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Acute Toxicity Study and Serum Biochemical Investigation of Leaf Extracts of *Chrysophyllum albidum* on Alloxan-induced Rats

[1]Amos Joseph, [1]Umar Tanko Mamza*, [3]Chiroma Ijuptil, and [2]Wiam Ibrahim

Author's Affiliations:
[1]Department of Pure and Applied Chemistry, Faculty of Physical Sciences, University of Maiduguri, Maiduguri, Borno State, Nigeria
[2]Department of Pharmacology and Toxicology, Faculty of Veterinary Medicine, University of Maiduguri, Borno State, Nigeria
[3]Department of Internal Medicine, College of Medical Sciences, University of Maiduguri, Borno State, Nigeria

***Corresponding Author: Dr. Umar Tano Mamza,** Department of Pure and Applied Chemistry, Faculty of Physical Sciences, University of Maiduguri, Borno State, Nigeria
E-mail: utmama@unimaid.edu.ng, drutmamza_2587@yahoo.com

ABSTRACT

This study investigates the acute toxicity and biochemical effects of the methanol leaf extract of *Chrysophyllum albidum* in Wistar albino rats. The extract was obtained using Soxhlet extraction and evaluated for toxicity via *intraperitoneal* and oral routes. The LD50 was determined to be 2,154 mg/kg for *intraperitoneal* administration, indicating moderate toxicity, while the oral LD50 was above 5,000 mg/kg, which is regarded as safe. Biochemical analyses revealed significant alterations in serum antioxidant enzyme levels, with increased glutathione (GPX) and malondialdehyde (MDA) levels, indicating oxidative stress. Treatment with the extract significantly reduced serum levels of liver enzymes (AST, ALT, ALP) and improved kidney function markers (urea, creatinine), suggesting hepatoprotective and nephroprotective effects. Additionally, the extract demonstrated potential antihyperglycemic and anti-hyperlipidemic properties, as evidenced by the normalization of serum electrolytes. These findings support the traditional use of *Chrysophyllum albidum* as a therapeutic agent with low acute toxicity and beneficial effects on metabolic disorders.

Keywords: Alloxan-induced rats, *Chrysophyllum albidum*, Diabetes, Toxicity, Biochemical

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INTRODUCTION

Plants and plants extracts have been used for centuries throughout the world in traditional cures and herbal remedies and as homeopathic medicines [1]. Due to the large chemical diversity among natural products, many research groups screen plant extracts for new promising therapeutic candidates for infectious diseases [2]. Herbal preparations assumed to be safe may contain contaminants such as heavy metals, aflatoxins and pathogenic microbes due to the

manner in which they are prepared or as a result of acquisition of metals (e.g. Cadmium) from the soil [3]. Natural products especially medicinal plants will continue to play an important role in meeting this demand through the expanded investigation of the world's biodiversity, much of which remains unexplored [4].

Medicinal plants should be used with precautions and toxicology studies should be conducted to increase the knowledge on the plant or plants preparation given to populations [5].

Chrysophyllum albidum commonly called white star apple belonging to the family of Sapotaceae is a lowland rain forest tree species and very useful medicinal plant common in the tropical and subtropical regions of the world [6]. In folklore medicine, *Chrysophyllum albidum bark* is employed for the treatment of yellow fever and malaria [7]. The leaf is used as an emollient and for the treatment of stomach ache, diarrhea and diabetes [8]. The plant could also be employed as sources of natural antioxidant boosters for the treatment of free radical implicated oxidative stress disorders [9].

Toxicity is the relative ability of a substance to cause adverse effects on living organisms, it describes the degree to which bioactive substances cause harm to living organisms as well as their symptoms, mechanisms and treatments [10]. Toxicology is the scientific study of the undesirable effects of chemical, physical or biological agents on living organisms; it involves observing and reporting symptoms that arise following exposure to toxic substances [11]. Acute toxicity is defined as the harmful effects produced by single exposure of drugs by any route for a short period of time (usually 24 hours) which could alter the functioning of the organism in general or individual organs. Acute toxicity studies in animals are considered necessary for any pharmaceutical intended for human use, results from acute toxicity test serve as a guide in dosage selection for long term toxicity studies as well as other studies that involve the use of animals [12].

Biochemical parameters encompass a diverse array of markers crucial for assessing physiological function and health status [13]. Superoxide Dismutase (SOD) is an antioxidant enzyme that protects cells from oxidative stress by converting superoxide radicals into oxygen and hydrogen peroxide. It plays a vital role in mitigating cellular damage caused by reactive oxygen species (ROS) [14]. Malondialdehyde (MDA) is a marker of lipid peroxidation, reflecting oxidative damage to cell membranes and lipids. Elevated MDA levels are associated with increased oxidative stress and cellular damage [15]. Glutathione Peroxidase (GPX) is an antioxidant enzyme that catalyzes the reduction of hydrogen peroxide and lipid peroxides, thereby protecting cells from oxidative damage. It plays a crucial role in maintaining cellular redox balance [16]. Catalase (CAT) is an antioxidant enzyme that catalyzes the decomposition of hydrogen peroxide into water and oxygen, thereby preventing the accumulation of hydrogen peroxide and mitigating oxidative stress [17]. Aspartate Aminotransferase (ASAT) and Alanine Aminotransferase (ALAT) are enzymes primarily found in liver cells. Elevated levels of these enzymes in the blood indicate liver damage or dysfunction, and they are commonly used as markers of liver health [18]. Alkaline Phosphatase (ALP) is an enzyme found in various tissues, including the liver, bones, and intestines. Elevated ALP levels may indicate liver or bone disorders, as well as certain cancers [19]. Albumin and total protein are markers of nutritional status and liver function. Low levels may indicate malnutrition, liver disease, or kidney dysfunction [20]. Total Bilirubin and Conjugated Bilirubin are breakdown product of heme metabolism. Elevated levels of total bilirubin and conjugated bilirubin may indicate liver or bile duct dysfunction [21]. Sodium, Potassium, Chloride, and Bicarbonate are electrolytes play essential roles in maintaining fluid balance, acid-base balance, and nerve and muscle function. Abnormal levels can indicate various health conditions, including dehydration, kidney disorders, and electrolyte imbalances [22]. Urea and Creatinine are waste products of protein metabolism excreted by the kidneys. Elevated levels may indicate impaired kidney function [23].

These biochemical parameters provide valuable insights into physiological processes and are

indispensable tools in clinical practice for diagnosing and managing various diseases and conditions. However, the safety of *Chrysophyllum albidum* is important in relation to its therapeutic actions, therefore, this study was aimed at determining the possible acute toxicity and biochemical changes of *Chrysophyllum albidum* methanol leaf extract in albino rats.

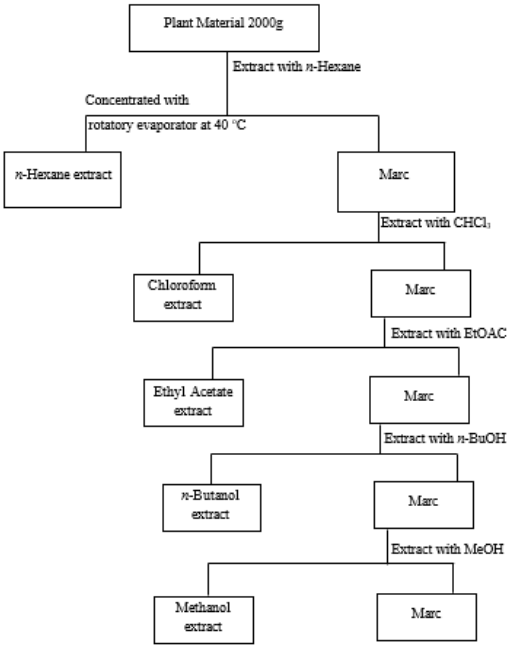
METHODOLOGY

Collection, Identification and Purification of Plant Materials

Fresh leaf sample of *Chrysophyllum albidum* was collected from Obio-Akpor Local Government Area, Port Harcourt, River State, Nigeria, and was identified by a Plant Taxonomist at the Department of Biological Sciences, University of Maiduguri, Borno State, Nigeria. The Specimen collected was air-dried under shade and pulverized using wooden mortar and pestle.

Plant Extraction

Soxhlet extraction technique was used for the extraction of plant material. Two thousand grams dry powdered plant material was subjected to successive soxhlet extraction with solvents of different polarity (*n*-hexane, chloroform, ethyl acetate, *n*-butanol and methanol). Firstly, powdered plant material was placed in the extraction chamber of the soxhlet apparatus. The extracting solvent (*n*-hexane) in the flask was heated until clear liquid contents of the chamber siphons into the solvent flask. The powdered plant material was extracted with 200 mL of solvent in the soxhlet extraction process. The *n*-hexane fraction was then filtered with Whatman No. 1 filter paper and concentrated using rotary evaporator (Buchi labortechnik AG, Switzerland) under reduced pressure set at 40 °C followed by oven at room temperature for 12 h. The marc was collected and dried at room temperature to remove *n*-hexane. The residue left was next extracted using chloroform, ethyl acetate, *n*-butanol and methanol following the same procedure as described before to get crude extract of chloroform ($CHCl_3$), ethyl acetate (EtOAC), *n*-butanol (*n*-BuOH) and methanol (MeOH) respectively (Scheme I). After extraction, the crude liquids were concentrated using rotatory evaporator at 40 ^{O}C which was kept for further analysis.



Scheme I: Flow Chart Extraction Profile and Fractionation of the leaf of *Chrysophyllum albidum*

Pharmacological Investigations of the Leaf Extracts of *Chrysophyllum albidum*

Experimental Animals

All the experiments that concerns anti-diabetic and toxicity evaluations was performed on laboratory animals (Wistar albino rats) in this study following standard procedures. The animals were handled according to the International Guiding Principle for Biomedical Research involving animals [24].

Albino rats (weighing 100-180 g) of both sexes were obtained from the animal house of the Pharmacology Department, Faculty of Pharmacy, University of Maiduguri, Borno State. The animals were housed in well-ventilated cages and kept under controlled environment conditions of temperature (25 ± 5 ^{O}C), relative humidity (50 ± 5 ^{O}C) and 12-hour light/dark circle at the animal house, Department of Veterinary Medicine, University of Maiduguri. The animals were fed with standard feed and allowed water, *ad libitum* and were given a period of acclimatization for two weeks before the commencement of the experiment. The study was conducted at the Department of Pharmacology and Toxicology, Faculty of Veterinary Medicine, University of Maiduguri, Borno State, Nigeria. The Ethic Clearance of using the experimental animals for this research was obtained from Ethic Clearance Committee of the Department of Veterinary Medicine, University of Maiduguri.

Acute Toxicity Study

The acute toxicity study was conducted in accordance with Lorke's method [25]. In this phase, specific doses (1600, 2900 and 5000 mg/kg body weight) of the methanol extract was administered to three rats (one rat per dose) to further determine the correct LD_{50} value. The extracts were dissolved in buffered saline solution and given via *intraperitoneal* route. All animals were observed on the day of treatment and surviving animals were monitored for signs of acute toxicity for 24 hours. Recovery and weight gain were seen as indications of having survived the acute toxicity. Determination of the LD_{50} of *Chrysophyllum albidum* was carried out at the Veterinary Department, University of Maiduguri.

The value of the LD_{50} was calculated with this formula: $LD_{50} = \sqrt{(a \times b)}$, where
a = Highest value that gave no mortality
b = Lowest dose that produced mortality

Extract Fractions and Alloxan Preparation

The plant extract was dissolved in 10 mL distilled water to give a stock solution of 200 mg/mL.

$$\text{Stock solution} = \frac{2000\ \text{mg}}{10\ \text{mL}} = 200\ \text{mg/mL}$$

$$\text{Volume to be administered} = \frac{\text{Dose x Body Weight in Kg}}{\text{Concentration of the Extract in mg}}$$

Biochemical analysis

Animals were subsequently anaesthetized in mild di-ethyl-ether and blood and tissue samples were isolated for various bioassay such as; Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, total protein, conjugated bilirubin, urea, creatinine, albumin, serum potassium, serum sodium, and lipid profile parameters using commercial test kits produced by Randox laboratories, U.K. Catalase (CAT) activity, Malondialdehyde (MDA) concentration, superoxide dismutase (SOD) and glutathione Peroxide (GPX) activities were all determined following previous methods described [26].

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 were excised from all the subjects (animals), washed in normal saline solution before preserved in sample bottles containing formalin for further analysis.

Statistical Analysis

The data generated from anti-diabetic study was compared with standard anti-diabetic drug (Glibenclamide) and the results obtained from these studies were statistically analyzed using

GraphPad Prism Version 9.0 (2020) and the effects were expressed as mean ± SEM values in all groups and were compared using one-way analysis of variance (ANOVA) followed by Dunnet's Multiple Comparison Test. For all analysis, the level of statistical significance was fixed as $p \leq 0.05$.

RESULTS

Acute Toxicity Evaluation (LD_{50}) of Methanol Leaf Extract of *Chrysophyllum albidum*

The toxicological evaluation of the plant extract seeks to discover its potential collateral effects, so as to ensure the safety of use. For the animals that were administered the extract via the *intraperitoneal* route in the first phase of treatment, the rats developed clinical signs of toxicity (loss of appetite, loss of stimuli sensitivity, loss of agility and immobility) after 30 minutes of the post treatment period with 100 mg/kg and 1000 mg/kg of the extract. There were no clinical signs of toxicity observed with the rats in the 10 mg/kg, either immediately or during the post treatment period and there was no mortality in the first phase. In the second phase of the treatment, rats administered with the extract developed clinical signs of toxicity (loss of appetite, loss of stimuli sensitivity, loss of agility and immobility) after 15 minutes of the post treatment period with 1600 mg/kg, and 2900 mg/kg of the extract. All the rats in the 2900 mg/kg group died after 2 hrs. of treatment. No mortality occurred in the 1600 mg/kg group during the 24 hrs. observation period (Table 1). From the results, the LD_{50} of the methanol leaf extract of *Chrysophyllum albidum* was calculated to be 2,154 mg/kg.

For the animals that were administered extract via the oral route, the results of the oral LD_{50} determination of methanol leaf extract of *Chrysophyllum albidum* is presented on Table 1 below. No mortality was recorded in the treated groups during the two phases of treatments. No clinical sign of toxicity was observed in all the animal groups (10, 100 and 1000 mg/kg) during the phase one. During the phase two, the animals treated with 1600 mg/kg, 2900 mg/kg and 5000 mg/kg body weight of the plant extract showed signs of irritability and weakness after 1 hour of administration. However, the animals recovered within two hours. The lack of mortality during the study indicates that the LD_{50} is above 5000 mg/kg body weight.

Table 1: Acute Toxicity Evaluation (LD_{50}) of Methanol Leaf Extract of *Chrysophyllum albidum*

Plant Material	Experiment	Dose (mg/kg)	Proportion of death after 24 hours	
			Intraperitoneal (*I.P*)	Oral (*P.O*)
Chrysophyllum albidum (Methanol leaf extract)	Phase 1	10	0/3	0/3
		100	0/3	0/3
		1000	0/3	0/3
Chrysophyllum albidum (Methanol leaf extract)	Phase 2	1600	0/3	0/3
		2900	3/3	0/3
		5000	-	0/3

LD_{50} =2,154 mg/kg

Effect of Methanol Leaf Extract of *Chrysophyllum albidum* on Alloxan-induced Diabetes in Serum Antioxidant Enzyme Levels in Wistar Rats

Glutathione and lipid peroxidation (MDA) activities were significantly increased following treatment with the extract ($p<0.05$), but the increased catalase observed in the diabetic untreated group was lowered significantly in groups treated with the extract. The activities of SOD were not significantly altered across the groups ($p>0.05$). GPX has showed relatively high values in treated groups compared to control indicating the plant extract is good for antidiabetic and antioxidant effects. The result of

the CAT has showed non-significance with the control. These results are presented in Table 2.

Effect of Methanol Leaf Extract of *Chrysophyllum albidum* on Alloxan-induced Diabetes in Serum Biochemistry in Wistar Rats

Serum biochemical parameters including AST, ALT, ALP and creatinine were significantly higher in the diabetic animals when compared with the normal control group ($P<0.05$). However, treatment with the extracts significantly lowered the values of these biochemical parameters by the end of treatment ($p<0.05$). The lowered total bilirubin values in the untreated rats were also significantly raised following treatment ($P<0.05$). but ALB, total protein, urea and conjugated bilirubin concentrations were not significantly altered (Table 3). The reduced value of creatinine in the treatment group is also a testament of the important of the plant in kidney function.

Effect of Methanol Leaf Extract of *Chrysophyllum albidum* on Alloxan-induced Diabetes in Serum Electrolytes in Wistar Rats

No significant change was observed between the K^+ and values of the diabetic untreated rats and the ones treated with the extracts after 21 days ($P>0.05$). However, Na^+ $Cl^-$and HCO^- concentrations were significantly lowered following treatment ($p<0.05$) [Table 4].

Table 2: Effect of Methanol Leaf Extract of *Chrysophyllum albidum* on Alloxan-induced Diabetes in Serum Antioxidant Enzyme Levels in Wistar Rats

S/N	Treatment	SOD	MDA	GPX	CAT
1.	Control	35.14±1.96*	25.04±3.27*	59.44±1.09*	14.00±1.42*
2.	Alloxan	39.00±0.99	29.92±1.81	83.00±4.20	17.78±0.94
3.	Drug	31.50±1.58*	37.44±3.55*	81.70±2.92*	18.42±1.23*
4.	100	37.38±3.55*	35.84±3.44*	112.54±3.53*	14.98±1.82*
5.	150	39.64±1.58	26.06±2.64*	89.32±1.75*	13.92±0.70*

Values are means ± SEM for N = 5. Values in the same column marked* are significantly different from that of the diabetic control group at $p< 0.05$.

Table 3: Effect of Methanol Leaf Extract of *Chrysophyllum albidum* on Alloxan-induced Diabetes in Serum Biochemistry in Wistar Rats

S/N	Treatment	AST	ALT	ALK. PHOS	ALB	T/P	T/B	C/B	Urea	Creatinine
1.	Control	17.80±2.78*	25.20±4.15*	9.76±2.21*	3.32±0.50	8.78±1.85	12.82±1.42*	6.58±0.23*	7.50±0.68	112.00±6.40*
2.	Alloxan	144.20±15.77	122.20±5.45	55.34±6.76	2.14±0.11	8.20±3.06	18.98±1.78	9.12±0.99	8.02±0.70	129.00±4.95
3.	Drug	40.00±5.61*	25.60±2.41*	19.56±1.78*	3.04±0.44	12.36±1.39*	16.78±0.36*	7.94±0.15*	7.24±0.77	116.00±1.58*
4.	100	79.80±7.40*	28.20±6.72*	29.62±5.98*	3.04±0.15	9.30±0.61	13.18±0.75*	6.80±0.64*	7.06±0.97	113.80±1.30*
5.	150	28.40±1.67*	65.00±7.28*	24.38±3.48*	3.06±0.59	9.18±1.14	12.10±2.20*	8.16±0.53*	6.32±1.20*	100.40±6.43*

Values are means ± SEM for N = 5. Values in the same column marked * are significantly different from that of the diabetic control group at $p< 0.05$.

Table 4: Effect of Methanol Leaf Extract of *Chrysophyllum albidum* on Alloxan-induced Diabetes in Serum Electrolytes in Wistar Rats

S/N	Treatment	Na^+	K^+	Cl^+	HCO^-
1.	Control	149.60±4.51*	7.28±0.84*	118.00±2.00*	22.20±1.92*
2.	Alloxan	193.20±7.29	8.90±0.69	128.40±1.67	23.40±0.89
3.	Drug	157.60±9.66*	6.38±0.55*	121.60±3.44*	21.80±1.30*
4.	100	168.00±8.46*	7.12±0.43*	118.80±1.79*	20.60±1.14*
5.	150	165.60±8.46*	8.62±0.74	109.60±1.67*	19.60±2.07*

Values are means ± SEM for N = 5. Values in the same column marked * are significantly different from that of the diabetic control group at $p< 0.05$.

DISCUSSION

Toxicity is an expression of being poisonous, indicating the state of adverse effect, led by the interactions between toxicants and cells [27].

This harm can range from mild irritation or reversible damage to severe illness, organ dysfunction, or even death, depending on factors such as the dose, duration of exposure, and individual susceptibility [28].

This study was designed to investigate the acute toxicity of methanol leaf extract of *Chrysophyllum albidum* via *intraperitoneal* and oral route toxicity analysis and its biochemical complications. For the *intraperitoneal* acute toxicity evaluation, there was a significant ($p\leq 0.05$) decline in the body weight of the treated animals both in phase one and phase two after 24 hrs. of treatment which was seen as a clinical sign of toxicity. In the initial hours of observation there was a significant ($p\leq0.05$) increase in the body weight of the treated animals both in phase one and phase two. This indicates that the extract has toxic effect on the Wistar rats and also has the ability to stimulate appetite of the rats and support weight gain at the dosages given. The acute toxicity of this study indicated that the methanol leaf extract of *Chrysophyllum albidum* is non-toxic when administered via the *intraperitoneal* route to the experimental animals since the LD_{50} was calculated to be 2,154 mg/kg (Lorke, 1983). In a similar study, the methanol leaf extract of *Chrysophyllum albidum* caused mortality and significant adverse effects via the *intraperitoneal* route and the toxic effect (LD_{50}) was calculated to be 244.95 mg/kg body weight [27], which was contrary to our findings.

For the oral acute toxicity evaluation, the LD_{50} of the methanol extract of *Chrysophyllum albidum* was estimated to be more than 5000 mg/kg. The dose produced no mortality after 24 hrs. of observation. It also had no adverse effects on the behavioral responses of the tested Wistar rats after 24 hrs. of observation. It has been suggested that any substance with an oral LD50 of above 5000 mg/kg should be regarded as safe [29]. It can therefore be inferred that, the plant under study is non-toxic. Although, the extract can be deduced to be safe, some dose dependent toxic manifestations were observed in the groups treated with 1600 mg/kg, 2900 mg/kg and 5000 mg/kg body weight of the extract following oral administration (*P.O*). This may be due to the effect of one or more of the chemical constituents present in the extract. The non-toxic observation that was made in the current studies following the evaluation of the acute toxicity aligns very well with other studies on toxicity of *Chrysophyllum albidum*. Previous research reported a non-toxic LD50 of methanol bark extract *of Chrysophyllum albidum* [30]. Another research also reported that the methanol leaf extract is non-toxic following oral route of administration to albino rats which is in agreement with this study [27]. The non-toxic effect of the plant could be due to its rich content of nutritional molecules. A report showed that

the whole plant is rich in Vitamin C, protein and mineral contents [31]. A study also reported that the methanolic extract of *Chrysophyllum albidum* seed cotyledon in Albino rats did not cause mortality or significant adverse effects at doses up to 5000 mg/kg body weight in acute toxicity tests [32]. Acute administration of the Seed cotyledon of *Chrysophyllum albidum* extract did not significantly affect the liver and kidney functions in the tested animals [33].

The result of catalase (CAT) in this study was insignificant 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 [34]. Complications arise 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 [35].

MDA concentration in this study significantly increase across the groups treated with *Chrysophyllum albidum* extract at lower concentration (100 mg/kg) when compared with diabetic group therefore proposing no defensive mechanisms of the extract at this concentration in averting lipid decomposition but it showed a promising effect at higher concentration (150 mg/kg) with lower MDA which indicate antioxidant and antidiabetic property. Previous research also reported a significant increase in MDA level of antioxidant and antidiabetic activities of the seed and leaf extracts of *Chrysophyllum albidum* which is in contrary to this study [8].

The antioxidant enzymatic activities; Superoxide dismutase (SOD) and glutathione peroxidase (GPX) were significantly higher in the groups treated with *Chrysophyllum albidum* compared with diabetic group. The observable reduction in SOD property in diabetic group could surmount to H2O2 or glycation inactivation of enzyme, which has been reported to occur in diabetes as a result of depletion owing to excessive use of these enzymes to mop up the hyperglycaemia-induced free radical generation [36]. Also, these enzymes are targets of glycation which can lead to inhibition of their enzymatic activity [36]. The increase in the GPX and SOD activities in the groups treated with *Chrysophyllum 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 [37].

Liver damage is usually assessed by the serum levels of ALT and AST [38]. High levels of AST and ALT indicate liver damage, cardiac infarction, and muscle injury. However, ALT is more specific to the liver and is thus a better parameter for detecting liver injury. Serum ALP, on the other hand, is related to the function of hepatic cells and biliary obstruction. High values of AST, ALT and ALP have been reported following alloxan-induced diabetes in rats [39]. This increase is mainly due to the leakage of these enzymes from the liver cytosol into the bloodstream [39]. The lowering effect of the extracts on the activities of these enzymes is, therefore, suggestive of their hepatoprotective potentials [40]. The kidney regulates the re-absorption of electrolytes into blood [41] but when its function is compromised, substances like chloride and potassium that are normally cleared accumulate in the biological fluid [42]. The kidney is an important organ in glucose homeostasis [43] and may be affected by beta-cell dysfunction [44]. Elimination of urea and creatinine from the plasma is one of the functions of kidney and is normally used for the assessment of renal competence [44]. The urea and creatinine concentration possess significant difference and the concentration of creatinine normally is constant but becomes elevated when renal function is impaired. The increase in creatinine levels of the distilled water treated diabetic rats might be due to impairment of renal functions ensuing from hyperglycaemia. A disturbance in electrolytes is associated with diabetes mellitus, as some electrolytes play essential roles in intermediary metabolism and cellular functions including osmosis and acid-base balance [45]. The lowering effect of the creatinine level by the extract is a testament of its nephroprotective property of the plant.

The high serum lipids values in the diabetic rats may be due to an increase in the mobilization of free fatty acids from peripheral fat deposits into the systemic circulation [46]. Hyperlipidemia is an established cause of complications in diabetes mellitus [47]. The lowering of total Na+ K+, Cl- and HCO- in the extract treated suggests that the extracts may contain bioactive substances with hypolipidaemic effects [48]. There is sufficient literature data to support the hypolipidaemic and anti-hyperlipidaemic effects of phytochemical agents like tannins, flavonoids, and saponins [49]. Therefore, the presence of these phytoagents in *Chrysophyllum albidum* may be responsible for the observed effects in diabetes mellitus. The fact that at all doses of both extracts reduced serum concentrations of Na+ K+, Cl- and HCO- suggests that the extracts may be of value in the control diabetic hyperlipidemia. These findings agree with the previous research that reported the anti-hyperlipidaemic activities of *Chrysophyllum albidum* in diabetic Rats [48].

Previous research also reported that this could serve as a reference for discussing both acute toxicity and biochemical effects [50]. Their study evaluated the acute toxicity of *Chrysophyllum albidum* methanol leaf extract and found it to be safe at tested doses. Additionally, the study assessed the extract's antioxidant properties, indicating increased SOD, GPX, and CAT activities, and reduced MDA levels, suggesting protection against oxidative stress. Regarding liver function markers, A recent study investigated the effects of *Chrysophyllum albidum* seed coat extract on biochemical parameters in rats [51]. They observed no adverse effects on liver function markers such as ASAT, ALAT, and ALP, indicating the safety of the extract.

The above normal levels of chloride (hyperchloremia) and potassium (hyperkalemia) observed in the diabetic control group suggests that the normal excretion of these electrolytes by the kidneys was adversely affected. Furthermore, the decrease in the levels of sodium and bicarbonate in the diabetic control group suggests that some aspects of tubular functioning as it relates to these electrolytes have been compromised. The bicarbonate ion maintains a healthy acidity level in the blood and other fluids in the body. The amelioration observed in groups treated with *Chrysophyllum albidum* and standard drugs suggests that these agents may possess some level of nephroprotective activities. This effect has indeed been reported for the *Chrysophyllum albidum* stem bark extract [48] and other medicinal plants [52].

CONCLUSION

The findings of this study supports the reported use of the methanolic leaf extract of *Chrysophyllum albidum as a* potential therapeutic agent with low acute toxicity and potential antihyperglycemic, anti-hyperlipidaemic and antioxidant properties. This possible mechanism of action could be the effects of their phytochemical components.

CONFLICT OF INTEREST

None declared

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