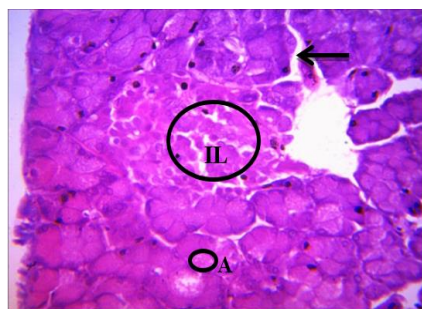


Plate 1: Normal control: Photomicrograph of pancreas section of normal control group (IL = Islet of langerhans, ID = Interlobular duct, A = Acinar).

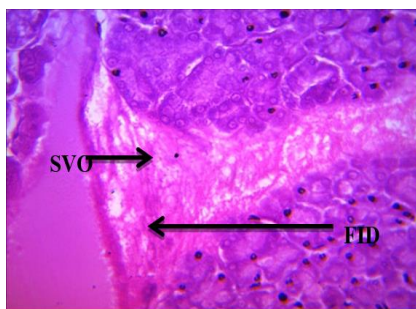


Plate 2: Diabetic control Photomicrograph of pancreas section of diabetic group (SVO = Severe interlobular oedema, FID = Fatty droplets in the interlobular duct).

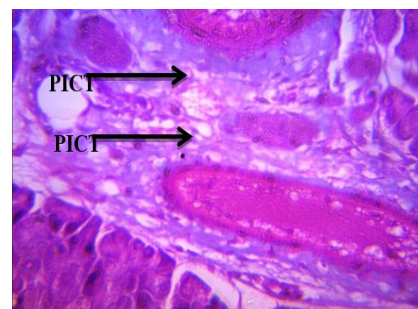


Plate 3: 10 mg/kg Metformin: Photomicrograph of pancreas section of 10 mg/kg body weight of Metformin group (PICT = Prominent interlobular connective tissue).

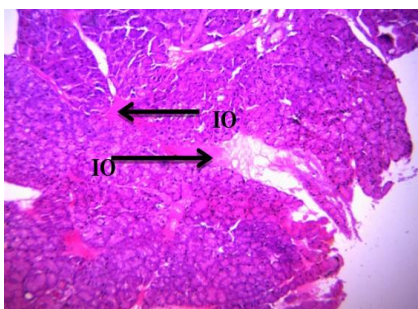


Plate 4: 10 mg/kg *C. albidum*: Photomicrograph of pancreas section of 10 mg/kg body weight of *C. albidum* (IO = Interlobular Oedema).

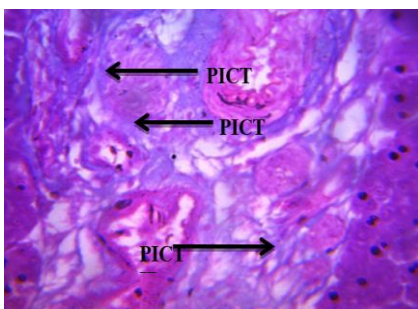


Plate 5: 30 mg/kg *C. albidum*: Photomicrograph of pancreas section of 30 mg/kg body weight of *C. albidum* (PICT = Prominent interlobular connective tissue).

DISCUSSION

Diabetes is being a chronic disorder and is characterized by an increase in blood glucose level and atypical carbohydrates, fat and protein metabolism linked with virtual or total deficiency of insulin discharge having numerous grades of insulin resistivity, follow by polydipsia, polyuria and [4]. This could be as a result of inadequate endogenous insulin synthesis in pancreatic beta cells (type-1 diabetes); or compromised insulin discharge (type-2 diabetes) [11].

In this study, an attempt was made in assessing the anti-diabetic property of the stem-bark of ethanol extract of *Chrysophyllum albidum* in streptozotocin induced high sugar level rats. The result of this study showed that the groups treated with 10 and 30 mg/kg body weight of *C. albidum* gave dose dependent increase. There were statistical differences ($p < 0.05$) across treated groups compared with normal control, 10 mg/kg metformin and diabetic control. The result observed in this study suggested *C. albidum* to possess hypoglycaemic property, thus stimulating cellular factors involved in the lysing of. *C. albidum* showed a prominent reduction in the blood glucose levels when compared with the untreated group (diabetic control). This possibly could be as a result of metformin involvement in the reduction of hepatic glucose synthesis rather than stimulating glucose breakdown [12]. The body does not immediately metabolize surplus glucose but rather altered to glycogen either stored in hepatic cells or the muscle pending when it is required for metabolism to produce energy. The reasons for this development are to avert hyperglycemic complications. Henceforth, the promotion of glycogen creation is a viable approach in avoiding or regulating diabetes [4]. Dose dependent increase observed in 10 and 30 mg/kg of *C. albidum* when compared with standard drug and diabetic control indicated the anti-diabetic effect of the plant extract. The effects are accomplished by exciting insulin secretion in pancreatic β -cells, blocking glucose intake, triggering glycogenesis in hepatic or could be owe to rise in glucose applications in the body [13]. Results showed is in line with previous work findings [14] which reported hypolipidemic and hypoglycemic properties of *C. albidum* seed cotyledon of ethanol extract in alloxan induced hyperglycemia, [15] hence it exhibited anti-hyperglycemic property in methanol seed cotyledon extract of *C. albidum* in in alloxan-induced high sugar level [16, 17] also it showed the antioxidant and anti-diabetic effect of leaf and seed extracts. [17] It was observed that 314.00 (diabetic control), 129.50

(positive control), 119.00 (*C. albidum*) and 109.00 (normal control). [18] Also showed the anti-diabetic and anti-oxidant property of *Vernonia amygdalinain* methanol leaves extract on alloxan-induced hyperglycemia in rats. [18] Further reported 122.30 (normal control), 482.50 (diabetic control), 442.00 (positive control) and 176 (extract) compared to 74.67 (basal control), 537.33 (diabetic control), 166.67 (standard drug) and 145.00 (30 mg/kg *C. albidum*) and 308.35 (10 mg/kg *C. albidum*) observed in this study.

The association involving chronic disorders and anaemia defect is properly characterized (Weiss and Goodnough, 2005). The prevalence of anaemia associated with *Diabetes mellitus* showed an increase in non-enzymatic glycosylation in red blood cells membrane, when compared with a report of hyperglycemia [10]. Oxidation involving certain proteins in *Diabetes mellitus* which triggered lipid peroxides increased leading to red blood cells haemolysis. Principal pathological effects of oxidative radical induced lipid peroxidation membrane such as enlarged membrane with inflexibility, decline in cellular distortion, decrease in erythrocyte existence and variability of lipid as reported [19].

The reduction in RBC, Hb, PCV and MCHC following treatment with *C. albidum* extract is an indication of reduced and abnormal erythropoiesis [20]. Administration of *C. albidum* extract to streptozotocin induced diabetic rats appreciably improved the level of MCH and MCHC. This proposes that certain phytoconstituents in the extract stimulated erythropoietin secretion or formation or triggered stem cells in bone marrow linking with MCV and MCH this conformed to earlier report of [21]. Result obtained showed a significant inclined in WBC, GRAN and LYM in diabetic control rats which became reduced in LYM of *C. albidum* extract treatment. This is attributed to the result showed the ability of the extract to restored insulin excitation, improve advanced glycation ends production (AGEs) and decrease oxidative stress (OS) within blood cells, findings from this study is in line with previous report of [22]. But with significant increment in WBC and GRAN, [20] reported that Leucocytes are activated by advanced glycation ends production (AGEs), oxidative stress, angiotensin II and pro-inflammatory cytokines which may be the cause of significant increase in WBC and GRAN. Report suggested that higher platelets count may contribute to vascular events in patient with insulin resistance [23]. However, treatment with *C. albidum* ethanol extract significantly ($p < 0.05$) reduced the platelets count dose dependently. The observation suggested that, the ability of the *C. albidum* ethanol extract to achieve glycemic control and protect against vascular events.

Oxidation is a complication characterized with inclined reactive oxygen species (ROS) recognized as being partially liable for diabetes and its conditions [24]. Oxidative stress genesis is based on diabetic patients also, with experimental high sugar level animals, which could be owing to glucose protein glycation [25]. Also, at higher level of glucose damage or depreciated natural occurring antioxidant protective system hence support oxidation and ultimately diabetes [26]. Hence, the repairs of antioxidant resistance system avert diabetes and possible complications. Several medicinal plants are known to possess numerous therapeutic properties with negligible adverse effects, a restraint of recent accessible oral drugs [27]. *C. albidum* possesses several medicinal effects, and most prominently, it displayed antioxidant property [28, 29]. Conversely, effort had been made in the assessment of antioxidant enzymes property in streptozotocin induced hyperglycemia treated with *C. albidum*.

The result of catalase (CAT) in this study was significantly higher in the groups treated with *C. albidum* when compared with the diabetic group but there was no significant difference ($p > 0.05$) in the treatments when compared with other groups including the diabetic control. Endogenous catalase mediates hydrogen peroxide (H_2O_2) decomposition to form water and oxygen [30]. Incline in catalase property proposed an *in vivo* antioxidant potential. An increased catalase effect of the treated groups (*C. albidum*) substantiates the capability of plant extract as free radicals scavenge via supportive catalase effect. Complications arises from oxidative stress associated with cell membranes, typically dented due to the cause of lipid

peroxidation by reactive oxygen species (ROS) and by-products such as thiobarbituric acid to produce reactive substances^[31]. Nevertheless, since ROS species exhibited reduced life span, their direct measurements are usually observed. Instead, by-products including malondialdehyde (MDA) can be considered as lipid peroxidation biomarkers^[32].

Malondialdehyde concentration in this study significantly increase across the groups treated with *C. albidum* stem-bark extract when compared with diabetic group therefore proposing no defensive mechanisms of the extract in averting lipid decomposition.^[17] Also reported a significant increase in MDA level of antioxidant and anti-diabetic activities of the seed and leaf extracts of *C. albidum*. In contrary to this finding,^[18] reported a decrease in MDA level of methanol leaf extract of *Vernonia amygdalina* in alloxan-induced diabetes wistar rats.^[33] Reported a significant reduction in MDA level of anti-hyperglycemic, anti-diabetic, and antioxidant effects of *garcinia pedunculata* in rats.^[34] Also reported a decrease in MDA level in effect of ethanol leaf extract of *Senna fistula* on some haematological parameters, lipid profile and oxidative stress in alloxan-induced diabetic rats. The excessive levels of MDA are attributed to increased production of ROS. Excessive lipid peroxidation causes lipid degradation that impairs cell membrane function, resulting in tissue damage and leading to many pathological conditions and cytotoxicity in the body^[35, 36].

The antioxidant enzymatic activities; Superoxide dismutase (SOD) and glutathione-S-transferase (GST) were significantly higher in the groups treated with *C. albidum* compared with diabetic group. The observable reduction in SOD property in diabetic group could summount to H₂O₂ or glycation inactivation of enzyme, which has been reported to occur in diabetes^[37] as a result of depletion owing to excessive use of these enzymes to mop up the hyperglycaemia-induced free radical generation. Also, these enzymes are targets of glycation which can lead to inhibition of their enzymatic activity^[37]. The decreased activity of GST observed in diabetic state may be because of the inactivation caused by reactive oxygen species (ROS).^[39, 40] also made observations similar to the findings of this study.

The increase in the GST and SOD activities in the groups treated with *C. albidum* shows its antioxidant effects. Several investigators exhibited antioxidant property of plant materials majorly as a result of free radicals scavenging property of phenolic constituents include, tannins, phenolic terpenes, flavonoids and polyphenols^[41]. Compounds of plant source such as flavonol and flavonoid are extremely originated in several vegetables or fruits with promising antioxidant potentials^[42]. The antioxidant property is owing to their possible capability to neutralize, quench and absorb radicals^[43]. This scavenging capacity of free radical might be ascribed to conjugated ring formation, redox activities and carboxylic group, previously reported to block lipid peroxidation^[44].

This study evaluates the histopathological effects of *C. albidum* extract in pancreas of wistar rats induced with diabetes. Histopathological alterations showed significant biomarkers in ecological scrutiny which permitted the examination of toxicity to toxicants on specific target organs. Pancreasis is a vital organ capable of digesting carbohydrates, proteins and lipids. It can synthesize many hormones and enzymes. It performs the vital duty of producing hormones most notably insulin to maintain the balance of blood glucose (sugar) and salt in the body. Thus, any alteration in organ functioning may unswervingly influence the existence and presentation of diverse organisms^[45]. The results of the histopathological alterations in the pancreas section (Plate 1) showed normal islet of langerhans, normal interlobular duct and normal acinar in normal control. Severe interlobular oedema (short arrows) and fatty droplets in the interlobular duct (Long arrow) were seen in the diabetic control (Plate 2). Interlobular oedema was also seen in the group treated with 10 mg/kg body weight of *C. albidum* (Plate 4). Prominent interlobar connective tissues were seen in standard drug (Metformin) and 30 mg/kg body weight of *C. albidum* (Plate 3 and 5) respectively. Fatty droplets and severe interlobular oedema observed in

pancreatic section of STZ-induced *Diabetes mellitus* (Diabetic group) in this study has been reported that prolong exposure of isolated islets or insulin secreting cells to its elevated level is associated with inhibition of glucose-stimulated insulin secretion and induction of cell death by apoptosis. Streptozotocin (STZ) a diabetogenic agent has been shown to produce free radicals^[46] and these free radicals trigger the production of counter-regulatory hormones which could cause weight loss^[47]. The alterations seen in the diabetic group may be due to the cytotoxic action of STZ mediated by reactive oxygen species (ROS). Oxidation as earlier stated is a complication characterized with increased ROS, known for its partial dependability for diabetes or further disorders^[25, 48]. The results showed a similar response with previous detected diabetes, glucose toxicity, in oxidative stress^[49, 50].^[49] Further affirmed β -cells are predominantly susceptible to oxidation due to reduced levels of antioxidant enzyme appearance. These are implicated in series of pancreatic β -cell malfunction, in pathological alteration in pancreatic islet β -cells, and in glucose toxicity^[49, 50]. Groups treated with *C. albidum* and standard drug (Metformin) showed improvement in the histopathological changes when compared with the diabetic group. Fatty droplets and severe interlobular oedema was not seen but prominent interlobar connective tissue was observed. Interlobar connective tissues observed in this study corroborate the findings of^[51].

CONCLUSION

In conclusion, anti-diabetic activity of *Chrysophyllum albidum* showed a prominent reduction in the blood glucose levels, antioxidant parameters with normal histopathological structure. However, it will be of interest to further investigate the active compounds present in the plant and the mechanism of actions.

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