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Antiplasmodial Activity of Combined Methanol Leaf Extracts of *Dacryodes edulis* and *Ficus capensis* in Swiss Albino Mice

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Abstract

Dacryodes edulis and *Ficus capensis* are medicinal plants commonly utilized in traditional Nigerian medicine to manage malaria and other ailments. This study evaluated the *in vivo* antiplasmodial activity of combined methanol leaf extracts of these plants against chloroquine-sensitive *Plasmodium berghei* NK-65 in Swiss albino mice using Peter's 4-day suppressive test. Thirty -six male mice were randomly divided into six groups (n = 6): Group 1 (normal control) received the vehicle only; Group 2 (negative control) was infected without treatment; Group 3 (positive control) received chloroquine (10 mg/kg/day), while Groups 4, 5, and 6 received the extract at doses of 250, 500, and 1000 mg/kg/day, respectively. Treatment was administered orally once daily. The combined extract significantly ($p < 0.05$) suppressed parasitaemia in a dose-dependent manner, achieving 60.48%, 69.07%, and 77.84% suppression, respectively, compared to 96.32% in the chloroquine-treated group. Biochemically, the extract reversed infection-induced elevations in serum liver enzymes (ALT, AST, ALP), with ALT levels reduced by 35.6% at a dose of 500 mg/kg. It also significantly decreased malondialdehyde (MDA) levels and restored reduced glutathione (GSH) levels in liver and brain tissues. Hematological indices such as hematocrit and red blood cell count were significantly improved at 250 and 500 mg/kg, though the highest dose (1000 mg/kg) led to elevated white blood cell counts, indicating possible immune stimulation. These findings provide scientific support for the traditional use of these plants in malaria treatment and suggest their potential as effective and affordable alternatives to conventional antimalarial therapies. Future studies should focus on evaluating the long-term safety profiles to facilitate the development of these agents into clinically viable antimalarials.

Keywords: Chloroquine, *Dacryodes edulis*, *Ficus capensis*, Malondialdehyde, *Plasmoduim berghei.*

1.0 Introduction

Malaria remains a significant public health challenge in many tropical and subtropical regions, particularly in sub-Saharan Africa, Asia, and Latin America, where it significantly contributes to morbidity and mortality [1]. Despite global efforts to control and eradicate malaria, recent statistics indicate approximately 247 million cases annually, resulting in over 619,000 deaths globally, with the majority being children under five years old in Africa [2]. The situation is exacerbated by the emergence and widespread resistance of *Plasmodium* parasites, especially *Plasmodium falciparum*, to conventional antimalarial drugs such as chloroquine, quinine, and, more recently, artemisinin-based combination therapies (ACTs) [2,3]. This scenario underscores the urgent need to identify and develop novel antimalarial agents with different modes of action, improved efficacy, and reduced side effects.

Plants have historically provided a rich source of bioactive compounds, many of which serve as templates for modern pharmaceuticals, including antimalarials [4]. Indigenous medicinal plants are widely used in traditional medicine across Africa

for treating malaria due to their availability, affordability, and cultural acceptability [5,6]. Current research focuses on plants traditionally used to combat malaria, particularly those rich in alkaloids, flavonoids, terpenoids, tannins, and glycosides—compounds known for their antiplasmodial and antioxidant properties [7-9].

Dacryodes edulis (African pear) and *Ficus capensis* (Wild fig) are prominent in Nigerian ethnomedicine. *D. edulis* is traditionally used to treat fever, dysentery and inflammation [10], with demonstrated pharmacological activities including antioxidant, antimicrobial and antisickling effects [10,11]. Similarly, *F. capensis* ("Opoto") is used traditionally for anemia, jaundice and infectious diseases [12], with reported antioxidant, anti-inflammatory and erythropoietic activities [13].

Despite their promising traditional uses, critical research gaps persist regarding *Dacryodes edulis* and *Ficus capensis*. Most prior studies have focused on individual plant extracts, overlooking the potential synergistic effects of combined therapy, which aligns more closely with traditional medicinal practices. Additionally, there is limited data on their comprehensive impact on malaria-induced oxidative stress and hepatotoxicity, and the specific bioactive compounds responsible for their antiplasmodial activity remain poorly characterized. This study addresses these gaps by investigating the combined antiplasmodial efficacy of methanol leaf extracts of *D. edulis* and *F. capensis* against *Plasmodium berghei* in mice. It evaluates dose-dependent effects on parasitemia suppression, oxidative stress markers such as malondialdehyde (MDA) and reduced glutathione (GSH), and liver function parameters. Furthermore, it characterizes the phytochemical profile of the combined extracts, thereby providing scientific validation for their traditional use in malaria management and in ongoing efforts to combat drug-resistant malaria through plant-based drug discovery.

2.0 Materials and Methods

2.1 Plant Collection and Authentication

Fresh *Dacryodes edulis* and *Ficus capensis* leaves were collected from a private farm in June 2017 from Uwasota, Benin City, Edo State, Nigeria. A taxonomist at the Department of Pharmacognosy, University of Benin, Benin City, Nigeria, authenticated the plants, where voucher specimens (UB-H-265 and UB-H-266) were deposited in the departmental herbarium for future reference.

2.2 Preparation of Plant Extracts

The freshly collected leaves were washed to remove debris and air-dried in the shade at room temperature (25 ± 2°C) until a constant weight was achieved. The dried leaves were hand-crushed into coarse pieces. Subsequently, 500 g of the crushed material (equal proportions of each plant powder) were macerated in 2 L of absolute methanol for 72 hours with intermittent shaking to ensure exhaustive extraction. The methanol extract was filtered through Whatman No.1 filter paper, and the filtrate was concentrated under reduced pressure at 45°C using a rotary evaporator. The resultant crude extract was weighed, and the percentage yield was calculated. The extract was then stored in airtight containers at 4°C, protected from moisture and light, until further use.

2.3 Phytochemical Screening

Qualitative phytochemical analysis of the methanol leaf extracts was performed using the standard protocols described by Trease and Evans as reported by Okugbo et al [14,15]. The extracts were screened for alkaloids (Wagner's and Dragendorff's reagents), tannins, saponins, reducing sugars, cardiac glycosides, flavonoids, terpenoids, steroids, and anthraquinones.

2.4 Experimental Animals

Male Swiss albino mice (Mus musculus, 18–30 g) were obtained in July 2017 from the Nigerian Institute of Medical Research (NIMR), Lagos, Nigeria. The mice were housed under standard laboratory conditions (temperature: 27 ± 2°C, relative humidity: ~70%, and a 12-hour light/dark cycle) and were provided with standard pelleted Growers mash from Olams Chikun Feeds Ltd, Lagos State, and water *ad libitum*. All experimental protocols involving animal handling and care adhered strictly to guidelines specified by the Institutional Animal Ethics Committee of the University of Benin, in alignment with internationally accepted standards as provided by the Canadian Council on Animal Care Guidelines and Protocol Review [16]. Animals were allowed to acclimatize for one week before experimentation.

2.5 Parasite Strain and Inoculation

The chloroquine-sensitive *Plasmodium berghei* NK-65 strain was obtained from the Nigerian Institute of Medical Research (NIMR), Lagos. Donor mice with 20–30% parasitaemia were anesthetized, and parasitized blood was collected by cardiac puncture into sterile heparinized tubes. The blood was diluted with sterile normal saline to achieve an inoculum containing approximately 1×10^7 parasitized erythrocytes per 0.2 mL. Each mouse was inoculated intraperitoneally with 0.2 mL of the prepared inoculum.

2.6 Acute Toxicity Study and Determination of Median Lethal Dose (LD50)

The acute toxicity of the extracts was determined to establish their median lethal dose (LD50) using Lorke's method [17]. with some modifications. The test was carried out in two phases.

Phase I: Nine (09) mice were divided into three groups (A, B, and C) of three mice each. The three groups were administered orally with graded concentrations (10, 100 and 1000 mg/kg body weight, respectively) of *Dacryodes edulis* leaf extracts. The animals were monitored for signs of toxicity such as tremors, weakness, loss of appetite and even death for 48 hours. Observation was continued for 7 days. This was also done for *Ficus capensis* leaf extract.

In the phase 2 experiment, Nine (09) mice were also divided into three groups (A, B, and C) of three mice each. The three groups were administered orally with graded doses of 1600, 2900 and 5000 mg/kg body weight of *Dacryodes edulis* leaf extracts.

This test was also done for the *Ficus capensis* leaf extracts.

All the animals were monitored for pain, distress, behavioral alterations and most importantly, death for 48 hours. Observation was continued for the next 14 days.

2.7 Evaluation of Antiplasmodial Activity (Suppressive Test)

Antiplasmodial activity was evaluated using Peters' standard 4-day suppressive test [18]. Mice were randomly divided into six groups of six mice each (n = 6):

Group 1: Normal control (non-parasitized, non-treated group., treated orally with 0.5 % Carboxymethylcellulose vehicle only).
Group 2: Negative control (Parasitized, non-treated group).
Group 3: Positive control (Parasitized, treated with chloroquine at 10 mg/kg/day).

Groups 4, 5, and 6: Parasitized mice treated with combined methanol leaf extracts at 250, 500 and 1,000 mg/kg/day, respectively.

On the first day of the experiment (termed 'day 0'), all mice were injected intraperitoneally with Plasmodium berghei NK 65-infected erythrocytes, except the mice in the non-parasitized, non-treated group.

Two hours after the infection of mice, the uninfected control (non-parasitized, non-treated, group 1) and the negative control (parasitized, non-treated- group 2) were given 0.5 mL Carboxyl methyl cellulose (CMC- 0.5%). The positive control (group 3) received 10mg/kg chloroquine. The three test groups were administered 250mg/kg, 500mg/kg, and 1000mg/kg of methanol extracts of the combined extracts for groups 4, 5, and 6, respectively. All administration was done orally by means of a gavage and was done for four consecutive days ('day 0- day 3').
On 'day 4' of the experiment, blood was collected from the tails of the mice and smeared onto a microscopic slide to make a thin film [19]. The blood films were allowed to dry, fixed with methanol (100%), and stained with Giemsa (10%) for 10 minutes. The stained films were then washed with phosphate buffer (pH 7.2) and allowed to dry [20].
The slides were then examined microscopically using ×100 magnification in oil immersion [20]. The parasitaemia was determined by counting a minimum of eight fields per slide with a minimum of 100 red blood cells (RBC) per field.

The percentage parasitaemia was expressed as mean ± SEM.

Mean parasitaemia = Number of mice in the group /Sum of parasitaemia values

The percentage parasitaemia was calculated using the modified Peter and Robinson [18] formula:

$$\%\ Parasitemia = \frac{Number\ of\ parasitized\ RBC}{Total\ Number\ of\ RBC}\ x\ 100$$

The average suppression of parasitaemia was calculated by comparing the average percentage parasitaemia in each group with that of negative control, using the formula of Abosi and Raseroke [21]:

$$A = \frac{(B - C)}{B}\ x\ 100$$

Where A = Average percentage suppression of parasitaemia

B = Average percentage parasitaemia in the negative control group

C = Average percentage parasitaemia in the test group

2.8 Sample Collection (Blood)

On day 5 of the experiment, animals were fasted overnight and sacrificed by cervical dislocation. Samples were then collected. Blood (1.8mL) was collected from the abdominal aorta and the heart via a 2mL syringe into plain sterile bottles and EDTA tubes (for hematological analysis). Blood samples in plain tubes were allowed to stand for 30 minutes to clot and centrifuged at 1,000g for 10 minutes at room temperature to obtain serum for biochemical assays.

2.9 Hematological Analysis

The samples were gently mixed to prevent clotting and immediately analyzed using an automated hematology analyzer (Mindray BC-2800Vet). The following hematological parameters were evaluated:

Packed Cell Volume (PCV/HCT) – determined using the microhematocrit method [22]. Capillary tubes filled with EDTA-treated blood were centrifuged at 12,000 rpm for 5 minutes, and PCV/HCT values were read using a hematocrit reader.

Hemoglobin (Hb) Concentration – estimated using the cyanmethemoglobin method [23]. Blood was mixed with Drabkin's reagent, allowed to stand for 10 minutes, and absorbance was read at 540 nm.

Red Blood Cell (RBC) Count and White Blood Cell (WBC) Count – obtained directly from the automated hematology analyzer [23].

2.10 Tissue Sample Collection

Liver and brain tissues were excised, rinsed in ice-cold physiological saline (0.9%), weighed, and homogenised (10% w/v for liver, 10% w/v for brain) in cold physiological saline. The homogenates were centrifuged at 4,000 rpm for 10 minutes, and the resulting supernatants were stored at 4°C until further biochemical analysis.

2.11 Biochemical Analysis

Malondialdehyde (MDA) levels, indicative of lipid peroxidation, were quantified using standard spectrophotometric methods [24]. Reduced glutathione (GSH) levels were assessed using the Ellman method [25]. Liver function tests, including alanine aminotransferase (ALT) [26], aspartate aminotransferase (AST) [26], alkaline phosphatase (ALP) [27], and Gamma-glutamyl transferase (GGT) [28], were measured spectrophotometrically using commercially available assay kits (Randox Laboratories, UK) following manufacturer protocols.

2.12 Data Analysis

Values were expressed as mean ± standard error of mean (SEM). Statistical comparisons between groups were performed using one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test to determine significant differences. Statistical significance was set at $p < 0.05$, and analyses were conducted using GraphPad Prism software (version 8.0, GraphPad Inc., USA).

3.0 Results

3.1 Phytochemical Analysis

Phytochemical screening of the combined methanol leaf extracts of *Dacryodes edulis* and *Ficus capensis* revealed the presence of cardiac glycosides, terpenoids, alkaloids, flavonoids, tannins, reducing sugars, and steroids. Notably, saponins were detected exclusively in *F. capensis* extract, while anthraquinones were absent in both extracts (Table 1).

Table 1: Phytochemical constituents of combined leaf extracts of *Ficus capensis* and *Dacryodes edulis*

Phytochemicals	*Ficus capensis*	*Dacryodes edulis*	*D.edulis + F.capensis*
Alkaloids (Wagner)	+	++	++
Alkaloids (Dragendroff)	++	++	++
Cardiac glycosides	++	++	++
Flavonoids	++	++	++
Reducing Sugars	++	++	++
Saponins	++	-	++
Steroids	++	+	++
Tannins	+++	+++	+++
Terpenoids	++	+++	+++
Anthraquinones	-	-	-

(Key: + trace; ++ moderate; +++ high; – absent)

3.2. Acute Toxicity Study Results

The oral administration of a single dose of the methanol extracts of either DE or FC, at different concentrations, to mice did not cause any visible signs of toxicity. No mortality was recorded at any dose used up to 72 hours after oral administration. The median lethal dose (LD50) of the extracts was estimated to be > 5,000 mg/kg body weight for both DE and FC.

3.2.1 Antiplasmodial Activity

The antiplasmodial activity of the extracts is shown in Table 2. The combined methanol leaf extracts demonstrated significant ($p < 0.05$) dose-dependent antiplasmodial activity against chloroquine-sensitive *Plasmodium berghei* NK-65 in infected mice. Percentage suppression of parasitaemia after five days of oral treatment at doses of 250, 500, and 1000 mg/kg/day was 60.48%, 69.07%, and 77.84%, respectively, compared to the untreated infected (negative control) group. The positive control (chloroquine, 10 mg/kg/day) showed the highest suppression at 96.32%.

Table 2: Antiplasmodial suppressive effects of the combined methanol leaf extract of *Ficus capensis* and *Dacryodes edulis*

Group	Mean Parasitaemia %	% Suppression
Negative Control	25.00	0.92
250 mg/kg body weight	9.88	60.48
500 mg/kg body weight	7.75	69.07
1000 mg/kg body weight	5.54	77.84
Chloroquine	0.92	96.32

3.3 Hematological Parameters

Figure 1 reveals the effects of the extracts on hematological parameters. Malaria infection significantly ($p < 0.05$) decreased hematocrit (HCT), red blood cell (RBC) count, and hemoglobin (Hb) levels, whereas white blood cell (WBC) counts were significantly increased in untreated infected mice compared to normal controls. Treatment with the extracts at 250 and 500

mg/kg/day significantly ($p < 0.05$) reversed these changes, restoring HCT, RBC, and Hb levels closer to normal. However, at 1000 mg/kg/day, a significant ($p < 0.05$) elevation in WBC count persisted, indicating possible immune response stimulation or mild extract-induced stress at higher doses.

3.4 Liver Function Enzyme Activities

Figure 2 shows the effects of the extracts on the liver function enzyme activities. The infection results in a significant ($p < 0.05$) elevation in serum levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Alkaline phosphatase (ALP) activities were compared to those of the normal control group, indicating hepatic impairment. Treatment with combined extracts significantly ($p < 0.05$) reduced these enzyme activities in a dose-dependent manner, indicating a potential hepatoprotective effect. However, chloroquine treatment increased gamma-glutamyl transferase (GGT) considerably, suggestive of mild drug-induced hepatotoxicity.

3.5 Oxidative Stress Indices

Figures 3 and 4 show the effects of the extracts on oxidative stress indices. Malaria infection significantly ($p < 0.05$) increased malondialdehyde (MDA) levels in liver and brain tissues, indicative of elevated lipid peroxidation, while significantly reducing reduced glutathione (GSH) levels, reflecting oxidative stress Treatment with the combined extracts at doses of 250 and 500 mg/kg/day significantly ($p < 0.05$) decreased MDA levels and elevated GSH content, ameliorating oxidative stress induced by infection. The highest dose (1000 mg/kg/day) showed less pronounced antioxidant effects, suggesting potential dose-related limitations.

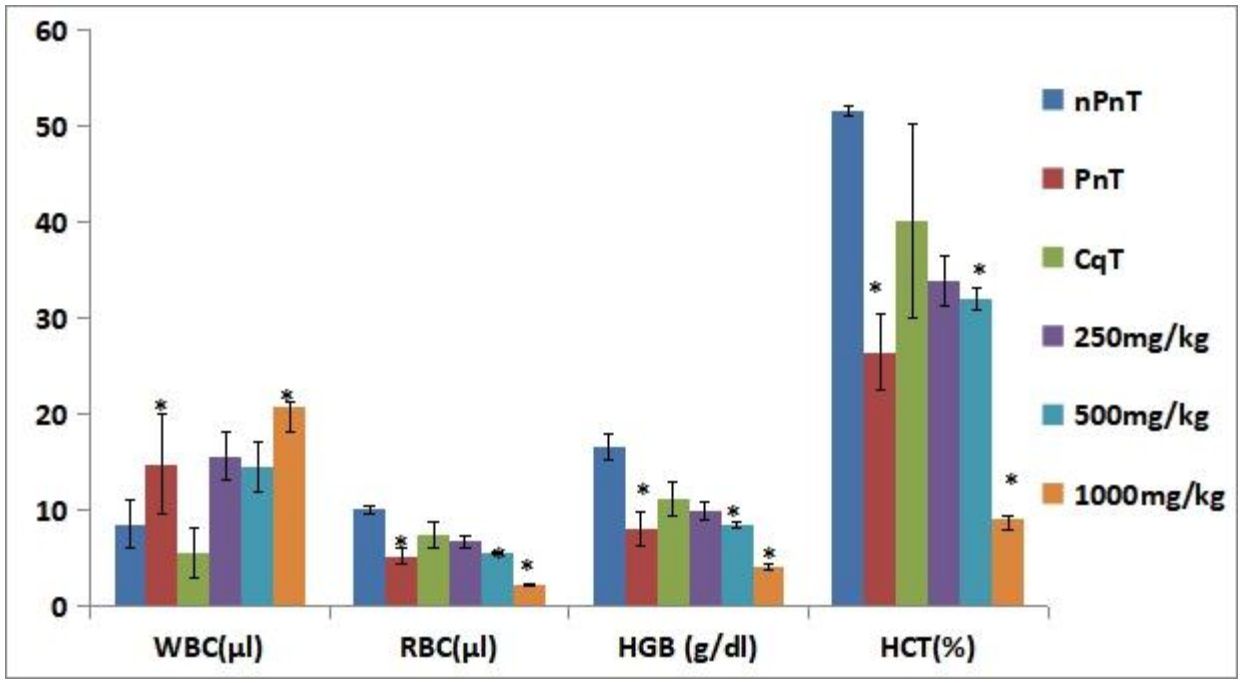


Figure 1: Effects of combined extracts on hematological parameters in *P. berghei*-infected mice. Data expressed as mean ± SEM (n=6). nPnT: Non-parasitized non-treated control; PnT: Parasitized non-treated; CqT: Chloroquine-treated. * Indicates significant difference ($p < 0.05$) compared to nPnT; # indicates significant difference compared to PnT.

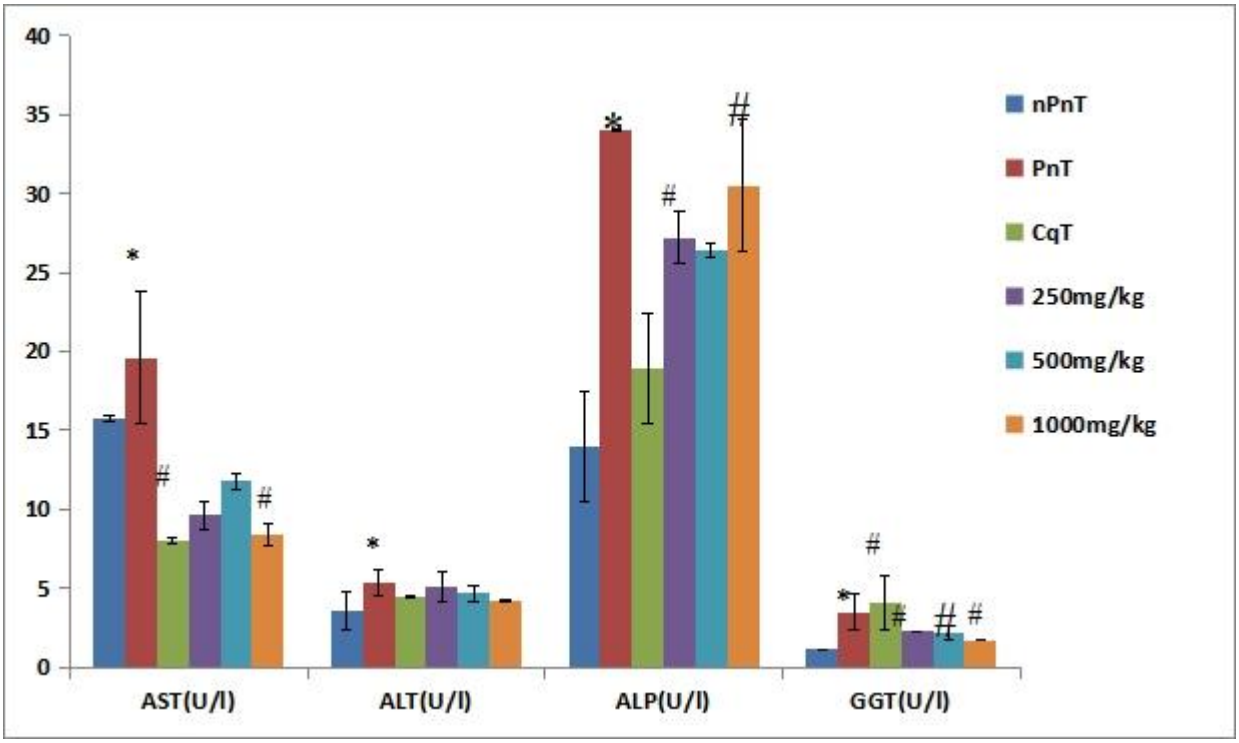


Figure 2: Effects of combined extracts on serum liver enzyme activities in *P. berghei*-infected mice. Data presented as mean ± SEM (n=6). nPnT: Non-parasitized non-treated control; PnT: Parasitized non-treated; CqT: Chloroquine-treated. * Indicates significant difference ($p < 0.05$) compared to nPnT; # indicates significant difference compared to PnT.

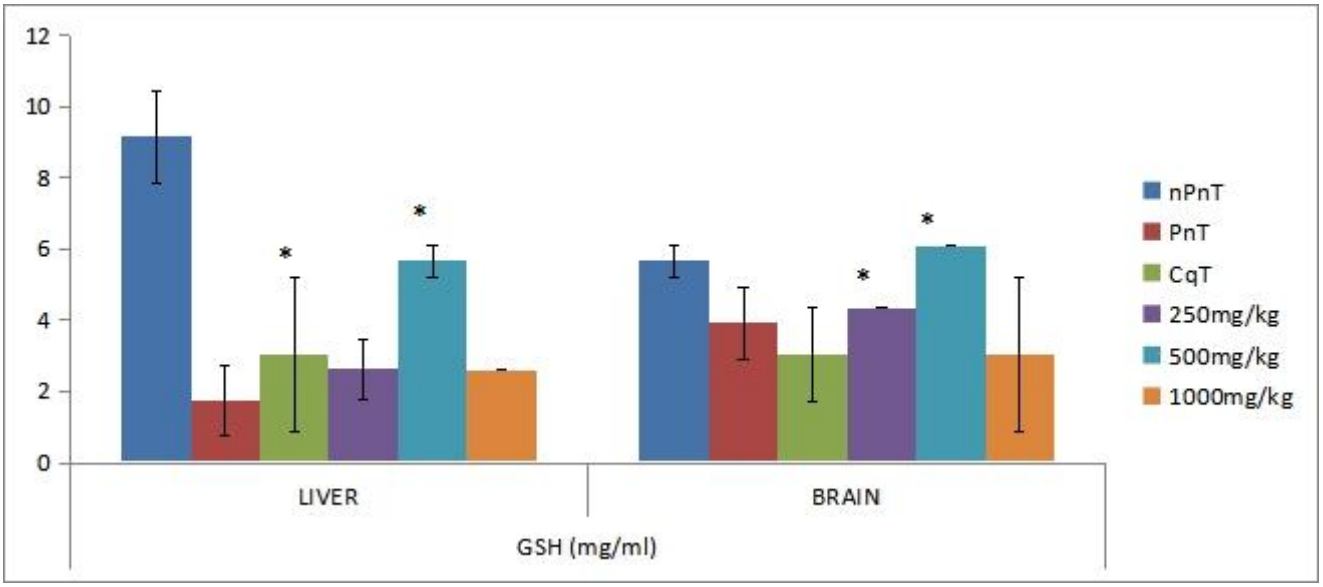


Figure 3: Effects of combined extracts on malondialdehyde (MDA) levels in liver and brain tissues of *P. berghei*-infected mice. Data presented as mean ± SEM (n=6). nPnT: Non-parasitized non-treated control; PnT: Parasitized non-treated; CqT: Chloroquine-treated. * Indicates significant difference ($p < 0.05$) compared to PnT.

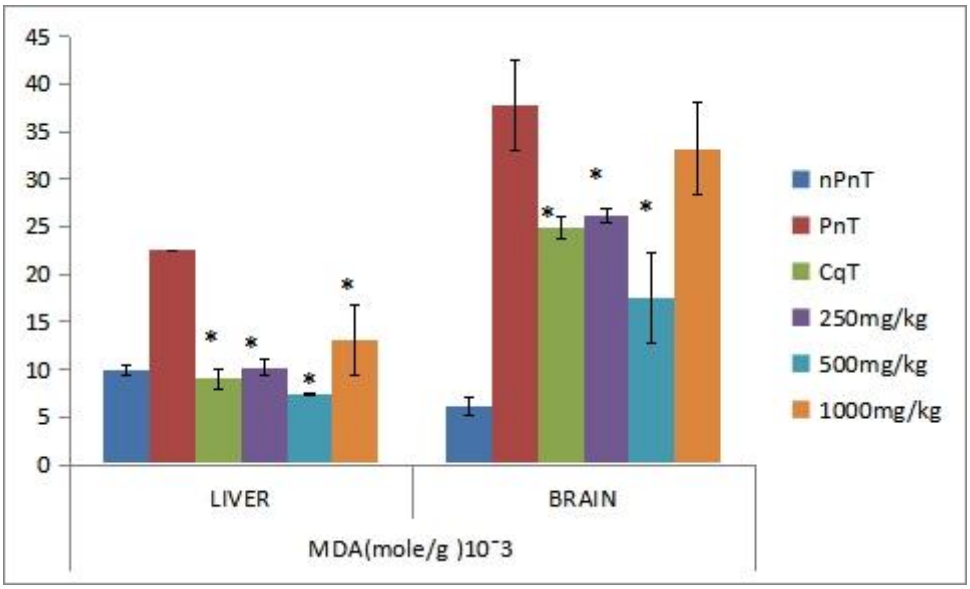


Figure 4: Effects of combined extracts on reduced glutathione (GSH) levels in liver and brain tissues of *P. berghei*-infected mice. Data presented as mean ± SEM (n=6). nPnT: Non-parasitized non-treated control; PnT: Parasitized non-treated; CqT: Chloroquine-treated. * Indicates significant difference ($p < 0.05$) compared to PnT.

4.0 Discussion

This study evaluated the antiplasmodial efficacy, hepatoprotective, and antioxidant potentials of combined methanol leaf extracts of *Dacryodes edulis* and *Ficus capensis* in mice infected with chloroquine-sensitive *Plasmodium berghei* NK-65.

Phytochemical screening revealed key secondary metabolites—alkaloids, flavonoids, terpenoids, cardiac glycosides, tannins, and reducing sugars—all of which have been previously associated with antimalarial and antioxidant activities [29–31]. The combined methanol leaf extract of *D. edulis* and *F. capensis* was confirmed to contain several secondary metabolites, notably alkaloids, flavonoids, terpenoids, and cardiac glycosides.

The antiplasmodial activity observed in many plants has been attributed to the single or combined action of these metabolites. These phytochemicals have also been linked to antiplasmodial effects via hemozoin inhibition and parasite membrane disruption [32]. The presence of these phytochemicals supports the ethnomedicinal use of both plants in traditional treatments against malaria and related symptoms.

During early infection, oral administration of extracts at 250 and 500 mg/kg/day concentrations caused chemosuppression of 60.47% and 69.07%, respectively, which was statistically significant ($P < 0.05$) compared to the negative control. The standard drug chloroquine (10 mg/kg/day) caused 96.32% chemosuppression, which was significantly higher ($P < 0.05$) compared to the extract-treated groups.

The highest concentration of extract used (1000 mg/kg/day) resulted in 77.84% chemosuppression, approaching the efficacy of the standard drug chloroquine (10 mg/kg/day). The observed antiplasmodial activity of the extracts is consistent with the traditional use of these plants as herbal medication against malaria. The plant extract may prevent the detoxification of free, oxidised haem (Fp-Fe III), one of the by-products of haemoglobin degradation, by intercalating with the iron-carboxylate bond that links the haem units of the malaria pigment (hemozoin), thereby inhibiting polymerisation [7-8].

The dose-dependent parasitaemia suppression (60.48–77.84%) observed in this study supports earlier reports on the antimalarial properties of these plants.

Dacryodes edulis has been previously shown to possess antimicrobial and anti-inflammatory effects, which may contribute to its antiplasmodial activity [10,11,35,36]. Similarly, *Ficus capensis* extracts have demonstrated erythropoietic and antipyretic activities, relevant in malaria-associated anemia and fever [12,35,36]. The combination of both extracts produced a more pronounced effect than previously reported for individual extracts [12, 35, 36], suggesting synergistic interactions among their bioactive compounds.

Notably, the observed 77.84% suppression at 1000 mg/kg was lower than that of chloroquine (96.32%), but still significant. This aligns with findings from other medicinal plants where crude extracts show moderate efficacy compared to standard drugs [35-36]. Although the suppressive effect was significantly lower than that observed with chloroquine (96.32% suppression), the results were nevertheless remarkable, demonstrating significant antimalarial potential.

Hematological parameters are critical indicators of health status during malaria infection, as the parasite invasion and replication within erythrocytes typically result in anemia, reduced hematocrit, and impaired red blood cell (RBC) function [38]. In untreated infected mice, significant reductions in hematocrit (HCT), RBC counts, and hemoglobin (Hb) levels were observed, consistent with established pathological features of malaria-induced anemia [38-39]. Treatment with the combined extracts at 250 mg/kg and 500 mg/kg markedly restored these parameters to near-normal levels, corroborating previous findings on *Ficus capensis* improving hematological indices in anemia models [12]. However, elevated white blood cell (WBC) counts at the highest dose (1000 mg/kg/day) may indicate mild immunological stimulation or early signs of subclinical toxicity, warranting further investigation. The most significant changes in hematological profiles corresponded with increasing parasitemia levels.

Elevated liver enzyme activities, such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP), in untreated parasitized mice indicated hepatic stress or injury induced by malaria infection [40]. Interestingly, administration of the extracts significantly normalized these enzyme activities, confirming the hepatoprotective capability of these plants. In contrast, chloroquine-treated mice exhibited considerably elevated gamma-glutamyl transferase (GGT) activity, reflecting mild drug-induced hepatic stress, consistent with previous studies [40]. Thus, the plant extracts not only offered antimalarial benefits but also conferred a hepatoprotective advantage, highlighting their therapeutic superiority.

The oxidative stress markers examined—malondialdehyde (MDA) and reduced glutathione (GSH)—revealed notable changes in infected untreated mice, characterized by significantly increased lipid peroxidation (elevated MDA levels) and depletion of antioxidant capacity (lowered GSH levels). Treatment with the extracts significantly attenuated lipid peroxidation and enhanced antioxidant defences, especially at the lower doses (250 and 500 mg/kg/day). The ability of these extracts to reduce oxidative stress can be attributed to their rich phytochemical content, notably flavonoids, terpenoids and tannins, which are well-documented antioxidants capable of scavenging free radicals and preventing oxidative damage [10, 11, 35].]. Lipid peroxidation in this study was assessed using the thiobarbituric acid reactive substances (TBARS) method, specifically by measuring malondialdehyde (MDA) levels.

P. berghei-infected mice recorded elevated levels of MDA in the brain and liver when compared to the extract-treated animals. The significant reduction ($p < 0.05$) in the level of MDA in extract-treated mice at doses of 250 and 500 mg/kg demonstrated the potential antimalarial benefits of these plants. It is possible that the extract contributed to the biosynthesis of antioxidant enzymes, thereby increasing the free radical scavenging ability and reducing membrane lipid peroxidation. Additionally, higher levels of GSH were recorded in the liver and brain of extract-treated infected mice at 250 and 500 mg/kg compared to the infected control. The extracts may exhibit antioxidant effects due to their rich phytochemical constituents.

Certain specific plant-derived bioactive agents function as metal chelators, possessing ortho-phenol and carboxyl groups that can bind essential parasite cations such as Ca^{2+}, Fe^{2+}, and Mg^{2+}. These cations serve as cofactors for the *Plasmodium* enzyme Ribonucleotide Reductase (RNR). The plant extracts may also contain constituents that inhibit *Plasmodium growth* by blocking the parasite's intracellular transport of choline, a necessary step for the biosynthesis of phosphatidylcholine, an essential molecule for Plasmodium [7]. In summary, the findings of this study confirm the traditional medicinal claims regarding the antimalarial efficacy of *Dacryodes edulis* and *Ficus capensis* leaf extracts. Furthermore, the observed hepatoprotective and antioxidant benefits add significant value, making

these leaf extracts promising candidates for the development of affordable, safe, and effective herbal therapies for malaria.

5.0 Conclusion

The present study demonstrated that combined methanol leaf extracts of *Dacryodes edulis* and *Ficus capensis* possess notable antiplasmodial activity against chloroquine-sensitive *Plasmodium berghei* NK-65 infection in mice. These extracts exhibited significant hepatoprotective and antioxidant properties, as evidenced by their ability to normalize biochemical and hematological parameters altered during malaria infection. These findings provide scientific support for the traditional use of these plants in malaria treatment and suggest their potential as effective and affordable alternatives to conventional antimalarial therapies. Future studies should focus on isolating and characterizing the active compounds responsible for these beneficial effects, determining optimal therapeutic doses, and evaluating long-term safety profiles to facilitate their development into clinically viable antimalarial agents.

Conflict of Interest: The Authors declare no conflict of interest.

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