Scientific Research Publishing

Journal of Biosciences and Medicines, 2025, 13(11), 188-200
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

Antidiabetic and Antioxidant Potentials of Aqueous Fresh Leaf Extract of *Chrysophyllum albidum* in Streptozotocin-Induced Diabetic Rats

Victor Ugadu Nwankwo[1], Kingsley Nwonu Agbafor[2*], Nkiru Nwamaka Ezeanni[2], David Chukwu Obasi[3], Emmanuel Nnaemeka Uhuo[4], Shedrack Ifeanyi Nwodo[5]

[1]Biotechnology Department, Ebonyi State University, Abakaliki, Nigeria
[2]Biochemistry Department, Ebonyi State University, Abakaliki, Nigeria
[3]Medical Biochemistry Department, David Umahi Federal University of Health Sciences, Uburu, Nigeria
[4]Biochemistry Department, Michael Okpara University of Agriculture, Umudike, Nigeria
[5]Chemical Science Department, Godfrey Okoye University, Enugu, Nigeria
Email: *nagbafor@gmail.com

How to cite this paper: Nwankwo, V.U., Agbafor, K.N., Ezeanni, N.N., Obasi, D.C., Uhuo, E.N. and Nwodo, S.I. (2025) Antidiabetic and Antioxidant Potentials of Aqueous Fresh Leaf Extract of *Chrysophyllum albidum* in Streptozotocin-Induced Diabetic Rats. *Journal of Biosciences and Medicines*, **13**, 188-200.
https://doi.org/10.4236/jbm.2025.1311013

Received: October 13, 2025
Accepted: November 8, 2025
Published: November 11, 2025

Abstract

Traditional medicine practitioners in Eastern Nigeria use various parts of *Chrysophyllum albidum* in management and treatment of several disorders, including liver and pancreatic ones. This study investigated antidiabetic and antioxidant potentials of aqueous fresh leaf extract of *Chrysophyllum albidum* in streptozotocin (STZ)-induced diabetic rats. Phytochemicals content and acute toxicity of the extract were measured by standard procedures. Forty-two (42) adult male albino rats, placed in seven groups (A, B, C, D, E, F and G) of six rats each, were used. Diabetes was induced in groups B - G by intraperitoneal administration of 50 mg/kg body weight of STZ. Groups D, E, F and G were treated with 200, 400, 600 and 800 mg/kg body weight of the extract respectively, while group C was given 500 mg/kg body weight of metformin. Treatment was by oral intubation, and lasted for twenty-one consecutive days. The results revealed percentage of cardiac glycosides > flavonoids > saponins > terpenoids > alkaloids > phenols > tannins in the extract. The median lethal dose (LD_{50}) of the extract was estimated to be greater than 5000 mg/kg b.wt. Induction of diabetes resulted to a significant ($P < 0.05$) increase in blood glucose, activity of amylase and lipase and pancreatic malondialdehyde (MDA) concentration, while plasma insulin and pancreatic catalase, glutathione re-

ductase and AMP kinase activity decreased significantly ($P < 0.05$). Treatment with metformin and different doses of the extract yielded a significant ($P < 0.05$) decrease in blood glucose, activity of amylase and lipase and pancreatic MDA, while plasma insulin and pancreatic catalase, glutathione reductase and AMP kinase activity increased significantly ($P < 0.05$). This effect of the leaf extract on blood glucose, insulin and activity of AMP kinase, amylase and lipase is indicative of antidiabetic property, while the effect on MDA level and activity of catalase and glutathione reductase suggests antioxidant property. These properties may be partly responsible for the various medicinal applications of fresh leaves of *Chrysophyllum albidum* including management/treatment of diabetes.

Keywords

Chrysophyllum albidum, Diabetes, Antioxidants, Phytochemicals and Albino Rats

1. Introduction

Medicinal plants also called medicinal herbs, have been discovered and used in traditional medicine practices since prehistoric times. Medicinal plants are rich in chemical compounds which they produce for their own defence and are known as secondary metabolites (phytochemicals), and their medicinal potencies are attributed to these chemical compounds [1]. A medicinal plant may contain a mixture of different phytochemicals, for example, saponins, which have the ability to lower cholesterol; alkaloids which are rich in nitrogenous compounds and are stimulants; tannins which are natural antibiotics; anthraquinones used as laxative and dye; cardiac glycosides which are good cardiovascular drugs; and phenols and flavonoids which are rich in antioxidants, which protect the cells, tissues and organs from the oxidative damages caused by free radicals [1].

Chrysophyllum albidum, commonly called African star apple, *udala* by Igbo tribe of South-Eastern Nigeria, *agbalumo* by the Yorubas of the South-Western Nigeria and *agwaluma* by the Hausas of the Northern Nigeria, belongs to the family, *Sapotaceae,* (which has up to 800 species). It is a lowland rain forest tree species [2]. It is common throughout the tropical central, East and West African regions and other parts of the world [3]. The leaves are simple, dark green above, pale tawny below when young and silver-white below when mature. The fruit is ovoid to sub-globose pointed at the apex, and up to 6 cm long and 5 cm in diameter [4].

In folklore medicine, *Chrysophyllum albidum* bark is employed for the treatment of yellow fever and malaria [5]. The leaf is used as an emollient and for the treatment of stomach ache and diarrhoea. The leaf and cotyledons from its seed are used as ointments in the treatment of vaginal and dermatological infections in Western Nigerian. The roots, barks and leaves of *C. albidum* are widely used as

an application to sprains, bruises and wounds in Southern Nigeria. The seeds and roots extracts of *C. albidum* are used to arrest bleeding from fresh wounds and inhibit microbial growth of known wound contaminants and also enhance wound healing process. The fresh leaves are squeezed in water and taken for diabetes and its complications [6].

Diabetes mellitus remains a significant global health concern, with its prevalence steadily increasing in both developed and developing countries. Characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both, diabetes imposes a substantial burden on individuals, families, and healthcare systems worldwide [7]. As reported by Lenzen [8], the diabetogenic activity of STZ (streptozotocin) has been shown to be mediated by generated reactive oxygen species. For instance, following its uptake into the beta cells, streptozotocin split into its glucose and methylnitrosourea moiety. Owing to its alkylating properties, the latter modifies biological macromolecules, fragments DNA, and destroys the beta cells, causing a state of insulin-dependent diabetes.

The pancreas is an organ, which is part of the digestive system, that produces insulin and enzymes involved metabolism. Enzymes, or digestive juices are secreted by the pancreas into the small intestine. The hormone, insulin, is secreted it into the blood stream, where it regulates glucose or sugar level. When blood glucose is high, insulin is released from the Islets of Langerhans. Insulin, among other things, will then facilitate the uptake of glucose into cells via increased expression and translocation of glucose transporter, GLUT-4 [9]. Amylases are calcium dependent metalloenzymes that randomly catalyze the hydrolysis of complex carbohydrates, e.g. glycogen. Amylase can be found in the salivary glands, pancreas and ovaries and is used in diagnosis of pancreatitis. Approximately, 40 percent of the amylase in the blood comes from the pancreas, which means that amylase blood test can help diagnose conditions that affect the pancreas. Amylase has been primarily used for the diagnosis of acute pancreatitis [10]. Lipases (triacylglycerol acylhydrolase) are a group of water soluble enzymes, which exhibit the ability of acting at the interface between aqueous and organic phases. They primarily catalyze the hydrolysis of ester bonds in water insoluble lipid substrates [11]. Serum lipase elevations have been reported to be positively associated with a correct diagnosis of acute pancreatitis, with diagnostic efficiencies of 94 per cent. A close correlation between elevations of serum lipase has been observed in both extrapancreatic and pancreatic disease processes. Serum lipase is a better test than serum amylase either to exclude or to support a diagnosis of acute pancreatitis [12]. AMP-activated protein kinases (AMPKs) act as a metabolic sensor in mammalian cells. The kinases are activated by a relative increase in cellular AMP level, *i.e.* increase in the AMP to ATP ratio. Activation of AMPK either by physiological stimulation such as contraction of skeletal muscles or by pharmacological agents leads to a significant increase of glucose transport mediated by translocation of the GLUT4 transporter molecule from intracellular membranes to the plasma membrane [13].

Oxidative stress is an imbalance between antioxidants and pro-oxidants, favouring the latter, and is recognised as a key mechanism that impairs molecular signalling pathways and enzyme activities, leading to tissue damage [14]. Reactive oxygen species (ROS) are the primary effector molecules of oxidative stress, which are produced under physiological states, such as during cell metabolism, and under pathological conditions. Endogenous sources of ROS include the mitochondria, plasma membrane, endoplasmic reticulum and peroxisomes, where enzymatic reactions and autoxidation of various compounds occur [15]. Catalase is a widespread enzyme in living organisms, playing a crucial role in protecting cells from damage caused by reactive oxygen species (ROS), particularly hydrogen peroxide. It catalyzes the decomposition of hydrogen peroxide into water and oxygen, effectively neutralizing this toxic by-product of cellular metabolism. Catalase has one of the highest turnover numbers of all enzymes; one catalase molecule can convert millions of hydrogen peroxide molecules to water and oxygen each second [16]. A characteristic feature of its structure is a heme system with a centrally-located iron atom. Its activity has been demonstrated in peroxisomes, mitochondria, endoplasmic reticulum and the cytosol in many types of cells [17]. Glutathione reductase (GR), also known as glutathione-disulfide reductase (GSR), catalyzes the reduction of glutathione disulfide (GSSG) to the sulfhydryl form glutathione (GSH), which is a critical molecule in resisting oxidative stress and maintaining the reducing environment of the cell. Glutathione reductase functions as dimeric disulfide oxidoreductase and utilizes an FAD prosthetic group and NADPH to reduce one molar equivalent of GSSG to two molar equivalents of GSH [18]. Malondialdehyde (MDA) is a chemical compound formed as a by-product of lipid peroxidation, a process where polyunsaturated fatty acids are damaged by free radicals. It's widely used as a biomarker for oxidative stress, reflecting damage to lipids in cells and tissues. MDA can interact with proteins, DNA, and RNA, potentially leading to toxic effects and contributing to conditions like cardiovascular disease [19].

Many ethno medicinal applications of various parts of *Chrysophyllum albidum* have not been studied scientifically. Most available reports on the antidiabetic potential of *Chrysophyllum albidum* focussed on other parts of the plant. The very few attempts on leaves did not monitor biomarkers of structural and functional integrity of the pancreas such as serum lipase and amylase activity. Hence, the present research was designed to investigate the use of the fresh leaves in management/treatment of diabetes (with additional focus on structural and functional parameters of the pancreas) and oxidative stress related disorders in albino rats.

2. Materials and Methods

The apparatus/equipment used were in good working conditions, while the chemicals and reagents were of high analytical grade.

2.1. Collection and Authentication of Plant Materials

Fresh leaves of *Chrysophyllum albidum* were collected from Amike-aba in Abakiliki

local government area, Ebonyi state. The plant sample was classified and authenticated by a plant taxonomist, Prof. Catherine V. Nnamani, of the Department of Applied Biology of Ebonyi State University, Abakaliki, Nigeria.

2.2. Preparation of Plant Extract

The method of extraction of Sofowora [20] as described by Agbafor *et al*. [21] was used. Five hundred (500) grams of the fresh leaves were washed with distilled water and pounded in a mortar with a pestle into a paste. The paste was soaked in 500 mls of distilled water for one hour, after which it was squeezed with muslin cloth to get a dark green solution. The solution was evaporated using rotor evaporator to get a gel, like solid. The solution of the extract was prepared by dissolving 20 gram of the gel-like solid in 100ml of distilled water to get a concentration of 0.2 g/ml.

2.3. Phytochemical Analysis of Extract

The phytochemical contents of the extract were determined using the method of A.O.A.C. [22].

2.4. Acute Toxicity Test of the Extract

The acute toxicity (LD_{50}) of the extract was measured by a modified method of Lorke [23]. Thirty-six (36) rats were randomized into six (6) groups of six rats each. Group A—Control, Group B—1000 mg/kg, Group C—2000 mg/kg, Group D—3000 mg/kg, Group E—4000 mg/kg and Group F—5000 mg/kg.

2.5. Induction of Diabetes

Diabetes was induced through single intraperitoneal injection of freshly prepared streptozotocin (STZ) (50 mg/kg b.w.) in 0.1 M citrate buffer (pH 4.5) to overnight starved rats [24]. Diabetic rats were permitted to drink 20% glucose solution overnight to overcome the initial drug induced hypoglycemic death. The blood glucose level was measured after three days, and rats with glucose levels >250 mg/dl were considered as diabetic. At the time of induction, control rats were injected with 0.2 ml of vehicle (0.1 M citrate buffer, pH 4.5) alone [25].

2.6. Experimental Design

Forty-two (42) adult male albino rats, placed in seven groups (A, B, C, D, E, F and G) of six rats each, were used**.** Diabetes was induced in groups B - G as explained above. Groups D, E, F and G were treated with 200, 400, 600 and 800 mg/kg body weight of the extract respectively, while group C was given 500 mg/kg body weight of metformin. Treatment was by oral intubation, once a day, and lasted for twenty-one consecutive days.

2.7. Summary of Experimental Design

Group:

A = Normal control (zero STZ and treatment).

B = Negative control (50 mg/kg STZ and zero treatment).
C = Positive control (50 mg/kg STZ + 500 mg/kg metformin).
D = 50 mg/kg STZ + 200 mg/kg extract.
E = 50 mg/kg STZ + 400 mg/kg extract.
F = 50 mg/kg STZ + 600 mg/kg extract.
G = 50 mg/kg STZ + 800 mg/kg extract.

2.8. Collection of Samples from the Animals

Blood and pancreas were collected from the animals under mild anaesthetic agent (chloroform).

2.9. Preparation of Pancreas Homogenate

The pancreas was washed in physiological saline several times until free of blood. The method described by Sretenovic *et al.* [26] was used to prepare the homogenate.

2.10. Measurement Parameters

Blood glucose level was determined using an Accu-Chek glucometer as described by Aziz and Hsiang [27]. The level of insulin and activity of α-amylase and lipase were measured in blood, while AMPK and antioxidant indices were determined in the homogenate. The activity of α-amylase was assayed by the method of Doehlert and Duke [28] following the protocol outlined in the kit used. Activity of lipase was measured according to the method of Yang and Biggs [29]. The insulin level was determined using the rat ELISA kit, following the protocol outlined in the kit [30]. Catalase (CAT) activity was assayed by monitoring the decomposition of H_2O_2 at 240 nm as described by Aebi [31]. Glutathione reductase (GR) was determined by the method of Benke *et al.* [32]. Malondialdehyde (MDA) levels were quantified by the method of Tsikas [33]. The phosphorylated AMPK (p-AMPK) activity was measured by the western blotting method adopted by Lim *et al.* [34] following the assay kit manufacturer's protocols.

2.11. Statistical Analysis

All results were analyzed using Graph-pad Prism 5. Data were expressed as mean ± standard deviation. The Means of the parameters were compared using (one-way ANOVA) and $P < 0.05$ was considered statistically significant.

3. Results and Discussion

The result of quantitative phytochemical analysis of the leaf extract is presented in Table 1. Alkaloids, cardiac glycosides, flavonoids, saponins, tannins and terpenoids were found in the extract. Cardiac glycosides were highest (26.55 ± 1.73 mg/100g), followed by flavonoids (17.24 ± 1.35 mg/100g), while tannins were the lowest (0.74 ± 0.08 mg/100g). The presence of these compounds may explain some of the various ethno medicinal applications of the leaves of *Chrysophyllum al-*

bidum. Alkaloids have many pharmacological activities including antihypertensive effects (many indole alkaloids), antiarrhythmic effect (quinidine, spareien), antimalarial activity (quinine), and anticancer actions (dimeric indoles, vincristine, vinblastine) and some alkaloids exhibit stimulant property such as caffeine and nicotine, morphine and are used as analgesic [35]. Tannin-containing plant extracts are used as astringents, against diarrhoea, as diuretics, against stomach and duodenal tumour, and as anti-inflammatory, antiseptic, antioxidant and haemostatic pharmaceuticals. Flavonoids play important roles as antioxidants (free radicals scavenger), anti-inflammatory agents, immune system modulators and cancer prevention agents [35]. Extensive research has been carried out into the membrane-permeability, immunostimulation, hypocholesterolaemic and anticarcinogenic properties of saponins, and they have also been found to be antioxidants, to impair the digestion of protein and the uptake of vitamins and minerals in the gut, to cause hypoglycaemia, and to act as antifungal and antiviral [36]. Terpenoids have medicinal properties such as anticarcinogenic (e.g. perilla alcohol), antimalarial (e.g. artemisinin), anti-ulcer, antimicrobial or diuretic (e.g. glycyrrhizin) activity [37]. Therapeutic uses of cardiac glycosides primarily involve the treatment of cardiac failure [38].

Table 1. Phytochemical constituents of the extract.

SN	Component	Concentration (mg/100g)
1	Alkaloids	5.68 ± 0.83
2	Tannins	0.74 ± 0.08
3	Flavonoids	17.24 ± 1.35
4	Saponins	14.19 ± 1.41
5	Terpenoids	9.62 ± 0.88
6	Cardiac glycosides	26.55 ± 1.73

Values are mean ± SD; N = 3.

Table 2 shows the result of the acute toxicity testing of the extract. Physical signs of toxicity were observed significantly at doses of 4000 and 5000 mg/kg b.wt of the extract. However, no death was recorded. Hence, the LD_{50} of the extract was estimated to be above 5000 mg/kg b.wt. Consequently, 200, 400, 600 and 800 mg/kg b.wt were adopted as the experimental doses.

The effect of the extract on antidiabetic indices is presented in Table 3. Blood glucose concentrations and activity of amylase and lipase enzymes recorded in the groups administered the extract were significantly ($P < 0.05$) lower than in the untreated diabetic group. On the other hand, plasma insulin concentrations and pancreatic AMPK activity in the treated groups were significantly ($P < 0.05$) higher than in the untreated group. These effects of the extract are indicative of an antidiabetic property. Diabetes is characterized by hyperglycemia resulting from de-

fects in insulin secretion, insulin action, or both [7]. Approximately, 40 percent of the amylase in the blood comes from the pancreas, which means that amylase blood test can help diagnose conditions that affect the pancreas. Elevated blood amylase activity suggests pancreatic toxicity [10]. Serum lipase elevations have been reported to be positively associated with a correct diagnosis of acute pancreatitis, with diagnostic efficiencies of 94 per cent [12]. When blood glucose is high, insulin is released from the Islets of Langerhans. Insulin, among other things, will then facilitate the uptake of glucose into cells via increased expression and translocation of glucose transporter, GLUT-4 [39]. Activation of AMPK leads to a significant increase of glucose transport mediated by translocation of the GLUT4 transporter molecule from intracellular membranes to the plasma membrane [40].

Table 2. Acute toxicity (LD_{50}) of the leaf extract.

Groups	Doses (mg/kg)	No. of animals	Observations
1 (control)	-	6	No observed changes
2	1000	6	No observed changes
3	2000	6	No observed changes
4	3000	6	No observed changes
5	4000	6	Reduced mobility & no mortality
6	5000	6	Reduced mobility & no mortality

Table 3. Antidiabetic parameters of the rats after treatment.

Groups	Glucose conc. (mg/dl)	Amylase activity (U/L)	Lipase activity (U/L)	Insulin conc. (ng/ml)	AMPK activity (U/mg protein)
A	109.32 ± 2.55^{d}	106.17 ± 3.22^{d}	218.49 ± 5.33^{e}	25.03 ± 1.26^{a}	26.44 ± 2.01^{a}
B	422.17 ± 9.54^{a}	238.91 ± 8.14^{a}	483.27 ± 9.87^{a}	6.49 ± 1.53^{c}	6.44 ± 1.05^{c}
C	121.28 ± 6.35^{d}	117.53 ± 3.87^{d}	220.36 ± 7.54^{e}	23.27 ± 2.15^{a}	22.88 ± 2.04^{a}
D	251.67 ± 7.40^{b}	187.34 ± 5.61^{b}	375.72 ± 8.80^{b}	13.48 ± 1.55^{b}	11.23 ± 1.80^{b}
E	207.25 ± 4.76^{c}	150.63 ± 6.21^{c}	284.68 ± 9.08^{c}	16.03 ± 2.11^{b}	13.84 ± 1.25^{b}
F	124.37 ± 5.15^{d}	123.18 ± 3.55^{d}	230.08 ± 9.15^{e}	24.01 ± 1.68^{a}	20.61 ± 2.30^{a}
G	142.38 ± 3.49^{d}	151.25 ± 2.39^{c}	254.29 ± 8.25^{d}	17.19 ± 2.02^{b}	14.35 ± 1.42^{b}

Values are mean ± SD; N = 6. Means in same column with different superscripts differ significantly ($P < 0.05$).

Results on the effects of the extract on antioxidant parameters are shown in Table 4. The catalase and glutathione activity obtained in the treated groups was significantly ($P < 0.05$) higher than in the untreated group, while the concentrations of MDA in the untreated groups were significantly ($P < 0.05$) lower than in the untreated group. These results reflect antioxidant property of the extract. Cat-

alase plays a crucial role in protecting cells from damage caused by reactive oxygen species (ROS), particularly hydrogen peroxide. It catalyzes the decomposition of hydrogen peroxide into water and oxygen, effectively neutralizing this toxic by-product of cellular metabolism [16]. Glutathione reductase (GR) catalyzes the reduction of glutathione disulfide (GSSG) to the sulfhydryl form glutathione (GSH), which is a critical molecule in resisting oxidative stress and maintaining the reducing environment of the cell [18]. Malondialdehyde (MDA), a product of lipid peroxidation, is widely used as a biomarker for oxidative stress, reflecting damage to lipids in cells and tissues. A decrease in tissue/organ MDA level is an antioxidant property. MDA can interact with proteins, DNA, and RNA, potentially leading to toxic effects and contributing to conditions like cardiovascular disease [19].

The antioxidant property of the extract may be partly responsible for its antidiabetic potential since generation of reactive oxygen species is part of diabetogenic ability of STZ. As reported by Lenzen [8], the diabetogenic activity of STZ (streptozotocin) has been shown to be mediated by generated reactive oxygen species which causes oxidative damage β-cells of the pancreas.

Table 4. Antioxidant parameters of the rats after treatment.

Group	Catalase activity (U/mg protein)	Glutathione reductase activity (U/mg protein)	Malondialdehyde conc. (nmol/g protein)
A	159.31 ± 8.50^{a}	16.71 ± 2.02^{a}	19.65 ± 1.76
B	64.60 ± 3.45^{d}	5.81 ± 1.03^{c}	68.18 ± 6.23^{a}
C	147.33 ± 5.26^{a}	18.92 ± 2.11^{a}	20.13 ± 4.55^{d}
D	91.30 ± 3.22^{c}	8.08 ± 1.11^{b}	44.10 ± 4.72^{b}
E	128.29 ± 4.37^{b}	10.81 ± 1.50^{b}	35.21 ± 5.02^{c}
F	150.14 ± 5.15^{a}	17.84 ± 1.14^{a}	18.87 ± 2.24^{d}
G	121.33 ± 4.24^{b}	12.13 ± 1.20^{b}	31.60 ± 4.14^{c}

Values are mean ± SD; N = 6. Means in same column with different superscripts differ significantly ($P < 0.05$).

These antidiabetic and antioxidant properties of the extract, which may be due to some of its chemical constituents (see above), were found to be dose-dependent. The effects recorded at 600 mg/kg b.wt of the extract were significantly ($P < 0.05$) higher than those of 800 mg/kg b.wt (**Table 3** and **Table 4**). This suggests that toxic or adverse of the extract may manifest at doses beyond 600 mg/kg b.wt. The suspected toxicity may be attributed to the relatively high content of cardiac glycosides of the extract. Although cardiac glycosides, eg, digitalis and digoxin, are drugs used today in cardiovascular medicine [41], they have a narrow therapeutic window due to their toxicity [42] [43]. Cardiac-glycoside-containing plants and their crude extracts have been used as arrow coatings, homicidal or suicidal aids, rat poisons, etc. [44]. However, more studies are necessary to establish this

suspected toxicity, and link it to the cardiac glycoside content. The effects produced by 600 mg/kg b.wt of the extract and those of 500 mg/kg b.wt. of metformin (standard antidiabetic drug) did not differ significantly ($P > 0.05$). Thus, the antidiabetic property of the fresh aqueous leaf extract of *Chrysophyllum albidum* may be comparable to that of metformin.

4. Conclusion

The antidiabetic and antioxidant properties of the extract, shown by this study, may be attributed to the chemical constituents of the leaves. The antioxidant property may contribute to the antidiabetic property by inhibiting actions of free radicals in the pancreas thereby enhancing its performance. These properties of the extract may contribute to explanations on the various ethno medicinal applications of leaves of *Chrysophyllum albidum.* Studies are on in our laboratory to identify the fraction(s) of the extract responsible for the observations/findings of the present research. We shall proceed to attempt to identify (by specific and detailed chemical analysis of the extract) specific bioactive compounds that may be implicated. This will give us an authoritative ground to establish these properties, and propose their possible biochemical mechanisms.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Dubey, N.K., Kumar, R. and Tripathi, P. (2004) Global Promotion of Herbal Medicine: India's Opportunity. *Current Science*, **86**, 37-41.

[2] Adebayo, A.H., Amos, O.A., Roseline, K., Olayemi, O.A., Titilayo, B.O. and Olugbenga, S.T. (2011) Antioxidant Activities of Leaves of *Chrysophyllum albidum* G. *Pakistani Journal of Pharmaceutical Sciences*, **24**, 545-551.

[3] Amusa, N.A., Ashaye, O.A. and Oladapo, M.O. (2013) Biodeterioration of the African Start Apple (*Chrysophyllum albidum*) in Storage and the Effect on Its Food Value. *African Journal of Agriculture*, **1**, 11-13.

[4] Oboh, G., Adebayo, A.A., Ejakpovi, I.I., Ogunsuyi, O.B. and Boligon, A.A. (2018) Phenolic Profiling and *in Vitro* Antioxidant, Anticholinesterase, and Antimonoamine Oxidase Properties of Aqueous Extract of African Star Apple (*Chrysophyllum albidum*) Fruit Parts. *Journal of Food Biochemistry*, **42**, e12568. https://doi.org/10.1111/jfbc.12568

[5] Florence, A.B. and Adiaha, A.H. (2015) Storage Effects and the Postharvest Quality of African Star Apple Fruits (*Chrysophyllum africana*) under Ambient Conditions. *African Journal of Food Science Technology*, **6**, 35-40.

[6] Okoli, B.J. and Okere, O.S. (2010) Antimicrobial Activity of the Phytochemical Constituents of *Chrysophyllum albidum* Plant. *Journal of Research in National Development*, **8**, 1035-1037.

[7] American Diabetes Association (2018) Classification and Diagnosis of Diabetes. Diabetes Care.

[8] Lenzen, S. (2007) The Mechanisms of Alloxan- and Streptozotocin-Induced Diabetes.

Diabetologia, **51**, 216-226. https://doi.org/10.1007/s00125-007-0886-7

[9] Peter, L., Theodor, H., Ulrich, F.W., Hryhoriy, L., Detlef, K.B., Merten, H., Natascha, C.N. and Thomas, K. (2017) Laproscapic versus Open Distal Pancreatectomy. *International Journal of Colorectal Disease*, **32**, 273-280.

[10] Azzopardi, E., Lloyd, C., Teixeira, S.R., Conlan, R.S. and Whitaker, I.S. (2016) Clinical Applications of Amylase: Novel Perspectives. *Surgery*, **160**, 26-37. https://doi.org/10.1016/j.surg.2016.01.005

[11] Hasan, F., Shah, A.A. and Hameed, A. (2009) Methods for Detection and Characterization of Lipases: A Comprehensive Review. *Biotechnology Advances*, **27**, 782-798. https://doi.org/10.1016/j.biotechadv.2009.06.001

[12] Chase, C.W., Barker, D.E. and Burns, R.P. (1996) Serum Amylase and Lipase in the Evaluation of Acute Abdominal Pain. *The American Surgeon*, **62**, 1028-1033.

[13] Garcia, D. and Shaw, R.J. (2017) AMPK: Mechanisms of Cellular Energy Sensing and Restoration of Metabolic Balance. *Molecular Cell*, **66**, 789-800. https://doi.org/10.1016/j.molcel.2017.05.032

[14] Sies, H., Berndt, C. and Jones, D.P. (2017) Oxidative Stress. *Annual Review of Biochemistry*, **86**, 715-748. https://doi.org/10.1146/annurev-biochem-061516-045037

[15] Moldovan, L. and Moldovan, N.I. (2004) Oxygen Free Radicals and Redox Biology of Organelles. *Histochemistry and Cell Biology*, **122**, 395-412. https://doi.org/10.1007/s00418-004-0676-y

[16] Chelikani, P., Fita, I. and Loewen, P.C. (2004) Diversity of Structures and Properties among Catalases. *Cellular and Molecular Life Sciences*, **61**, 192-208. https://doi.org/10.1007/s00018-003-3206-5

[17] Habib, L.K., Lee, M.T.C. and Yang, J. (2010) Inhibitors of Catalase-Amyloid Interactions Protect Cells from β-Amyloid-Induced Oxidative Stress and Toxicity. *Journal of Biological Chemistry*, **285**, 38933-38943. https://doi.org/10.1074/jbc.m110.132860

[18] Deponte, M. (2013) Glutathione Catalysis and the Reaction Mechanisms of Glutathione-Dependent Enzymes. *Biochimica et Biophysica Acta* (*BBA*)—*General Subjects*, **1830**, 3217-3266. https://doi.org/10.1016/j.bbagen.2012.09.018

[19] Cordiano, R., Di Gioacchino, M., Mangifesta, R., Panzera, C., Gangemi, S. and Minciullo, P.L. (2023) Malondialdehyde as a Potential Oxidative Stress Marker for Allergy-Oriented Diseases: An Update. *Molecules*, **28**, Article No. 5979. https://doi.org/10.3390/molecules28165979

[20] Sofowora, A.E. (1993) The State of Medicinal Plants in Nigeria. University of Ibadan Press.

[21] Agbafor, K.N., Ogbanshi, M.E. and Akubugwo, E.I. (2014) Phytochemical Screening, Hepatoprotective and Antioxidant Effects of Leaf Extracts of *Zapoteca portoricensis*. *Advances in Biological Chemistry*, **4**, 35-39. https://doi.org/10.4236/abc.2014.41006

[22] AOAC (1997) Official Methods of Analysis of the Association of Official Analytical Chemists. 20th Edition, Association of Official Analytical Chemists.

[23] Lorke, D. (1983) A New Approach to Practical Acute Toxicity Testing. *Archives of Toxicology*, **54**, 275-287. https://doi.org/10.1007/bf01234480

[24] Gupta, R. and Gupta, R.S. (2009) Hypolipidemic Activity of *Pterocarpus marsupium* in Streptozotocin Induced Diabetes. *Journal of Complementary and Integrative Medicine*, **6**, 1-28.

[25] Jayaprasad, B., Sharavanan, P.S. and Sivaraj, R. (2016) Antidiabetic Effect of Chloroxylon Swietenia Bark Extracts on Streptozotocin Induced Diabetic Rats. *Beni-Suef University Journal of Basic and Applied Sciences*, **5**, 61-69.

https://doi.org/10.1016/j.bjbas.2016.01.004

[26] Sretenovic, J., Joksimovic Jovic, J., Srejovic, I., Zivkovic, V., Mihajlovic, K., Labudovic-Borovic, M., *et al*. (2021) Morphometric Analysis and Redox State of the Testicles in Nandrolone Decanoate and Swimming Treated Adult Male Rats. *Basic and Clinical Andrology*, **31**, Article No. 17. https://doi.org/10.1186/s12610-021-00134-8

[27] Aziz, S. and Hsiang, Y.H. (1983) Comparative Study of Home Blood Glucose Monitoring Devices: Visidex, Chemstrip Bg, Glucometer, and Accu-Chek Bg. *Diabetes Care*, **6**, 529-532. https://doi.org/10.2337/diacare.6.6.529

[28] Doehlert, D.C. and Duke, S.H. (1983) Specific Determination of α-Amylase Activity in Crude Plant Extracts Containing β-Amylase. *Plant Physiology*, **71**, 229-234. https://doi.org/10.1104/pp.71.2.229

[29] Yang, J. and Biggs, H.G. (1971) Rapid, Reliable Method for Measuring Serum Lipase Activity. *Clinical Chemistry*, **17**, 512-518. https://doi.org/10.1093/clinchem/17.6.512

[30] Latha, M. and Pari, L. (2004) Effect of an Aqueous Extract of Scoparia Dulcis on Blood Glucose, Plasma Insulin and Some Polyol Pathway Enzymes in Experimental Rat Diabetes. *Brazilian Journal of Medical and Biological Research*, **37**, 577-586. https://doi.org/10.1590/s0100-879x2004000400015

[31] Aebi, H. (1984) Catalase *in Vitro*. In: Packer, L., Ed., *Methods in Enzymology*, Academic Press, 121-126. https://doi.org/10.1016/s0076-6879(84)05016-3

[32] Benke, G.M., Cheever, K.L., Mirer, F.E. and Murphy, S.D. (1974) Comparative Toxicity, Anticholinesterase Action and Metabolism of Methyl Parathion and Parathion in Sunfish and Mice. *Toxicology and Applied Pharmacology*, **28**, 97-109. https://doi.org/10.1016/0041-008x(74)90135-5

[33] Tsikas, D. (2017) Assessment of Lipid Peroxidation by Measuring Malondialdehyde (MDA) and Relatives in Biological Samples: Analytical and Biological Challenges. *Analytical Biochemistry*, **524**, 13-30. https://doi.org/10.1016/j.ab.2016.10.021

[34] Lim, C.T., Lolli, F., Thomas, J.D., Kola, B. and Korbonits, M. (2012) Measurement of AMP-Activated Protein Kinase Activity and Expression in Response to Ghrelin. In: *Methods in Enzymology*, Elsevier, 271-287. https://doi.org/10.1016/b978-0-12-381272-8.00017-9

[35] Mamta, S., Jyoti, S., Rajeev, N., Dharmendra, S. and Abhishek, G. (2013) Phyto-Chemistry of Medicinal Plants. *Journal of Pharmacognosy and Phytochemistry*, **1**, 168-182.

[36] Morrissey, J.P. and Osbourn, A.E. (1999) Fungal Resistance to Plant Antibiotics as a Mechanism of Pathogenesis. *Microbiology and Molecular Biology Reviews*, **63**, 708-724. https://doi.org/10.1128/mmbr.63.3.708-724.1999

[37] Dudareva, N., Pichersky, E. and Gershenzon, J. (2004) Biochemistry of Plant Volatiles. *Plant Physiology*, **135**, 1893-1902. https://doi.org/10.1104/pp.104.049981

[38] Wang, Z., Wang, M., Mei, W., Han, Z. and Dai, H. (2008) A New Cytotoxic Pregnanone from Calotropis Gigantea. *Molecules*, **13**, 3033-3039. https://doi.org/10.3390/molecules13123033

[39] Watson, R.T., Kanzaki, M. and Pessin, J.E. (2004) Regulated Membrane Trafficking of the Insulin-Responsive Glucose Transporter 4 in Adipocytes. *Endocrine Reviews*, **25**, 177-204. https://doi.org/10.1210/er.2003-0011

[40] Rahmi, R., Machrina, Y. and Yamamoto, Z. (2022) The Effect of Various Training on the Expression of AMPK and GLUT4 in Type 2 Diabetes. *Macidonian Journal of Medical Sciences*, **10**, 1-5.

[41] Khandelwal, R., Vagha, J.D., Meshram, R.J. and Patel, A.A. (2014) Comprehensive Review on Unveiling the Journey of Digoxin: Past, Present, and Future Perspectives. *Cureus*, **16**, e56755.

[42] Shi, L., Sun, L.D. and Odel, J.G. (2018) Colored Floaters as a Manifestation of Digoxin Toxicity. *American Journal of Ophthalmology Case Reports*, **10**, 233-235. https://doi.org/10.1016/j.ajoc.2018.02.024

[43] Serge Barold, S. (2018) Alternans during Fascicular Ventricular Tachycardia Due to Digitalis Toxicity. *Journal of Electrocardiology*, **51**, 450-451. https://doi.org/10.1016/j.jelectrocard.2018.01.011

[44] Hack, J.B., Wingate, S., Zolty, R., Rich, M.W. and Hauptman, P.J. (2025) Expert Consensus on the Diagnosis and Management of Digoxin Toxicity. *The American Journal of Medicine*, **138**, 25-33.e14. https://doi.org/10.1016/j.amjmed.2024.08.018