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Research Article

Hepatoprotective and Nephroprotective Effects of *Chrysophyllum albidum* Aqueous Fresh Leaf Extract in Albino Rats

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ABSTRACT

Chrysophyllum albidum fruit is widely consumed and used in many parts of Africa for the management and treatment of various diseases, including liver and kidney impairments. Hence, this study determined the effects of *C. albidum* aqueous fresh leaf-extract on the hepatic and renal markers of albino rats. Sixteen adult male albino-rats were grouped into four with four rats each. Normal control was group A, while those administered with dosages of 200 mg/kg, 400 mg/kg and 600 mg/kg body weight of *C. albidum* aqueous fresh leaf extract twice daily via oral intubation for seven consecutive days were respectively groups B, C and D. Blood collected through cardiac puncture from the rats were used for liver and kidney function assays. Liver function markers tested were alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), total protein and total bilirubin. The kidney function markers tested were urea, creatinine, sodium, bicarbonate and potassium. The activities of ALP, AST and ALT significantly ($p < 0.05$) decreased, as well as the concentrations of total protein, total bilirubin, urea, creatinine, bicarbonate (HCO_3^-), sodium (Na^+) and potassium (K^+) in the extract-treated groups (B, C, D) in accordance to the dosage, unlike the normal control (A). Our findings suggest that *C. albidum* leaf has both hepatoprotective and nephroprotective effects, hence, may be useful for managing and treating of liver and/or kidney diseases.

Keywords: *Chrysophyllum albidum, Liver, Liver function markers, Kidney, Kidney function markers, Body weight.*

INTRODUCTION

Plants are important sources of food and therapy. Therefore, in addition to being the primary source of food, plants are medicinal agents. This is because of the phytochemicals they contain (Obasi *et al*., 2020).

Chrysophyllum albidum or African star apple is a fruit that matures for consumption mainly in the dry season. It is a member of the Sapotaceae family, and grows high with a height and mature girt of 25 - 37 meters and 1.5 to 2.0 meters respectively (Imaga and Urua, 2013; Anang *et al*., 2019). *C. albidum* as a medicinal plant, is used in different places in Nigeria, including some countries in African because of its therapeutic effects such as hypoglycemic, antimalarial, antioxidant and antibiotic; with evidence that it contains several phytochemicals (Ogunleye *et al*., 2020). The different names of *C. albidum* in different parts of Nigeria are: Hausa – Agwaluma; Yoruba – Agbalumo; Igbo, Ibiobio and Efik – Udara; Igala – Ehya; Urhobo-Utieagadava; Ijaw and Edo/Benin - Otien (Ogunleye *et al*., 2020).

Reasonable amounts of resin and anacardic acid that can serve in wood protection are found in C. albidum fruit (Oboh *et al*., 2009). The fruit pulp is flesh and gives a light refreshment when taken like a meal (Amusa *et al*., 2003). It can be exploited in soft drinks' production or fermented for alcohol generation (Ajewole and Adeyeye, 1991).

Furthermore, *C. albidum* seed provides oil, which has several applications (Ugbogu and Akukwe, 2008). It has been shown that the tree-bark ameliorates yellow fever and Plasmodium infections, whereas the leaf serves as a remedy for dermatological problems, diarrhea and stomachache (Idowu *et al*., 2006); while its cotyledons serve as medicinal cream against infections of the vagina (Akubugwo and Ugbogu, 2007), as well as antidiabetic and antihyperlipidemic agent (Olorunnisola *et al*., 2008). C. albidum has antimicrobial activity, containing eleagnine demonstrated to be responsible for bacterial growth inhibition (Idowu *et al*., 2003; Duyilemi and Lawal, 2009). Anti-inflammatory, anti-nociceptive and antioxidant activities of eleagnine have been reported (Idowu *et al*., 2006). There was a report that resistant strains of *Staphylococcus aureus* were inhibited by high concentration of *C. albidum* pulp aqueous extract than a synthetic antibiotic, ciprofloxacin (George *et al*., 2018). The pulp contains more vitamin C than pawpaw, mango, hog plum and pineapple (Edem *et al*., 1984; Ellong *et al.*, 2015). Furthermore, *C. albidum* has been proven to contain more nutrients and antioxidants than some common tropical fruits (Abiodun and Oladapo, 2011; Bello and Henry, 2015). Myricetin rhamnoside, an excellent antioxidant, was isolated from *C. albidum* leaf extract. (Adebayo *et al*., 2010; Adebayo *et al*., 2011).

Irrespective of different information on *C. albidum*, there are not many information on the hepatoprotective and nephroprotective activities of its aqueous fresh leaf extract. Liver and kidney related diseases are among the many diseases affecting both adults and youths nowadays, leading to death when not well managed. Also, some synthetic drugs are harmful to the liver and kidney, making their use in the disease treatment difficult, and the need for natural remedy. Therefore, this study investigated the effect of *Chrysophyllum albidum* aqueous fresh leaf-extract on the hepatic and renal function markers of albino rats.

MATERIALS AND METHODS

Plant sample collection and extract preparation

Fresh leaves of *C. albidum* used in this study were collected from a tree in Ebonyi State in January, 2022. The method of extraction of *C. albidum* as described by Agbafor (2004) was adopted. The fresh leaves of *C. albidum* weighing 190 g were washed, cut into small pieces and homogenized using mortar and pestle to obtain the paste. The paste was poured into a conical flask, and was added 300 ml of water, left soaked for 1 hour before filtration to get a green solution. Rotary evaporator was used to evaporate the solution to obtain a gel-like extract. For the preparation of the extract solution, extract of 125 g was added into a beaker containing 250 ml of water and was stirred to dissolve to get 0.5 g/ml of aqueous *C. albidum* fresh leaf-extract. The extract was transferred into a sealed clean container and kept at an ambient temperature in a dry place before use.

Animal management

Twenty (20) male adult albino rats of weights 141 - 170 g were purchased and kept in the laboratory for 7 days before the experiment. The animals were sustained with clean water and feed (growers mash – manufactured by Eastern Premier Feed Limited). Weights of the animals were checked prior to the experiment and daily throughout the period of experiment with an electronic weighing balance. The weights determined the volume of extract administered.

Experimental design

Sixteen (16) acclimatized adult male albino-rats were grouped into four with four rats each. Normal control was group A, while other groups were administered with dosages of 200 mg/kg (A), 400 mg/kg (B) and 600 mg/kg (C) b.w. (body weight) respectively of C. albidum aqueous fresh leaf extract twice daily via oral intubation for seven consecutive days.

Collection of blood sample

After the seven days of experiment, the rats were sacrificed and blood was collected through the heart into anticoagulant-free bottles. The blood was left to clot before spun in the centrifuge at 2500 rpm for 15 minutes, after which, the serum was decanted and kept for liver and kidney function assessments.

Liver function markers

Liver function markers tested were alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), total protein and total bilirubin, using the standard procedures in the Randox kits manual.

Kidney function markers

The kidney function markers tested were urea, creatinine, bicarbonate, sodium and potassium concentrations, according to the standard procedures in the manual of Randox kits.

Statistical analyses

The calculations were done using SPSS 23 version. One-way ANOVA and the test procedures of Duncan were used. The results were presented as ± SEM (Standard error of the Mean) of samples' triplicates. Differences were considered statistically significant at error probability, $P < 0.05$.

RESULTS

Physical activity

There were obvious decreased physical activities among groups C (400 mg/kg) and D (600 mg/kg b.w. of *C. albidum* aqueous fresh leaf-extract from the fifth day of the experiment); unlike in groups B (200 mg/kg b.w of *C. albidum* aqueous fresh leaf extract) and A (normal control).

Body Weight

C. albidum aqueous fresh leaf-extract effect on the average weights of the rats in each group during the days of experiment is shown in Table 1. The body weights decreased gradually in accordance to the dosage of *C. albidum* in groups B, C and D respectively, while weight gain occurred in the control group A.

Liver Function Markers.

Table 2 is the result of the effect of aqueous fresh leaf extract of *C. albidum* on serum liver function markers of albino rats. The activities of AST, ALP and ALT decreased significantly ($P < 0.05$), as well as the concentrations of the total protein and total bilirubin, compared to the normal control in a dose-dependent fashion.

Table 1. Effects of *C. albidum* Aqueous Fresh Leaf-Extract on the Weights of Rats After Seven Days of Administration.

Days	Group A (g)	Group B (g)	Group C (g)	Group D (g)
1	158.12 ± 3.44	150.37 ± 7.02	153.12 ± 3.12	161.50 ± 6.51
2	162.50 ± 4.25	151.12 ± 7.31	152.50 ± 4.33	158.50 ± 5.42
3	165.62 ± 3.26	149.61 ± 6.21	146.50 ± 3.06	155.37 ± 4.96
4	170.12 ± 3.44	148.87 ± 7.09	144.50 ± 3.06	150.72 ± 6.67
5	176.87 ± 4.25	145.62 ± 5.81	140.12 ± 2.57	140.87 ± 5.66
6	178.50 ± 5.40	140.50 ± 4.33	138.12 ± 2.13	133.62 ± 5.65
7	185.12 ± 3.87	133.75 ± 5.81	132.50 ± 2.28	124.37 ± 6.88

Values are ± SEM; n = 4. Group A = normal control, group B = 200 mg/kg b.w, group C = 400 mg/kg b.w, group D = 600 mg/kg b.w. of *C. albidum* aqueous fresh leaf extract.

Table 2. Effect of *C. albidum* Aqueous Fresh Leaf Extract on Liver Function Markers of Rats After Seven Days of Administration

Groups	ALT (U/L)	AST (U/L)	ALP (U/L)	T. Bil (µmol/l)	Total Protein (g/l)
A	29.94 ± 1.21^{d}	41.37 ± 2.26^{d}	36.12 ± 1.24^{d}	2.84 ± 0.38^{d}	8.85 ± 0.41^{d}
B	26.66 ± 0.53^{c}	34.97 ± 1.48^{c}	32.61 ± 1.22^{c}	2.20 ± 0.24^{c}	7.55 ± 0.37^{c}
C	20.65 ± 0.56^{b}	30.62 ± 1.43^{b}	26.97 ± 1.18^{b}	1.62 ± 0.18^{b}	6.23 ± 0.42^{b}
D	15.76 ± 2.15^{a}	19.19 ± 1.97^{a}	20.03 ± 1.19^{a}	1.06 ± 0.15^{a}	5.15 ± 0.24^{a}

Values are ± SEM; n = 4. Values with different superscripts down the columns are significant at $P < 0.05$. Group A = normal control, group B = 200 mg/kg b.w, group C = 400 mg/kg b.w, group D = 600 mg/kg b.w. of *C. albidum* aqueous fresh leaf-extract. (ALP = alkaline phosphatase, AST = aspartate aminotransferase, ALT = alanine aminotransferase, T. Bil = total bilirubin).

Kidney Function Markers: *C. albidum* aqueous fresh leaf-extract effect on the kidney function markers of the rats in each group during the days of experiment is shown in Table 3. Serum concentrations of creatinine, urea, bicarbonate, sodium and potassium had significant ($P < 0.05$) decrease in the test animals according to dosage, but were higher in the normal control

Table 3. Effect of *C. albidum* Aqueous Fresh Leaf Extract on Kidney Function Markers of Rats After Seven Days of Administration

Groups	Urea (mg/dl)	Creat mg/dl)	Na (mmol/l)	K (mmol/l)	HCO_3^- (mmol/l)
A	25.10 ± 1.23^d	6.67 ± 0.28^d	111.47 ± 8.37^d	4.15 ± 0.41^c	26.10 ± 1.63^d
B	23.53 ± 1.34^c	6.03 ± 0.53^c	97.67 ± 5.64^c	2.99 ± 0.39^b	19.22 ± 0.99^c
C	22.21 ± 1.60^b	5.26 ± 0.46^b	89.12 ± 1.63^b	2.22 ± 0.42^b	15.94 ± 0.82^b
D	20.55 ± 1.22^a	4.18 ± 0.22^a	86.76 ± 1.50^a	1.24 ± 0.37^a	14.59 ± 0.56^a

Values are ± SEM; n = 4. Values with different superscripts down the columns are significant at $P < 0.05$. Group A = normal control, group B = 200 mg/kg b.w, group C = 400 mg/kg b.w, group D = 600 mg/kg b.w. of *C. albidum*

DISCUSSION

There was a relative reduction in physical activities in groups given 400 and 600 mg/kg b.w. of *C. albidum* aqueous fresh leaf-extract (C and D), from the fifth day to the last day of the experiment unlike in groups A and B. Also, there was a gradual increase in wight in the control group A from the first to the seventh day of the experiment, whereas the groups given 200, 400 and 600 mg/kg b.w. of the extract (B, C and D) respectively experienced weight loss according to the dosage (Table1). The actual cause of the weight loss is not very clear. However, there was a report that certain phytochemicals can cause decreased physical activities and loss of appetite in laboratory animals (Agbafor, 2004). The case of weight loss could be attributed to decreased feed and water intake. Also, similar observations were made in a study where albino rats were treated with ethanolic extract of lemon grass (Agbafor and Akubugwu, 2007). Weight losses in albino rats administered with *Vitex doniana* and *Mucuna pruciens* leaf extracts have been reported (Agbafor and Nwachukwu, 2011).

There was significant ($P < 0.05$) decreases in serum activities of AST, ALP and ALT, as well as in total protein and total bilirubin concentrations in the groups given 200, 400 and 600 mg/kg b.w of aqueous extract of *C. albidum* fresh leaf (B, C and D) compared to the control group A, according to dosage. The decreases in the activities and levels of the liver function markers are indicative that *C. albidum* has a hepatoprotective effect. However, the mechanism of these actions has to be investigated.

The activities of ALT and AST are usually used as indices for liver disease (Shi *et al.*, 2010; Ozer *et al.*, 2008). Higher ALT levels are found in the liver more than other organs, and it is leaked into the extracellular space to the blood when liver injury occurs (Ozer *et al.*, 2008). ALT is a marker for hepatocellular necrosis (Singh *et al.*, 2011), as well as AST, although AST is less specific (Ozer *et al.*, 2008). Apart from the liver, AST is present in various organs such as kidney, brain, heart and muscle; and becomes elevated in the serum when injury occurs in any of the organs (Nathwani *et al.*, 2005). Cholestasis and hepatobiliary effects are detected by elevation in ALP, including bilirubin levels with or without elevation of ALT level (Ramaiah, 2007; Saukkonen *et al.*, 2006). High levels of serum ALP in humans are linked to cholestasis of drug origin (Wright and Vandenberg, 2007). Elevated serum or tissue bilirubin level causes jaundice and occurs in infectious liver diseases like hepatitis or bile-duct obstruction (Edem and Usoh, 2009). Increased bilirubin level is a sign of hepatocellular damage, and its measurement is useful in determining hepatic excretory function, and in haemolytic anaemia assessment. Bilirubin-UDP-glucuronyltransferase catalyzes the conjugation of bilirubin with glucuronic acid in the liver, making it soluble and further excreted into the bile (Saidu *et al.*, 2010). Dehydration may lead to a rise in plasma total protein concentration, including infection-induced elevated plasma immunoglobulin level (Saidu *et al.*, 2010).

Therefore, any substance with the potential to reverse, reduce or prevent the elevations of serum liver enzymes such as AST ALP and ALT, including serum levels of total protein and total bilirubin, is regarded to be hepatoprotective. For example, marked elevations of serum activities of liver enzymes, and elevated levels of serum bilirubin, albumin and total protein were observed in diabetic rats but were reduced and reversed to near normal range after treatment with 0.57 ml/kg b.w. of Ruzu herbal bitters, a hepatoprotective polyherbal mixture (Obasi and Ogugua, 2021). Hence, *C. albidum* can as well be said to be hepatoprotective.

The serum levels of creatinine, sodium, urea, bicarbonate and potassium decreased significantly ($P < 0.05$) in the rat groups given 200, 400 and 600 mg/kg b.w. of *C. albidum* aqueous fresh leaf-extract (B, C and D) according to dosage, but increased significantly ($P < 0.05$) in the normal control group (A). These decreases in the kidney function markers in the treated groups are suggestive that *C. albidum* enhances glomerular filtration rate and normal kidney function.

Creatinine, a major byproduct of muscle metabolism, is excreted by the kidney. Kidney failure is marked by high serum creatinine level (Aliyu *et al.*, 2006). Therefore, creatinine level is essential in assessing healthy kidney, being a byproduct of muscular energy metabolism in the presence of creatine phosphate with adenosine triphosphate (ATP) (Allen, 2012). Increased serum level of urea indicates azotemia. Excess nitrogen arising from protein and amino acid degradation in the liver is converted to urea, which is filtered in the kidney from the blood in the glomerulus, and partially reabsorbed before eventual excretion (Corbett, 2008; Gowda *et al.*, 2010). Serum urea is a vital renal function marker in a case of increased serum urea nitrogen-creatinine for differential diagnosis of pre-renal and acute renal failure conditions (Rosner and Kline, 2006). Sodium and potassium are the main extracellular and intracellular ions respectively, crucial in fluid and electrolyte balance in human body. Serum elevations of sodium and potassium could be associated with renal impairment (Clausen and Poulsen, 2013). Renal failure affects the excretion and levels of sodium and potassium in the blood, resulting in their elevated levels known as hypernatremia (high blood sodium) and hyperkalemia (high blood potassium) respectively.

Reduction of elevated kidney function marker in diabetic rats by a nephroprotective polyherbal mixture, Ruzu herbal bitters, was reported (Obasi and Ogugua, 2020). Therefore, *C. albidum*, based on the observed effects on the kidney markers of albino rats, probably by enhancing kidney function, can be regarded to be nephroprotective.

CONCLUSION

In this study, it was observed that different doses of *Chrysophyllum albidum* aqueous fresh leaf extract caused decreased activities and levels of the liver and kidney function markers assessed. Thus, revealing that aqueous fresh leaf extract of *Chrysophyllum albidum* possesses hepatoprotective and nephroprotective effects, and could be pharmacologically important in managing liver and/or kidney diseases.

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This study has not received any external funding.

CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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