Trop J Nat Prod Res, March 2018; 2(3):126-131 **ISSN 2616-0684 (Print)**
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

In Vivo Antiplasmodial and Toxicological Effects of Extracts of Fruit Pulp of *Chrysophyllum albidium* G. Don (Sapotaceae)

Chibueze P. Ihekwereme*, Chinelo O. Melidem, Ijeoma C. Maduka, Jude N. Okoyeh

Department of Pharmacology & Toxicology, Faculty of Pharmaceutical Sciences, Nnamdi Azikiwe University, Awka, Nigeria.

ARTICLE INFO

Article history:
Received 30 December 2017
Revised 28 February 2018
Accepted 06 March 2018
Published online 07 March 2018

ABSTRACT

Plant parts of *Chrysophyllum albidium* is reported to possess antimalarial properties. However, knowledge gaps still exist in the antimalarial efficacy and safety of some solvent fractions of the fruit pulp. The aim of this study is to explore the antimalarial and toxicological potentials of the methanol extract of the pulp of *C. albidum.* Prophylactic and curative antiplasmodial activities of the methanol extract of the fruit pulp were evaluated using rodent malaria model. Repeated dose toxicity studies were conducted for 28 days using OECD 407 guidelines. The effect of the extract on animal weight, hematological and biochemical parameters were estimated. The oral acute toxic dose of the pulp extract was beyond 5000 mg/kg. The extract demonstrated prophylactic activities at 100 mg/kg (27.94%) and 200 (67.79%) mg/kg doses. The highest curative antimalarial activity was at 15 mg/kg dose on day 4 (72.43 %) and day 7 (83.80 %). The repeated dose toxicity assay did not show that the extract is harmful to the experimental animals. The extract reduced the PCV and hemoglobin level at 15 and 50 mg/kg dose, but not at 150 mg/kg. The Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) levels significantly decreased at the end of the study. This study used a murine model of malaria to demonstrate that the methanol extract of the fruit pulp of *C. albidum* possesses prophylactic and curative properties. The repeated dose toxicity study did not show any toxicity to the experimental animals.

Keywords: *Chrysophyllum albidium*, Parasitemia, Antimalarial, Antiplasmodium.

Introduction

Malaria control has become global due to monumental damages and mortality arising from poor control. The number of people infected with malaria in sub-Sahara Africa is estimated to be 114 million in 2015.[1] Between 2013 and 2015, it was reported that about 510 million insecticide-treated nets (ITN) were distributed in sub-Sahara Africa.[1] There are economic benefits that will be gained from reduced malaria morbidity and mortality.[1]

Malaria is caused by *Plasmodium* species of *malariae, ovale, vivax, and falciparum*. Another species of Plasmodium, *P. knowlesi*, is gradually increasing its burden as a cause of human malaria.[2] Of these, *P. falciparum* causes more maternal and infant mortality than non-*falciparum* infections.[3] The parasite vector, the female Anopheles mosquitoes, plays an important role in transmitting the infection. The parasite spends its lifecycle partly in the mosquito and partly in the human host. The mosquito injects parasites from its salivary glands into the human bloodstream as it attempts to take a blood meal. The parasites then enter the liver cells, reproduce and release one of its forms (merozoites) into the blood. The merozoites invade the red blood cells. Another Anopheles mosquito taking a blood meal from an infected human will ingest these parasites and allow the parasites to complete their life cycle in the mosquito.

Malaria control has many challenges. Vector control measures including the use of barriers such as treated nets and insecticides have been deployed. Insecticide use has suffered vector resistance [4] while the use of nets are associated with physical and psychological discomforts.[5] Some users complain of increased sweating when sleeping under the nets while others feel "caged" and "imprisoned". Parasite control in infected humans is usually by chemotherapy, which on its own has equally recorded treatment failures arising from parasite resistance.[6,7]

Chloroquine, mepacrine, sulphadoxine, pyrimethamine, lumefantrine and quinine are among popular drugs used previously in malaria chemotherapy. Current approved treatment is a combination therapy involving an artemisinin and another antimalarial drug. Resistance to previously used drugs is one key reason for the new treatment approach. Unfortunately, there are reports of failure of the approved treatment regimen.[8] This has created the need for the discovery of new, safe and effective antimalarial drugs. It has been suggested that drugs acting through a new mechanism of action might be preferred.[9]

Use of herbs in disease control predates recorded history. Various herbs and herbal formulations have been used against malaria. Several reports have shown that several plants found in malaria endemic areas possess antimalarial property.[10] These include *Vernonia amygdalina* (Asteraceae), *Spathodea campanulata (*Bignoniaceae*), Ficus mucuso (*Moraceae*), Uvaria puguensis* (Annonaceae), and *Polygonum senegalense* (Polygonaceae).[10]

Chrysophyllum albidum, commonly referred to as the African star apple, belongs to the family Sapotaceae. It grows in several tropical African countries including Nigeria, Uganda, Niger Republic, Cameroon and Cote d' Ivoire where it is found in lowland rain forest zones.[11] In South East Nigeria, where it is called "*Udara*", the fruit is commonly consumed especially by pregnant women. Elsewhere, the plant is used in ethnomedicine for treating malaria.[12] The seed cotyledon possesses antinociceptive, anti-inflammatory and antioxidant activities[13] while the leaf extract contains antiplatelet and hypoglycemic properties.[13] The stem bark also possesses antimicrobial properties.[14,15] The methanol bark extract contains antiplasmodial substances suggesting that antimalarial constituents may be found elsewhere in the plant.[17] Compounds found in

*Corresponding author. E mail: cp.ihekwereme@unizik.edu.ng
Tel: +234 7089817404

Citation: Ihekwereme CP, Melidem CO, Maduka IC, Okoyeh JN. *In Vivo* Antiplasmodial and Toxicological Effects of Extracts of Fruit Pulp of *Chrysophyllum albidium* G. Don (Sapotaceae). Trop J Nat Prod Res. 2018; 2(3):126-131. doi.org/10.26538/tjnpr/v2i3.5

the seed cotyledon include three alkaloids: eleagnine (1, 2, 3, 4-tetrahydro-1-methyl-*β*-carboline); tetrahydro-2-methylharman (1, 2, 3, 4-tetrahydro-1, 2-dimethyl-β-carboline) and skatole (3-methylindole).[16] Stigmasterol, epicatechin, epigallocatechin and epicatechin dimer (procyanidin B5) have been isolated from the stem-bark.[16] Previous preliminary studies have shown that the fleshy pulp of the fruit and ethanol extract of the seed possess antimalarial constituents.[7] The aim of this study is to explore the antimalarial and toxicological potentials of the methanol extracts of the pulp of *C. albidum.*

Materials and Methods

Plant material
Fresh leaves and fruits of *C. albidum* were harvested from a tree in August 2016 in Agulu, Anambra State, Nigeria, and were authenticated in the Department of Pharmacognosy and Traditional Medicine, Faculty of Pharmaceutical Sciences, Nnamdi Azikiwe University, Awka, where a voucher specimen coded PCG474/A/043 was deposited.

Preparation of extract
The fruits were washed to remove debris or soil. The pulps were carefully removed and mashed. The mashed pulp (2 kg) was macerated in methanol for five days with intermittent stirring. The procedure for maceration was as follows: About 400 g of the mashed pulp was weighed and transferred into a clean bottle. About 350 mL of methanol was added to the bottle. The mixture was covered and allowed to stand and was agitated periodically for some minutes. This was done using five different containers which add up to 2 kg. The different portions of the extract were added together. The extract was filtered, concentrated in a water bath at 50ºC and stored in a refrigerator.

Animals
Swiss albino mice of either sex were used for the study. All the animals were obtained from the animal house of the Department of Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, Nnamdi Azikiwe University, Awka. The experimental animals were housed under standard environmental conditions of temperature (26 - 30°C), a 12 h dark–light cycle and allowed free access to drinking water and food pellets (Vital feeds, Nigeria). The animals were acclimatized for seven days before use.

Acute toxicity
The acute toxicity test of the extract was carried out on 13 mice (17 – 28 g, 4-6 weeks old) using Lorke's methods.[18]

Parasite inoculation
P. berghei (NK 65) was obtained from National Institute for Pharmaceutical Research and Development (NIPRD), Abuja, Nigeria. Blood drawn from mice infected with *P. berghei* was used to infect the animals. Standard inoculums of 1 x 10^7 P. berghei infected erythrocytes in 0.2 ml were prepared by diluting the infected blood with 0.9% normal saline. The mice were inoculated by intraperitoneal injection with a blood suspension (0.2 mL) containing 1 x 10^7 parasitized erythrocytes.[19] The parasite was maintained by serial passage of blood on a weekly basis from infected to non-infected mice.

Prophylactic study
A previously described method was used with some modifications.[20] The animals used for the study were 20 albino mice of both sexes, weighing between 11 g – 27 g and 4 - 6 weeks old. The animals were randomly placed in 4 groups (n = 5). Test groups were dosed daily either with 100 mg/kg or 200 mg/kg of the pulp extract. A dose (22.5 mg/kg) of sulphadoxine / pyrimethamine (1500 mg/75 mg) (AmalarTM, Elbe Pharma Nig. Ltd) was administered daily as the positive control while distilled water served as the negative control. The dose of the positive control was determined from the dose used clinically for treating a 70 kg man[21,22]. All drugs were administered orally by gavage once a day for 3 days. On the fourth day, the mice were infected intraperitoneally. After which the parasitemia was monitored at 72 h post infection.

Curative study
At 72 h post infection, when the level of parasitemia was observed to be > 4%, the animals (16 – 26 g, 4 – 6 weeks old) were divided into groups (n = 5). There were 4 test groups which orally received either 15, 50, 150 or 500 mg/kg doses of the pulp extract. Two control groups were used namely, negative (infected and treated with 0.09 mL distilled water), and positive (infected and treated with 8 mg/kg arthermeter/lumefantrine). Lonart (Artemether 20 mg plus Lumefantrine 120 mg), a co-formulation tablet by Greenlife Pharmaceuticals, Nigeria. Blood samples were collected from the animals on day 4 and day 7 post treatment.

Parasitemia monitoring
Parasitemia was monitored using a previously described method [23]. Blood samples were collected from the tip of the tails of the animals. Thin blood films were dried and fixed (for 15 min) using methanol, and subsequently stained with 10 % Giemsa for 25 min. The stained films were washed off using phosphate buffer, pH 7.2 and allowed to dry. The films were then immersed in oil and viewed at 100x magnification. The parasitemia level was determined by counting the number of parasitized erythrocytes out of 100 erythrocytes in random fields of the microscope.[24]

Repeated Dose Toxicity Study
Toxicity study (28-day repeated oral toxicity study) was carried out according to OECD 407 guidelines.[25] The mice (12 – 35 g) were divided into four groups (n = 5). Test groups received daily oral dose of extracts of either 15 mg/kg body weight (low dose), 50 mg/kg bw (intermediate dose) or 150 mg/kg bw (high dose) for 28 days, using a cannula attached to a syringe. The control group received 0.09 mL distilled water. The mice were observed daily for mortality and morbidity until the completion of the experiment. Toxicity was assessed using body weight, hematological and biochemical analysis. Mean body weights of the mice were recorded on day 0, 7, 14, 21 and 28. Weight differences were calculated by subtracting the pretreatment mean weight from the post-treatment mean weight. The resulting value was expressed as a percentage of the pretreatment weight.

Biochemical analysis
Serum alanine aminotransferase (ALT) and serum aspartate aminotransferase (AST) were estimated by the method of Reitman and Frankel[26] using ALT and AST test kit (Span Diagnostic Ltd). The absorbance of the samples was read at 546 nm using a UV spectrophotometer. The concentration values were extrapolated from a graph of concentration against wavelength absorbance of known concentrations.

Statistical analysis
The results were analyzed using GraphPad Instat Version 3.10 for Windows (GraphPad softwares Inc., San Diego, CA, USA). The results were presented as mean ± standard error of mean (SEM) and were subjected to one-way analysis of variance (ANOVA) followed by Dunnett multiple comparison test. Differences between means were considered significant at $P < 0.05$. The percentage parasitemia was calculated using the formula:

$$\% \text{ Parasitemia} = \frac{\text{Total number of parasitized erythrocytes}}{\text{Total number of erythrocytes counted}} \text{ X } 100$$

Average percentage of chemosuppression was calculated using the formula:

$$\% \text{ Suppression} = \frac{\text{Parasitemia in negative control} - \text{Parasitemia in test group}}{\text{Parasitemia in negative control}} \text{X } 100$$

Results and Discussion

Acute toxicity
The yield of the methanol extract of the pulp was 16.44 %. The acute toxic dose of the pulp extract is beyond 5000 mg/kg per oral since all the animals survived even at 5000 mg/kg. This shows that the extract might be considered relatively safe at very high doses. This agrees with the large quantities of the fruit pulp eaten by consumers without any restraints. Previously, the oral LD_{50} of the methanol leaf extract (2739 mg/kg) and the expressed juice from the pulp (> 5000 mg/kg) have been reported.[7,12] The methanol leaf extract is more toxic than the expressed juice from the pulp and methanol pulp extract (oral LD_{50} > 5000 mg/kg). This difference in toxicity between the leaf and fruit pulp reflects the distribution of phytoconstituents in the plant.[7] It also follows that pharmacological activities observed for the plant might be different for different parts of the plant.

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Prophylactic study

The methanol extract showed chemoprophylactic antimalarial activity against *P. berghei* infection in mice with a mean parasitemia of 9.44 ± 1.18 and 4.22 ± 0.26 at 100 and 200 mg/kg doses respectively. When compared to the negative control, it translates to 27.94 and 67.79% parasite inhibition at 100 and 200 mg/kg doses of the extract, respectively (Table 1). Mean parasitemia for the positive and negative control values were 1.74 ± 0.06 (86.72%) and 13.1 ± 0.26 (0.00%), respectively. All the values were statistically significant ($P < 0.01$).

The pulp juice suppressed early infection by 72.97 % at 500 mg/kg[7] while 67.79 % suppression was recorded at 200 mg/kg methanol pulp extract. The drop in the level of parasitemia in the prophylactic study shows the fruit pulp could prevent the development of clinical malaria. Drugs that have demonstrated such activities in preclinical studies are known to be useful clinically.[20] The trend in its prophylactic activity suggests a dose-dependent activity.

Curative study

The crude extract exerted a considerable ($P < 0.01$) curative effect at the tested doses. Mean parasite counts (Tables 2) at day 4 were 8.80 ± 0.24 (500 mg/kg), 5.10 ± 0.73 (150 mg/kg), 4.15 ± 0.76 (50 mg/kg), and 4.00 ± 0.70 (15 mg/kg). Lower counts were obtained on day 7 with mean parasites values of 3.20 ± 0.63 (500 mg/kg), 4.50 ± 0.52 (150 mg/kg), 3.95 ± 0.27 (50 mg/kg), and 2.35 ± 0.23 (15 mg/kg). The parasite percentage inhibition (Table 3) on day 4 and day 7 did not depend on the dose used. Results of day 4 showed an inverse relationship with the dose at the range 50 – 500 mg/kg, whereas on day 7, it appeared to be dose-dependent at that same range. The highest activity on day 4 (72.43%) and day 7 (83.80%) were exerted by the least dose (15 mg/kg) used. This dose inhibited more parasites than the positive control on both days. From the result, the methanol pulp extract had 30.16% (500 mg/kg) at day 4. Previous reports show that at day 4, the expressed juice of the pulp recorded 88.46% (500 mg/kg) and 92.31% (1000 mg/kg).[7] The activity of expressed pulp juice is enhanced even at higher doses. Our result suggests that the methanol pulp extract does not have such property. It has been suggested that the expressed pulp juice, which is recommended traditionally for consumption during pregnancy may be serving as an intermittent preventive therapy against malaria infection.[7]

From the curative study, the extract demonstrated a good to moderate activity even at doses as low as 15 mg/kg.[10] Higher doses gave lower parasite clearance values. The doses used seem to suggest the extract might have potent activity at much lower doses.

Table 1: Chemoprophylactic antimalarial activity of the methanol extract of the pulp of *Chrysophyllum albidium*.

Treatment Group	Dose	Parasite Count	% Suppression
Group 1 (pulp)	100 mg/kg	9.44 ± 1.18^{xx}	27.94
Group 2 (pulp)	200 mg/kg	4.22 ± 0.26^{xx}	67.79
Positive control (S/P)	22.5 mg/kg	1.74 ± 0.06^{xx}	86.72
Negative control	Water	13.1 ± 0.26	0.00

Values are expressed as means ± SEM, n = 5, ^{xx} = significant at $p < 0.01$ compared to the negative control.

Repeated Dose Toxicity Study

Consumption of toxic substances or anti-nutritive phytoconstituent usually reduce total body weights, food consumption and activity. It may also alter circulating leukocyte counts.[27] This occurs due to the presence of substances that are inhibitory or poisonous to normal metabolic activities.[28] None of the animals died. There was no morbidity observed in any of the animals.

Mean Body Weight

The result of the body weight measurement is presented in Table 4. The body weight of the control and group treated with 15 mg/kg increased significantly ($P < 0.05$) but the groups treated with 50 mg/kg and 150 mg/kg did not increase significantly as shown in tables 4 and 5. The percentage weight difference showed that as the dose increases there was reduction in body weight. It does appear the extract did not affect the terminal weight of the animal. This opinion is supported by the values obtained from all the groups except the 150 mg/kg group. Their respective mean weights appear to normalize across the different dose levels at about the 28th day of treatment. Even though the result of the 150 mg/kg dose showed a negative growth, it could be that the animals were already mature at the pretreatment stage unlike the others and hence was not expected to gain weight. The slight weight loss (7.72%) may be due to age and may not be taken to suggest the extract is toxic.

Hematological analysis

The result of the PCV shows there were reduction in value at 15 and 50 mg/kg which was significant from the 14th day (Table 5). There was no observable effect of the extract at the 150 mg/kg dose. The same trend was observed in the hemoglobin level (Table 6). There were reductions in HB values at 15 and 50 mg/kg and there was no observable effect of the extract at the 150 mg/kg dose. The effect of the extract on PCV and hemoglobin share similar trends. The reduction in PCV on Day 14 at 15 and 50 mg/kg (but not 150 mg/kg) dose suggests this effect may be dose related. The WBC count shows there is a general increase for all the test and control groups. This general increase implies that the extract may not adversely affect the WBC count.

Table 7 shows that there is a general increase in the WBC count for all the test and control groups which began from day 7 up till the 28th day. On Day 28, the negative control had the highest count (5.66 ± 0.56) while the 15 mg/kg group had the lowest count (4.11 ± 0.17).

Biochemical analysis

The Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) significantly decreased at the end of the study (Tables 8 and 9). The results on Day 0 were compared with day 14 and day 28. There was no significant difference on day 14 for all the groups, unlike day 28 where there was a significant difference ($P < 0.01$) for most of the groups. However, for AST treated with 50 mg/kg and 150 mg/kg there was no difference ($P < 0.01$) throughout the study when compared to day 0. Increased ALT levels in the blood are associated with hepatocellular damage, while increased blood AST level is less specific than ALT as an indicator of liver problem.[29] The decrease in the levels of the liver enzymes suggests the extract is safe for the organ. This is similar to the ethanol leaf extract which doses (250 - 1000 mg/kg) significantly reduced ($p < 0.05$) plasma levels of AST and ALT.[13] This is unlike the fractions of the methanol leaf extract which were observed to be toxic to the liver.[12]

Table 2: Curative antimalarial activity of the methanol extract of the fruit pulp of *Chrysophyllum albidium.*

Treatment	Dose	Mean parasite count		
		Day 0	Day 4	Day 7
Group 1	500 mg/kg	12.60 ± 0.24	8.80 ± 0.24^{xx}	3.20 ± 0.63^{xx}
Group 2	150 mg/kg	15.00 ± 0.84	5.10 ± 0.73^{xx}	4.50 ± 0.52^{xx}
Group 3	50 mg/kg	12.60 ± 0.40	4.15 ± 0.76^{xx}	3.95 ± 0.27^{xx}
Group 4	15 mg/kg	14.51 ± 0.88	4.00 ± 0.70^{xx}	2.35 ± 0.23^{xx}
Positive control (A/L)	8 mg/kg	13.65 ± 0.40	4.95 ± 0.44^{xx}	3.70 ± 0.37^{xx}
Negative control	Water	10.70 ± 0.26	10.50 ± 0.27^{ns}	10.45 ± 0.63^{ns}

Values are expressed as means ± SEM, n = 5, ^{xx} = significant at $p < 0.01$ compared to day 0, ns = not significant at $p < 0.01$ compared to day 0. A/L - Artemether 20 mg plus Lumefantrine 120 mg (a co-formulation tablet).

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Table 3: Percent chemosuppression (Curative) of malaria parasite by extract *on* day 4 and day 7.

Group	Day 4 (%)	Day 7 (%)
Group 1 (500 mg/kg)	30.16	74.60
Group 2 (150 mg/kg)	66.00	70.00
Group 3 (50 mg/kg)	67.06	68.65
Group 4 (15 mg/kg)	72.43	83.80
Positive control	63.74	72.89
A/L (8 mg/kg)		
Negative control	1.87	2.34

A/L - Artemether 20 mg plus Lumefantrine 120 mg (a co-formulation tablet).

There seems to be something unique about the 15 mg/kg dose. In the curative study, it recorded the highest parasite clearance rate both at day 4 (72.43%) and day 7 (83.80%). It showed more activity than the positive control drug. It also caused the lowest mean body weight (22.93 ± 1.74) recorded on day 28, lower than the negative control (25.65 ± 1.51). At the 15 mg/kg dose, the extract significantly reduced the PCV on days 14, 21 and 28 unlike at 50 mg/kg where there was a significant reduction only on days 14 and 21. A similar trend was seen on the HB level. On the other hand, the 15 mg/kg group had the lowest WBC count from day 14 till day 28.

Table 4: Effect of methanol extract of the fruit pulp of *C. albidium* pulp on mean body weight (g).

Groups	Day 0	Day 7	Day 14	Day 21	Day 28	% weight difference on Day 28
Control	12.86 ± 0.29	19.40 ± 0.96**	22.12 ± 1.01**	22.12 ± 0.95**	25.65 ± 1.51**	99.45
15 mg/kg	14.90 ± 0.33	19.36 ± 0.38**	22.02 ± 0.70**	21.70 ± 1.20**	22.93 ± 1.74**	53.69
50 mg/kg	20.72 ± 1.08	24.02 ± 1.66	25.63 ± 1.67	24.62 ± 1.10	24.85 ± 2.10	19.76
150 mg/kg	31.34 ± 1.22	25.86 ± 2.75	26.84 ± 2.47	27.34 ± 2.75	28.92 ± 2.64	-7.72

Values are expressed as means ± SEM, n = 5, ^{xx} = significant at $p < 0.01$ compared to day 0.

Table 5: Effect of methanol extract of the fruit pulp of *C. albidium* on Packed Cell Volume.

Groups	Day 0 (%)	Day 7 (%)	Day 14 (%)	Day 21 (%)	Day 28 (%)
Control	33.40 ±1.08	33.20 ± 0.80	34.20 ± 2.48	34.00 ± 1.30	31.60 ± 2.23
15 mg/kg	34.20 ± 0.73	32.20 ± 1.20	30.80 ± 0.37*	35.20 ± 1.02	27.20 ± 0.66**
50 mg/kg	34.60 ± 0.81	33.60 ± 1.29	26.00± 1.30**	29.40 ± 1.50*	30.40 ± 0.81
150 mg/kg	33.20 ± 0.86	31.80 ±1.91	32.00 ± 0.37	35.60 ± 0.75	33.00 ± 0.75

Values are expressed as means ± SEM, n = 5, ** = significant at $p < 0.01$ compared to day 0, *= significant at $p < 0.05$ compared to day 0

Table 6: Effect of methanol extract of the fruit pulp of *C. albidium* on hemoglobin level.

Groups	Day 0 (%)	Day 7 (%)	Day 14 (%)	Day 21 (%)	Day 28 (%)
Control	11.13 ± 0.36	11.26 ± 0.27	11.40 ± 0.83	11.33 ± 0.43	10.33 ± 0.95
15 mg/kg	11.40 ± 0.24	10.73 ± 0.40	10.27 ± 0.13*	11.73 ± 0.34	9.25 ± 0.16**
50 mg/kg	11.53 ± 0.27	11.20 ± 0.43	8.67 ± 0.44**	9.80 ± 0.50*	10.17 ± 0.35
150 mg/kg	11.07 ± 0.29	10.6 ± 0.64	10.60 ± 0.13	12.13 ± 0.25	11.20 ± 0.25

Values are expressed as means ± SEM, n = 5, ** = significant at $p < 0.01$ compared to day 0, *= significant at $p < 0.05$ compared to the day 0.

Table 7: Effect of methanol extract of the fruit pulp of *C. albidium* on white blood cells.

Groups	Day 0 ($x10^9$/L)	Day 7 ($x10^9$/L)	Day14 ($x10^9$/L)	Day21 ($x10^9$/L)	Day28 ($x10^9$/L)
Control	1.46 ± 0.08	3.07 ± 0.33*	3.7 ± 0.22**	5.50 ± 0.65**	5.66 ± 0.56**
15 mg/kg	1.95 ± 0.06	3.29 ± 0.16**	2.75 ± 0.16**	3.93 ± 0.05**	4.11 ±0.17**
50 mg/kg	1.52 ± 0.08	4.43 ± 0.19**	3.21 ± 0.19**	4.10 ± 0.20**	4.71 ±0.19**
150 mg/kg	1.50 ± 0.09	3.42 ± 0.11**	4.13 ± 0.210**	5.30 ± 0.59**	5.34 ± 0.53**

Values are expressed as means ± SEM, n = 5, ** = significant at $p < 0.01$ compared to day 0, *= significant at $p < 0.05$ compared to day 0

Table 8: Effect of methanol extract of the fruit pulp of *C. albidium* on Alanine aminotransferase (ALT)

Groups	Day 0 (U/L)	Day 14 (U/L)	Day 28 (U/L)
Control	24.02 ±2.28	22.55 ±1.10	11.40 ±0.70**
15 mg/kg	31.21 ±3.92	26.90 ±0.82	14.54 ±5.59**
50 mg/kg	21.66 ±2.12	18.77 ±1.24	13.02 ±1.53**
150 mg/kg	21.24 ±1.63	19.66 ±1.27	10.43 ± 0.77**

Values are expressed as means ± SEM, n = 5, ** = significant at $p < 0.01$ compared to day 0.

Table 9: Effect of methanol extract of the fruit pulp of *C. albidium* on Aspartate aminotransferase (AST)

Groups	Day 0 (U/L)	Day 14 (U/L)	Day 28 (U/L)
Control	84.48 ±2.76	73.72 ± 9.67	32.53 ± 3.56**
15 mg/kg	85.57 ± 2.94	78.46 ± 4.15	40.95 ± 3.60**
50 mg/kg	59.04 ± 4.36	49.60 ± 7.90	47.92 ± 13.79
150 mg/kg	45.79 ± 6.26	42.86 ± 5.19	30.96 ± 0.72

Values are expressed as means ± SEM, n = 5, ** = significant at $p < 0.01$ compared to day 0,

Conclusion

In conclusion, this study has shown that the methanol extract of the fruit pulp of *C. albidum* possesses prophylactic and curative properties against murine models of malaria. The repeated dose toxicity study showed that the extract is not harmful to the experimental animals. These findings show the consumers of the fruit could be enjoying some level of protection against malaria infection. Further studies to isolate and characterize the antimalarial principles as well as elucidate its mechanism of antimalarial action is recommended.

Conflict of interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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