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In vitro antiplasmodial, anthelmintic activities and toxicological profile of the leaves, roots, and stem bark of *Ficus bubu* Warb.

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Abstract

Background: *Ficus bubu* is a fig tree belonging to the Moraceae family, whose leaves, roots, and stem bark contain bioactive compounds identified through qualitative and quantitative phytochemical screening. While these parts are known for their antioxidant activities, scientific data on their antiplasmodial and anthelmintic activities, as well as toxicological profiles, have not yet been reported.

Methods: Acute toxicity testing was performed on all three plant parts. Additionally, subacute toxicity testing was carried out on the stem bark, which showed the most promising activities.

Results: The results revealed that the stem bark extract exhibited promising antiplasmodial activity (IC_{50} = 9.07 µg/mL) against the 3D7 strain and good activity (IC_{50} = 17.97 µg/mL) against the Dd2 strain. In contrast, the root extracts showed moderate activity (IC_{50} = 21.43 µg/mL) against 3D7 and marginal potency (IC_{50} = 63.87 µg/mL) against Dd2 strain, while leaf extracts displayed poor activity on both strains. The stem bark extract exhibited anthelmintic activity comparable to that of the reference drug praziquantel (at 500 µg/mL) while the root extract showed slightly lower activity. Furthermore, leaf extracts exhibited moderate anthelmintic activity. Acute toxicity doses of leaf, root, and bark extracts were well tolerated, with no deaths observed. Thus, with an oral LD_{50} greater than 5000 mg/kg, the substances can be considered practically non-toxic. The stem bark extract (10B3Fb), which showed the strongest biological activity, was used for the subacute toxicity study. Observation of behavioral parameters over 28 days showed that rats remained normal throughout the study. Weight gain generally increased in all groups.

Conclusion: The stem bark extract (10B3Fb) had favorable effects on lipid regulation, liver and kidney function, as well as hematological and histological parameters in both females and males. No signs of toxicity or tissue damage were observed, confirming its safety.

Keywords: *Ficus bubu*; antiplasmodial activity; anthelmintic activity; acute toxicity; subacute toxicity.

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Background

Malaria is an infectious disease caused by parasites of the genus *Plasmodium*, transmitted to humans through the bite of infected *Anopheles* mosquitoes. This illness is characterized by fever, chills, muscle pain, headaches, and asthenia. In the absence of treatment, it can advance to severe stages, leading to serious complications and, in some cases, death [1]. Malaria is a widespread epidemic in sub-Saharan Africa, where member countries organize annual conferences to coordinate control strategies [2]. In March 2024, at a ministerial conference in Yaoundé, countries accounted for more than 70% of cases and 73% of global malaria deaths from reported approximately 166 million cases and 423,000 deaths in 2022. Malaria remains a major public health concern in sub-Saharan Africa, causing over 90% of malaria-related worldwide. In Cameroon, the Ministry of Public Health reported an increase of prevalence at a rate of 26.1% in 2022, with more than 2 million cases and 1,756 deaths in 2023 [3]. Despite a decline in mortality, the number of malaria cases continues to rise. The reduction in malaria incidents remains minimal, particularly in countries with limited resources [3,4].

Helminth infections are common in many parts of the world, especially in developing countries. These infections can invade multiple organs, such as the intestines, liver, and lungs, leading to a wide spectrum of symptoms ranging from abdominal pain, digestive disorders, and weight loss to severe complications [5]. Geohelminthiasis, caused by soil-transmitted helminths, is transmitted by eggs present in human feces, which contaminate soil particularly in areas with poor sanitation. Globally, geohelminthiasis is one of the most common infections, affecting more than 1.5 billion people, nearly 24% of the world's population [6,7]. These infections primarily affect the poorest and most disadvantaged communities with limited access to safe drinking water, sanitation, and hygiene in tropical and subtropical regions. The highest prevalence occurs in sub-Saharan Africa, China, South America, and Asia. More than 260 million preschool children, 654 million school-age children, 108 million adolescent girls, and 138.8 million pregnant or breastfeeding women live in areas of high transmission that require treatment and preventive measures [7,8].

In addition to existing measures to eradicate malaria and reduce geohelminthiasis, the emergence of drug resistance complicates control efforts. Consequently, research and technological innovation are focusing on biodiversity, particularly medicinal plants with therapeutic properties that remain underexplored, highlighting antiplasmodial and, anthelmintic potential. Within this context, we became interested in *Ficus bubu* Warb. (Moraceae), a species renowned for its therapeutic uses [9,10]. To date, no studies have investigated its antiplasmodial or anthelmintic activities or its toxicological profile. However, previous research has demonstrated antimicrobial and antiproliferative activities [11,12]; as well as circadian rhythm effects on the phytochemical content and antioxidant potential of ethanol extracts [13]. Therefore, this study aims to evaluate the antiplasmodial and anthelmintic activities and assess the toxicological profile of the leaves, roots, and stem bark of *Ficus bubu* Warb., with the goal of identifying new therapeutic avenues for the treatment of these parasitic infections.

Methods

Plant material

The plant material consists of the leaves, roots, and stem bark of *Ficus bubu* Warb., harvested at 6 a.m., 12 p.m., and 6 p.m., respectively. Each plant part was collected at these three times of day near the Melen market in Yaoundé, Central Province, Cameroon. The sample with the best phytochemical and antioxidant results were selected for antiplasmodial and anthelmintic assays. The plant was identified and authenticated at the National Herbarium of Cameroon on January 10, 2024, by Mr. NGANSOP T. Eric (Botanist, Scientific and Technical Executive) as *Ficus bubu* Warb. (Moraceae), by comparison with R. Letouzey's voucher specimen no. 12153, registered as specimen no. 29050/SRF/Cam.

Malaria parasite

The antiplasmodial activity of the plant extracts was evaluated on *Plasmodium falciparum* strains 3D7 (chloroquine- and artemisinin sensitive) and Dd2 (chloroquine-resistant and artemisinin-sensitive). These strains were maintained in continuous culture at the Pasteur Center in Yaounde, Cameroon, where the assays were performed.

Helminth parasite

For the anthelmintic study, *Taenia solium* in the L3 larvae were used. They were collected from pig feces sampled at a slaughterhouse in Douala, Cameroon, and identified by a biologist.

Animals

Wistar rats, nulliparous and non-pregnant, aged 8-12 weeks, were obtained from the Faculty of Sciences, University of Douala, and used for toxicity studies.

Extraction

Leaves, roots, and stem bark were harvested, weighed, reweighed again, and ground into fine powder following the methods of Allal (2018) and Zaiter (2017) [14,15]. Ethanol extracts were prepared according to Mugiraneza et *al.* (2009) [16]. For each harvest, 1 kg of powdered material was macerated in 5 l of 70% ethanol for 48 h at room temperature. Each mixture was filtered through 1 mm Whatman filter paper, and the filtrates were evaporated under reduced pressure at 79°C using a rotary evaporator. Extraction yields were calculated as:

$$\tau = \frac{\mathbf{m}}{\mathbf{M}} x\ \mathbf{100}$$

Where τ: extraction yield, M: powder mass, and m: extract mass

Antiplasmodial activity

Antiplasmodial activity was tested against *Plasmodium falciparum* 3D7 and Dd2 strains, supplied by the Pasteur Center in Yaounde. For preliminary screening, percentage inhibition at 100 µg/ml was determined on the 3D7 strain using the SYBR Green I method. SYBR Green-I lysis buffer (50 µL, diluted 1/3) was added per 100 µL of treated culture [17]. Plates were incubated in the dark for 1

h, and fluorescence was mesured at 485/535 nm. Percentage inhibition was then calculated relative controls (C^- = artemisine-treated. C^+ = solvent-treated) as:

% Inhibition = $(C^+ - X) / (C^+ - C^-) \times 100$

where **X** = fluorescence of the extract.

Culture methods followed Makler & Hinrichs (1993) and Efange et *al*. (2020) for 3D7 [18,19] and modified Trager & Jensen (1976) and Boyom et *al*. (2011) for Dd2 [17,20].

Parasites were maintained in fresh human O+ red blood cells at 2% hematocrit in RPMI 1640 medium supplemented with 2 mM L-glutamate, $NaHCO_3$, 25 mM HEPES, 0.65 mM hypoxanthine, 20 µg/mL gentamicin, 5% Albumax II, 20 mM glucose, and 2–4% erythrocytes [17-21]. Synchronization was achieved using 5% sorbitol, which lyses mature forms while preserving ring-stage parasites [22,23].

Stock solutions of extracts (1 mg/mL) were prepared in 10% DMSO, filtered through 0.22 µm membranes, and serially diluted to obtain eight concentrations (20 µg/mL to 0.256×10^{10} µg/mL) with a final DMSO concentration ≤ 0.2%

Assays were performed in 96-well plates with 100 µL total volume, 1% parasitemia (3D7) or 2% (Dd2), and 0.2% DMSO. Artemisinin (1 µM) and chloroquine were used as references. Negative controls contained DMSO (0.2%) and positive controls contained chloroquine (3D7) or artemisinin (Dd2). Absorbance values of parasite lactate dehydrogenase (LDH) were measured at 620 nm after 48 h (3D7) [18,21].

For Dd2, after 72 h, plates were frozen at −20°C, thawing, treated with SYBR Green I lysis buffer, incubated for 30 min in the dark, and fluorescence was measured at 485/538 nm [17,20].

Anthelmintic activity

L3 larvae of *Taenia solium* were obtained by coproculture from pig feces collected daily for six weeks at Ndokoti market, Douala. Larvae were isolated using the Baermann technique [24].

Larval inhibition was assessed following Rabel et *al*. (1994) with modifications [25]. Approximately 1000 L3/mL were incubated at 23°C with extracts at 1200, 600, 300, 150, and 75 µg/mL (three replicates per concentration) in 96-well plates. Negative controls contained larvae without extract, and praziquantel (500, 250, 125 µg/mL) served as reference. After 6, 12, and 24 h, 50 µL aliquots were transferred to cavity slides for microscopic counting at 40× magnification. Larval inhibition was calculated as:

$$IL = \frac{T - M}{T} x\ 100$$

Where T = total larvae in controls and M = larvae surviving in treated wells.

Acute toxicity of Ficus bubu leaves, roots, and stem bark

Acute toxicity was assessed in female Wistar rats according to OECD guideline 425 (2008) [26]. Twenty-one rats (8–12 weeks) were divided into 7 groups: one control and two groups each receiving 2000 or 5000 mg/kg of leaf, root, or bark extract (Figure 1).

Single oral doses were administered by gavage. Rats were observed intensively for 4 h, then daily for 14 days, with attention to coat, motility, tremors, body weight, grooming, respiration, noise sensitivity, stool appearance, and mortality [27]. Body weight was recorded every 2 days. On day 15, rats were euthanized with ketamine/diazepam overdose, and organs were excised, weighed, and examined macroscopically [27,28].

Subacute toxicity of Ficus bubu stem bark

Subacute toxicity was evaluated according OECD Guideline 407 (2008) [29,30]. Twenty-four rats (nulliparous, non-pregnant) were divided into 4 groups (n = 6, 3 males and 3 females each):

- Group I: distilled water (1 mL/100 mg body weight, control).
- Groups II–IV: stem bark extract at 200, 400, or 800 mg/kg body weight (Figure 2).

Treatments lasted 28 days. Rats were weighed and observed for behavioral changes throughout. At the end, animals were euthanized and samples collected for organ, biochemical, hematological, and histological analyses [31–33].

Biochemical tests included lipid profile (total cholesterol, HDL, triglycerides) and liver/kidney function (transaminases, ALP, γ-GT, total and direct bilirubin, total protein, urea, creatinine). Hematological parameters included RBC, HGB, HCT, WBC, MCV, Lym, GRA, MCHC, MCH, PLT, and MPV. Histological sections of the liver, kidneys, heart, lungs, and spleen were also examined.

Results

Extraction

Extraction was carried out using 70% ethanol, a polar solvent. Several harvests were carried out as part of the study of the plant's biological behavior. The plant material was weighed at each stage of process —from fresh parts, dried away from sunlight to the powdered material and final extracts to determine extraction yield (Table 1). *Ficus* species are characterized by abundant sap flow during harvesting. In the case of *Ficus bubu*, thick white latex exuded profusely from the leaves, stem bark, and even roots.

After concentration in a rotary evaporator, viscous extracts were obtained: greenish black for the leaves, brown for the roots, and dark brown for the stem bark. Each extract was stored in glass bottles covered with Whatman No.2 paper for one month and weighed regularly until constant masses. This allowed extraction yields to be calculated and each extract to be coded accordingly.

Antiplasmodial activity

Single-dose screening of (100 µg/mL) against the chloroquine-sensitive *P. falciparum* strain 3D7 was first performed to assess the antiplasmodial potential of *F. bubu* extracts and percentages of inhibition where 22, 89, 92, and 109 for leaves harvested at 6 a.m., Roots harvested at 12 noon, stem bark harvested at 6 p.m., and artemisinin respectively. For the 3D7 strain, extracts were tested at 100, 50, 25, 12.5, 6.25, 3.125, 1.5625, and 0.78125 µg/mL (Table 2). Stem bark extract (10B3Fb) displayed the strongest activity, followed by the root extract (10R2Fb). Leaf extracts were less active, with sensitivity similar to that of chloroquine. Dose–response curves derived from logarithmic concentrations (Figure 3) yielded IC_{50} values of > 100 µg/mL (leaves), 21.43 µg/mL (roots), and 9.07 µg/mL (stem bark). Artemisinin and chloroquine showed IC_{50} values of 0.009 and 0.005 µg/mL, respectively. For the Dd2 strain, extracts were tested under the same conditions (Table 3). Stem bark extract (10B3Fb) again showed the highest activity,

particularly at higher concentrations. Root extract (10R2Fb) was moderately active, while leaf extracts were largely inactive, similar to chloroquine, which is known to be ineffective against this strain.
Dose–response curves (Figure 4) yielded IC_{50} values of > 100 µg/mL (leaves), 63.87 µg/mL (roots), and 17.97 µg/mL (stem bark). Artemisinin and chloroquine had IC_{50} values of 0.01 and 0.17 µg/mL, respectively.
Resistance indices (R), calculated as the IC_{50} ratio Dd2/3D7 (Table 4), were 1.98 for stem bark extracts, close to artemisinin (1.11), and lower than root extracts (2.98). These values were markedly below that of chloroquine (31.35), confirming the relative efficacy of stem bark extracts.

Anthelminthic activity

The inhibition effects of ethanol extracts from *F. bubu* leaves, roots, and stem bark on *Taenia solium* L3 larvae are shown in Figure 5. Extracts were tested at 1200, 600, 300, 150, and 75 µg/mL, while praziquantel (500, 250, and 125 µg/mL) served as the reference.
Praziquantel at 500 µg/mL eliminated all larvae (100% inhibition), with 89.33% and 71.67% inhibition at 250 and 125 µg/mL, respectively. Stem bark extracts exhibited similar activity, with inhibition rate of 96.33%, 91.00%, 86.33%, 75.67%, and 70.33% across the five concentrations. Root extracts followed, with 81.33%, 80.00%, 68.00%, 58.0%, and 54.00% respectively. Leaf extracts were least active, with inhibition percentages of 61.33%, 51.00%, 41.33%, 38.67%, and 32.00%. Statistical analyses showed no significant difference between stem bark praziquantel, while root extract displayed moderate differences. Leaf extracts showed significant, very significant, or high differences compared with controls.

Acute toxicity of F. bubu leaves, roots, and stem bark

Lethal dose 50 (LD_{50})

Ethanolic extracts administered orally to female Wistar rats at 2000 mg/kg and 5000 mg/kg were well tolerated. No deaths occurred at these limit doses.

Behavioral parameters

Rats receiving leaves, roots, and stem bark extracts (2000 and 5000 mg/kg) showed no abnormal changes in grooming, motility, tremors, stool appearance, or other parameters. No deaths were recorded.

Body weight gain

As shown in Figure 6, rats gained weight progressively during the 14-day experiment, regardless of dose or plant part tested. Statistical analysis revealed no significant difference in weight gain between treated and control groups ($p = 0.9999 > 0.05$).

Relative organs weight

Figures 7-11 show the mean relative weights (± SEM) of the heart, lungs, liver, spleen, and kidneys of treated and control rats. No significant differences were observed ($p > 0.05$ for all comparisons). Slight increases in organ weight suggested exposure to active compounds, but values were comparable across treatment groups and doses.

Subacute toxicity of F. bubu stem bark

Clinical parameters

Rats treated with 200, 400, and 800 mg/kg extract for 28 days showed no abnormal changes in grooming, motility, nutrition, respiration, stool appearance, or eyes no deaths occurred.

Body weight changes

Figures 12 and 13 show progressive weight gain in both sexes. No significant differences were observed between extract-treated groups and controls.

Relative organ weights

Figures 14 and 15 show organ weight data. In females, liver weights decreased slightly with dose, suggesting hepatoprotective effects, while other organs remained stable. In males, the Fb800 group showed increased liver and lung weights ($p < 0.01$) and the Fb200 group showed a slight increase in spleen weight ($p < 0.05$). No significant changes were noted for kidneys or hearts.

Lipid profile

Tables 5 and 6 show extract effects on lipid metabolism. In females, HDL cholesterol increased significantly in all treated groups ($p < 0.05$–0.01). No significant changes were observed for total cholesterol or triglycerides. In males, both total cholesterol and HDL cholesterol increased significantly in treated groups, while triglycerides showed minor changes.

Liver and kidney function

Tables 7 and 8 summarize biochemical data. A slight increase in total bilirubin (BT) was observed in females at Fb 800 ($p < 0.05$), and an increase in protein levels (PT) in males at Fb200 ($p < 0.01$) and Fb 800 ($p < 0.05$). No significant changes were observed in other liver (ASAT, ALAT, PAL, γ-GT) or kidney (urea, creatinine) parameters.

Hematological parameters

Tables 9 and 10 show hematological results. In females, slight decreases in platelet counts were observed at Fb400 and Fb800 ($p < 0.05$). In males, platelet counts increased significantly in all treated groups ($p < 0.001$). No other parameters were significantly affected.

Histopathology

Figures 16 and 17 show organ histology. In all groups, liver, kidney, heart, lung, and spleen structures appeared normal, with no evidence of toxicity. Hepatic parenchyma, renal glomeruli, cardiac fibers, pulmonary alveoli, and splenic white pulp were preserved across treated and control groups.

Discussion

Malaria and helminth infections remain major public health problems, particularly in sub-Saharan Africa, where morbidity and mortality rates are still very high despite considerable control efforts. In this study, the *in vitro* antiplasmodial and anthelmintic activities, as well as the toxicological profile of *Ficus bubu* Warb. extracts were evaluated.

The extraction yields were 7.41%, 10.67%, and 7% for extracts 10L1Fb, 10R2Fb, and 10B3Fb, respectively. These values are higher than those reported by Mbosso *et al.* (2015, 2016), who obtained yields of 5.3%, 4.2%, and 3.7% from methanol extracts of the fruit, leaves, and bark of *F. bubu* [12,34].

Following evidence of circadian effects on the phytochemical content and antioxidant potential of *Ficus bubu* extracts [13], leaf samples harvested at 6 a.m. (10L1Fb), root samples harvested at noon (10R2Fb), and stem bark samples harvested at 6 p.m. (10B3Fb) were selected for antiplasmodial, anthelmintic, and acute toxicity testing. Extract 10B3Fb, which showed the most promising biological profile, was used for subacute toxicity testing. A review of the literature revealed that antimicrobial and antiproliferative activities of methanol extracts had been investigated previously [12,34]. Phytochemical analysis revealed the presence of bioactive compounds such as alkaloids, flavonoids, polyphenols, and tannins, known for their pharmacological properties. Similar results have been reported in other *Ficus* species, suggesting that these metabolites contribute to the observed biological activities.

The antiplasmodial assays demonstrated that stem bark extracts had the strongest activity against both *P. falciparum* strains. According to Singh *et al.* (2015), plants were classified for their antiplasmodial potential as (a) highly active (IC_{50} ≤ 5 µg/mL), (b) promising (IC_{50} 5.1–10 µg/mL), (c) good activity (CI_{50} 10.1–20 µg/mL), (d) moderate activity (IC_{50} 20.1–40 µg/mL), (e) marginal potency (IC_{50} 40.1–70 µg/mL), and (f) poor or inactive (IC_{50} > 70.1 µg/mL) [35], the results classify bark extracts as promising to good with IC_{50} values of 9.07 µg/mL (3D7) and 17.97 µg/mL (Dd2). Root extracts showed moderate activity, while leaf extracts were weak or inactive. Compared with reference molecules, these values indicate that although the extracts are less potent than artemisinin and chloroquine, they nevertheless show promising activity, particularly in the stem bark. The resistance indices obtained suggest that the activity of stem bark extracts remains stable between sensitive and resistant strains, which is an encouraging feature in the context of increasing resistance to conventional drugs. The presence of alkaloids, flavonoids, and other compounds likely explains this activity, consistent with findings in *Ficus elastica* (IC_{50} = 9.5 µg/mL) [21].

The anthelmintic assays confirmed the activity of the extracts, particularly the stem bark, which exhibited inhibition levels close to praziquantel at equivalent concentrations (inhibition rates of 96.33%, 91.00%, 86.33%, 75.67%, and 70.33% at 1200, 600, 300, 150, and 75 µg/mL, respectively). Root extracts showed moderate activity, while leaf extracts were weaker. The activity depends on both concentration and exposure time, similar to results reported for *Ficus exasperata* on *Haemonchus contortus* [36]. Secondary metabolites such as alkaloids, flavonoids, saponins, and tannins are known to disrupt helminth membranes, enzyme systems, and motility [25], which likely explains the activity of *F. bubu* against *Taenia solium* larvae. These results support the traditional use of *Ficus* species in the management of parasitic infections and suggest that *F. bubu* may be a source of new anthelmintic agents.

Toxicological analysis showed that extracts were practically non-toxic, with LD_{50} values > 5000 mg/kg, in line with the Hodge and Sterner classification (5000 < LD_{50} < 15000 mg/kg) [37]. No signs of significant toxicity were observed, consistent with studies on *Ficus sycomorus* [38]. Subacute toxicity tests on bark extracts (200–800 mg/kg for 28 days) revealed no mortality, abnormal behavior, or significant variations in body weight, organ weights, or hematological and biochemical parameters. These findings agree with Etame *et al.* (2018) [28]. Minor variations observed in liver and lung weights (Fb 800 males) were attributed to feeding errors rather than extract toxicity. Lipid profile analyses showed increased HDL cholesterol and slight reductions in triglycerides, suggesting a favorable effect on lipid metabolism. Steroids detected during phytochemical screening may explain the cholesterol increase [39]. Liver function markers (AST, ALT, ALP, γ-GT, bilirubin) remained within normal limits, confirming hepatoprotection. Similarly, kidney markers (urea, creatinine) showed no significant changes. Hematological analysis revealed slight platelet variations (decrease in females, increase in males), consistent with earlier findings [38], but however all within safe ranges. Histological analysis of liver, kidney, heart, lung, and spleen tissues confirmed normal architecture without signs of damage, consistent with Souhila (2022) [40]. Overall, *F. bubu* stem bark extracts demonstrated promising antiplasmodial and anthelmintic activities with a favorable toxicological profile.

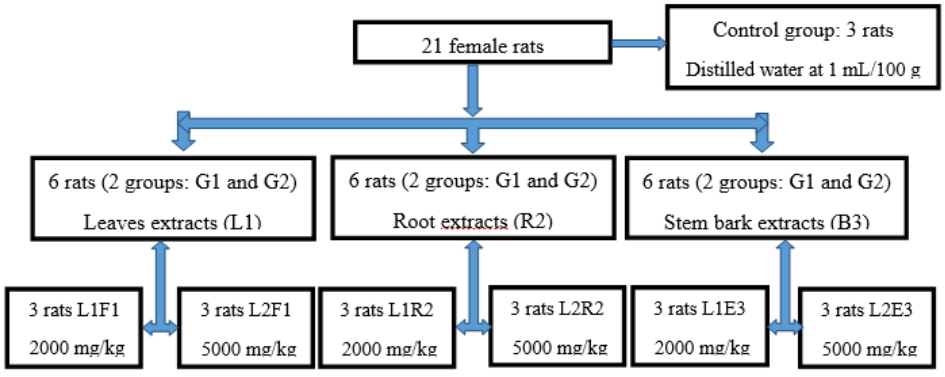

Figure 1. Allocation of batches for the acute toxicity study of *Ficus bubu* leaves, roots, and stem bark.

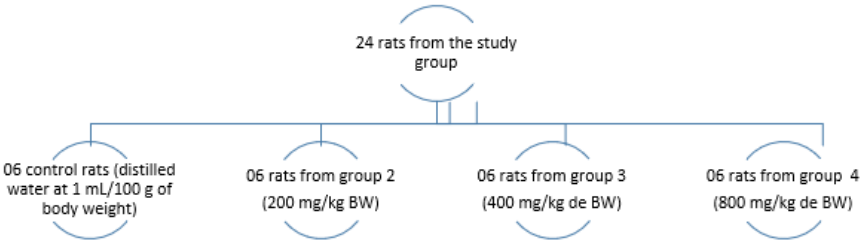

Figure 2. Subacute toxicity study protocol.

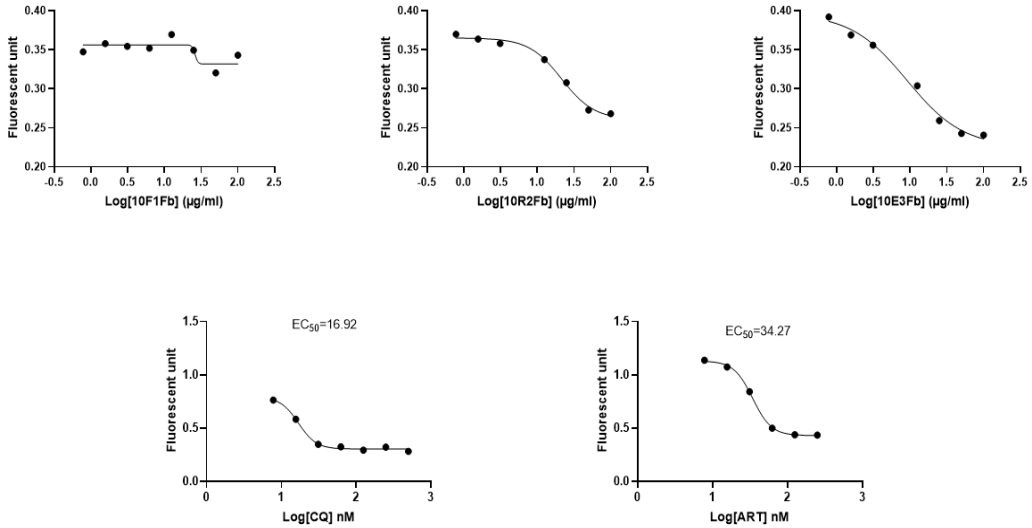

Figure 3. Inhibitory concentrations obtained from *F. bubu* leaves, roots, and stem bark extracts against the Pf 3D7 strain.
Legend: 10L1Fb = Leaves extract of *Ficus bubu* harvested at 6 a.m.; 10R2Fb = Roots extract of *Ficus bubu* harvested at 12 noon; 10B3Fb = Stem bark extract of *Ficus bubu* harvested at 6 p.m.; CQ = chloroquine; ART = artemisinin.

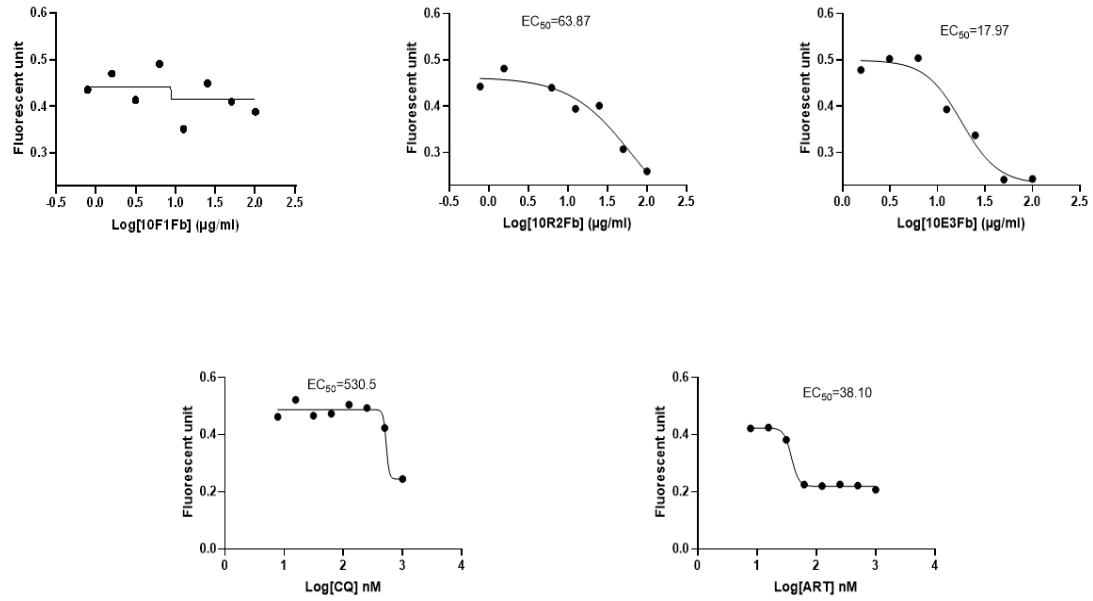

Figure 4. Inhibitory concentrations obtained from *F. bubu* leaves, roots, and stem bark extracts against the Pf Dd2 strain.
Legend: 10L1Fb = Leaf extract of *Ficus bubu* harvested at 6 a.m.; 10R2Fb = Root extract of *Ficus bubu* harvested at 12 noon; 10B3Fb = Stem bark extract of *Ficus bubu* harvested at 6 p.m.; CQ = chloroquine; ART = artemisinin.

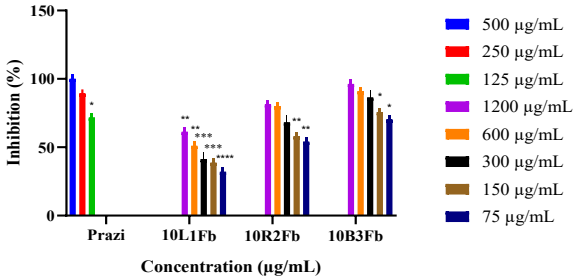

Figure 5. Percentage inhibition of *F. bubu* extract concentrations on *Taenia solium* larvae.
$p > 0.05$ = not significant; $p < 0.05$ (*) = marginally significant; $p < 0.01$ (**) = significant; $p < 0.001$ (***) = highly significant; $p < 0.0001$ (****) = extremely significant.

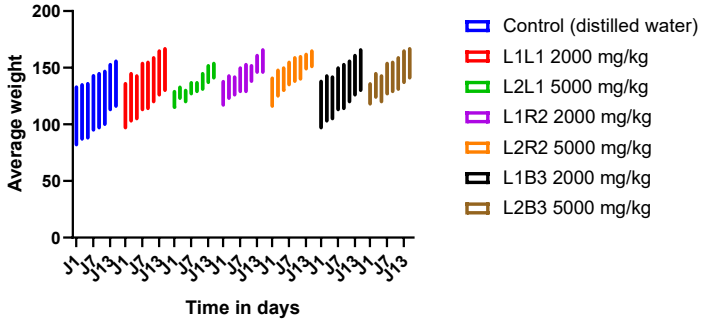

Figure 6. Weight gain in rats during acute toxicity.
Legend: L1L1 = Batch 1 leaf extract; L2L1 = Batch 2 leaf extract; L1R2 = Batch 1 root extract; L2R2 = Batch 2 root extract; L1B3 = Batch 1 stem bark extract; L2B3 = Batch 2 stem bark extract.

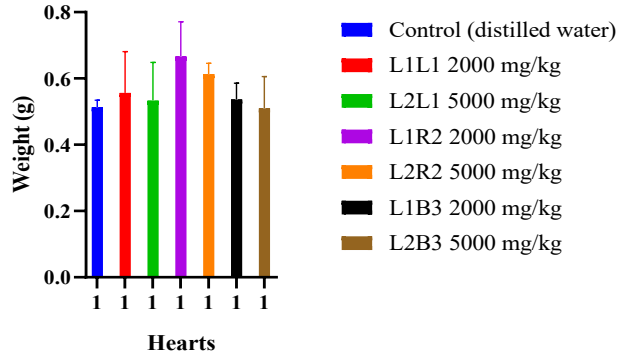

Figure 7. Comparative diagrams of hearts.
Legend: L1L1 = Batch 1 leaf extract; L2L1 = Batch 2 leaf extract; L1R2 = Batch 1 root extract; L2R2 = Batch 2 root extract; L1B3 = Batch 1 stem bark extract; L2B3 = Batch 2 stem bark extract.

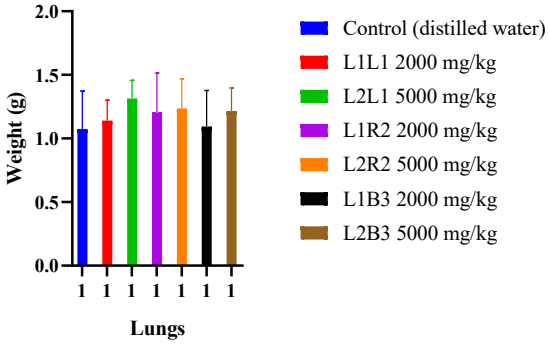

Figure 8. Comparative diagrams of lungs
Legend: L1L1 = Batch 1 leaf extract; L2L1 = Batch 2 leaf extract; L1R2 = Batch 1 root extract; L2R2 = Batch 2 root extract; L1B3 = Batch 1 stem bark extract; L2B3 = Batch 2 stem bark extract.

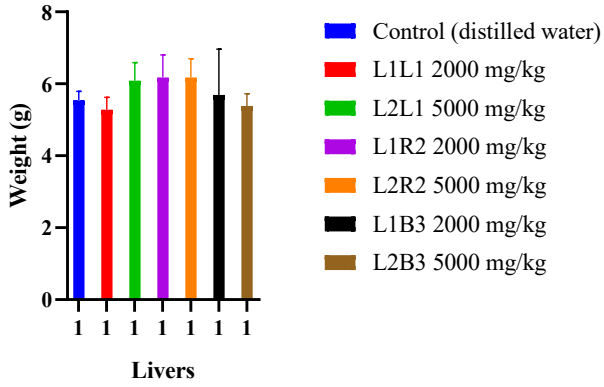

Figure 9. Comparative diagrams of livers.
Legend: L1L1 = Batch 1 leaf extract; L2L1 = Batch 2 leaf extract; L1R2 = Batch 1 root extract; L2R2 = Batch 2 root extract; L1B3 = Batch 1 stem bark extract; L2B3 = Batch 2 stem bark extract.

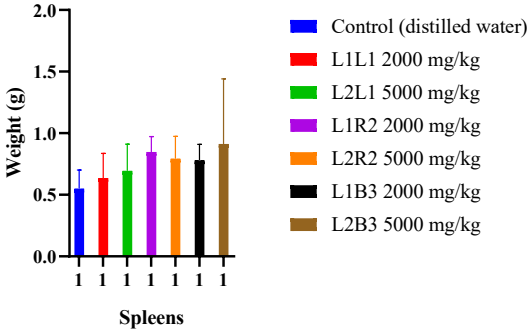

Figure 10. Comparative diagrams of spleens.
Legend: L1L1 = Batch 1 leaf extract; L2L1 = Batch 2 leaf extract; L1R2 = Batch 1 root extract; L2R2 = Batch 2 root extract; L1B3 = Batch 1 stem bark extract; L2B3 = Batch 2 stem bark extract.

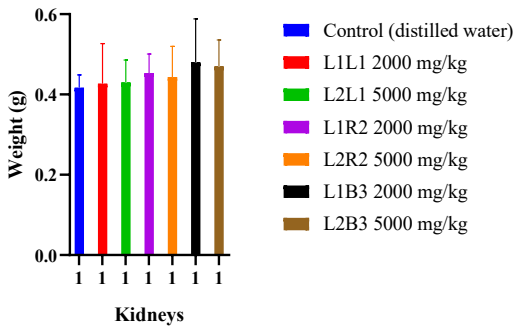

Figure 11. Comparative diagrams of kidneys.
Legend: L1L1 = Batch 1 leaf extract; L2L1 = Batch 2 leaf extract; L1R2 = Batch 1 root extract; L2R2 = Batch 2 root extract; L1B3 = Batch 1 stem bark extract; L2B3 = Batch 2 stem bark extract.

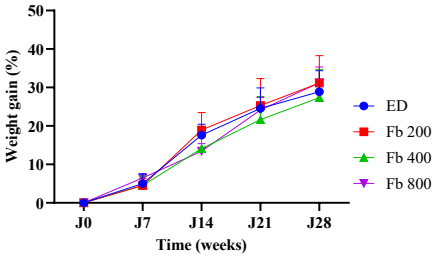

Figure 12. Weight gain in female rats.
Legend: Each point represents the mean ± SEM; ED = normal control rats receiving distilled water; Fb 200, 400, and 800 = rats receiving ethanolic extract of *F. bubu* stem bark harvested at 6 p.m. at doses of 200, 400, and 800 mg/kg, respectively.

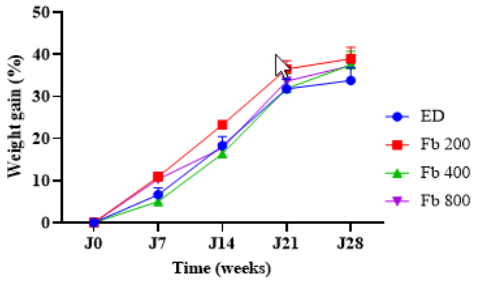

Figure 13. Weight gain in male rats.
Legend: Each point represents the mean ± SEM; ED = normal control rats receiving distilled water; Fb 200, 400, and 800 = rats receiving ethanolic extract of *F. bubu* stem bark harvested at 6 p.m. at doses of 200, 400, and 800 mg/kg, respectively.

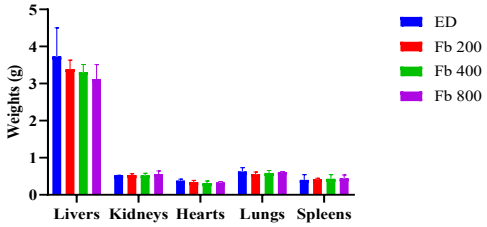

Figure 14. Effects of ethanolic extract of *F. bubu* on the relative weight of certain organs in female rats.
Legend: ED = normal control rats given distilled water; Fb 200, 400, and 800 = rats given ethanolic extract of *F. bubu* stem bark harvested at 6 p.m. at doses of 200, 400, and 800 mg/kg, respectively; $p > 0.05$ = not significant; $p < 0.05$ (*) = slightly significant; $p < 0.01$ (**) = significant; $p < 0.001$ (***) = very significant; $p < 0.0001$(****) = extremely significant

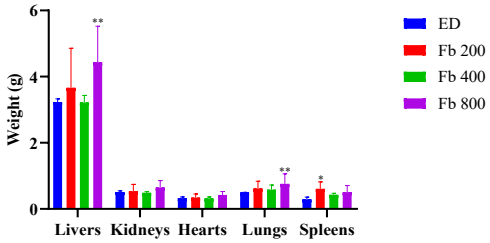

Figure 15. Effects of ethanolic extract of *F. bubu* on relative weight of some organs of male rats.
Legend: ED = normal control rats given distilled water; Fb 200, 400, and 800 = rats given ethanolic extract of *F. bubu* stem bark harvested at 6 p.m. at doses of 200, 400, and 800 mg/kg, respectively; $p > 0.05$ = not significant; $p < 0.05$ (*) = slightly significant; $p < 0.01$ (**) = significant; $p < 0.001$ (***) = very significant; $p < 0.0001$ (****) = extremely significant.

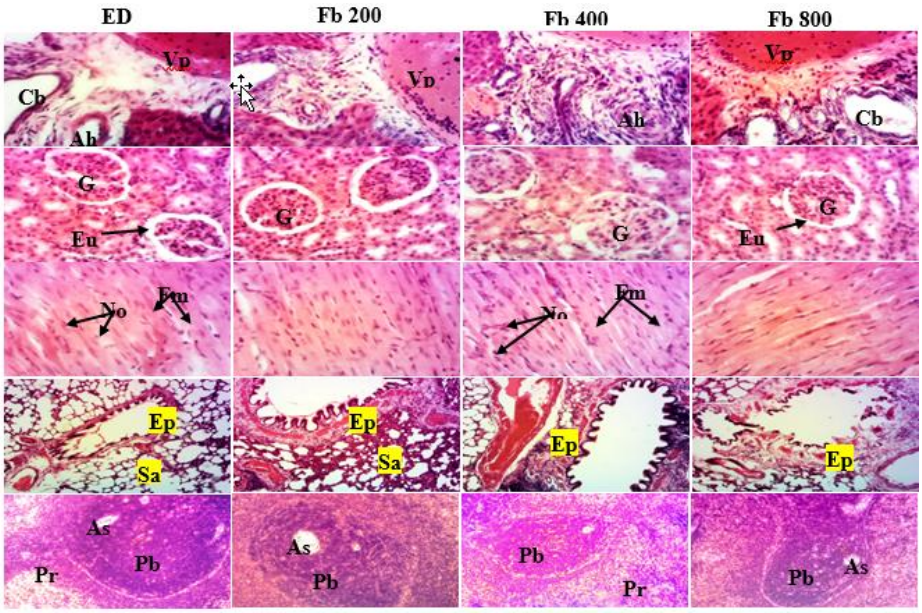

Figure 16. Effects of *F. bubu* ethanol extract on the structure of the liver, kidney, heart, lungs, and spleen in female rats
Legend: Liver: He = Hepatocyte; Vp = Portal vein; Cb = Bile canaliculus; Kidneys: Eu = Urinary space; G = Glomerulus; Heart: Fm = Muscle fiber; No = Nuclei; Lung: Ep: Pulmonary epithelium; Sa = Alveolar sac; Spleen: As = Splenic artery; Pb = White pulp, Pr = Red pulp.

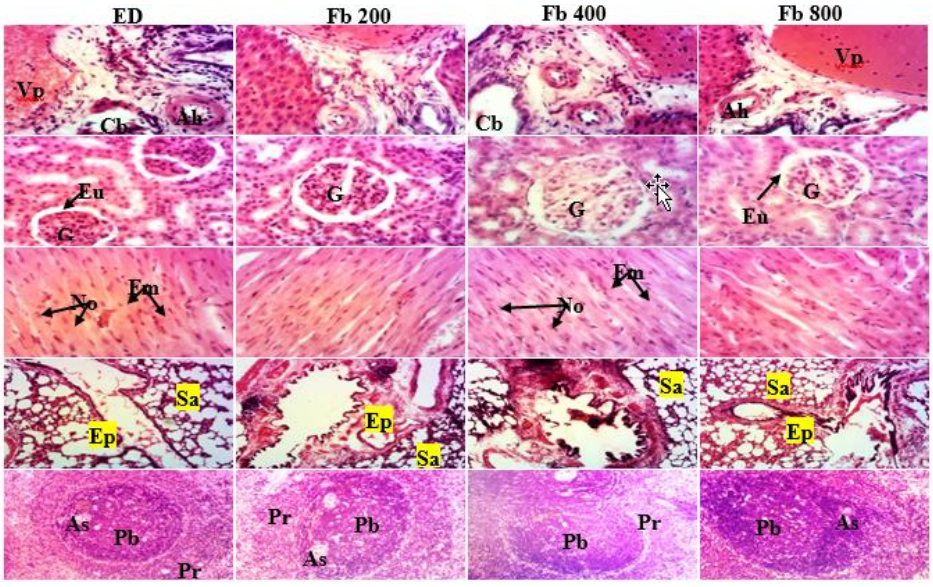

Figure 16. Effects of *F. bubu* ethanol extract on the structure of the liver, kidney, heart, lungs, and spleen in male rats
Legend: Liver: He = Hepatocyte; Vp = Portal vein; Cb = Bile canaliculus; Kidneys: Eu = Urinary space; G = Glomerulus; Heart: Fm = Muscle fiber; No = Nuclei; Lung: Ep: Pulmonary epithelium; Sa = Alveolar sac; Spleen: As = Splenic artery; Pb = White pulp, Pr = Red pulp.

Table 1. Extraction yield.

	Leaves 6 a.m.	Roots 12 p.m.	Bark 6 p.m.
	L1Fb	**R2Fb**	**B3Fb**
Fresh parts (g)	2011	1210	2981
Dry parts (g)	1300	600	1400
Crushed (g)	1200	450	1300
Extracts (g)	89	48	91
Yield (%)	7.41	10.67	7

Table 2. Antiplasmodial activity on strain 3D7.

Compound concentrations (µg/mL)	**10F1Fb**	**10R2Fb**	**10E3Fb**	**Reference drug concentrations (nM)**	**CQ**	**ART**
100	0.3430	0.2681	0.2408	**1000**	0.3340*	0.4408*
50	0.3205	0.2728	0.2428	**500**	0.2830	0.6568*
25	0.3495	0.3080	0.2593	**250**	0.3232	0.4361
12.5	0.3696	0.3374	0.3040	**125**	0.2949	0.4391
6.25	0.3521	0.3399	0.3080	**62.5**	0.3254	0.5012
3.125	0.3545	0.3581	0.3560	**31.25**	0.3497	0.8428
1.5625	0.3580	0.3638	0.3689	**15.625**	0.5842	1.0740
0.78125	0.3474	0.3699	0.3921	**7.8125**	0.7643	1.1380

Legend: 10L1Fb = *Ficus bubu* leaves harvested at 6 a.m.; 10R2Fb = *Ficus bubu* roots harvested at 12 noon; 10B3Fb = *Ficus bubu* stem bark harvested at 6 p.m.; CQ = chloroquine; ART = artemisinin.

Table 3. Antiplasmodial activity on strain Dd2.

Compound concentrations (µg/mL)	**10F1Fb**	**10R2Fb**	**10E3Fb**	**Reference drug concentrations (nM)**	**CQ**	**ART**
100	0.3886	0.2597	0.2434	**1000**	0.2450	0.2072
50	0.4105	0.3077	0.2420	**500**	0.4232	0.2217
25	0.4498	0.4012	0.3375	**250**	0.4932	0.2259
12.5	0.3519	0.3944	0.3934	**125**	0.5049	0.2204
6.25	0.4914	0.4400	0.5039	**62.5**	0.4734	0.2254
3.125	0.4143	0.5348*	0.5024	**31.25**	0.4665	0.3818
1.5625	0.4703	0.4813	0.4785	**15.625**	0.5220	0.4245
0.78125	0.4361	0.4425	0.4190*	**7.8125**	0.4623	0.4219

Legend: 10L1Fb = *Ficus bubu* leaves harvested at 6 a.m.; 10R2Fb = *Ficus bubu* roots harvested at 12 noon; 10B3Fb = *Ficus bubu* stem bark harvested at 6 p.m.; CQ = chloroquine; ART = artemisinin.

Table 4. Results of the *in vitro* antiplasmodial activity of *Ficus Bubu*

Extract	Preparation	%GI (100 µg/mL)	Pf3D7 IC_{50} (µg/mL)	PfDd2 IC_{50} (µg/mL)	Resistance index (Dd2/3D7)
10R2Fb	DMSO	89	21.43	63.87	2.98
10F1Fb	DMSO	22	> 100	> 100	-
10E3Fb	DMSO	92	9.07	17.97	1.98
ART	DMSO	-	0.009	0.01	1.11
CQ	H2O	-	0.005	0.17	31.35

Table 5. Effects of ethanolic extract of *F. bubu* on some lipid profile parameters in female rats

	ED	Fb 200	Fb 400	Fb 800
CT (mg/dL)	99.20 ± 6.96	106.50 ± 8.01	106.80 ± 5.19	104.20 ± 3.04
HDL-C (mg/dL)	59.91 ± 2.01	70.81 ± 0.23*	68.13 ± 1.06*	72.60 ± 0.70**
TG (mg/dL)	22.65 ± 2.91	22.21 ± 3.53	23.82 ± 3.85	18.58 ± 2.91

Legend: Each value represents the mean ± SEM; *p < 0.05 = not significant, **p < 0.01 = significant compared to ED; TC = Total cholesterol; HDL-C = HDL cholesterol; TG = Triglycerides; ED = distilled water; Fb 200, 400 and 800 = rats given ethanolic extract of *F. bubu* stem bark harvested at 6 p.m. at doses of 200, 400 and 800 mg/kg respectively.

Table 6. Effects of ethanolic extract of *F. bubu* on some lipid profile parameters in male rats

	ED	Fb 200	Fb 400	Fb 800
CT (mg/dL)	109.50 ± 4.08	119.60 ± 4.62**	123.00 ± 1.72**	115.40 ± 4.23**
HDL-C (mg/dL)	72.26 ± 3.37	75.44 ± 1.48*	85.59 ± 3.33**	84.00 ± 7.10**
TG (mg/dL)	20.5 ± 52.35	20.29 ± 3.17	29.36 ± 2.07*	16.34 ± 2.70*

Legend: Each value represents the mean ± SEM; *p < 0.05 = not significant, **p < 0.01 = significant compared to ED; TC = Total cholesterol; HDL-C = HDL cholesterol; TG = Triglycerides; ED = distilled water; Fb 200, 400 and 800 = rats given ethanolic extract of *F. bubu* stem bark harvested at 6 p.m. at doses of 200, 400 and 800 mg/kg respectively.

Table 7. Effects of ethanolic extract of *F. bubu* on some parameters of liver and kidney function in female rats

	ED	Fb 200	Fb 400	Fb 800
ASAT (U/L)	109.60 ± 4.95	105.40 ± 2.04	108.00 ± 3.93	107.10 ± 3.29
ALAT (U/L)	92.65 ± 1.26	93.04 ± 3.83	96.74 ± 2.17	91.49 ± 4.04
PAL (U/L)	73.45 ± 1.90	70.59 ± 5.26	58.29 ± 4.17	65.53 ± 1.50
γ-GT (U/L)	10.66 ± 0.31	11.53 ± 0.62	11.03 ± 0.21	10.71 ± 0.60
BD (mg/dL)	0.14 ± 0.02	0.15 ± 0.01	0.19 ± 0.01	0.18 ± 0.01
BT (mg/dL)	0.53 ± 0.04	0.49 ± 0.04	0.54 ± 0.07	0.79 ± 0.02*
PT (mg/dL)	0.69 ± 0.01	0.70 ± 0.01	0.74 ± 0.02	0.70 ± 0.01
CREA (mg/dL)	1.74 ± 0.18	1.71 ± 0.12	1.14 ± 0.15	1.51 ± 0.04
UREE (mg/dL)	33.08 ± 1.57	28.80 ± 1.66	27.13 ± 2.12	26.62 ± 1.77

Legend: AST = aspartate aminotransferase; ALT = alanine aminotransferase; ALP = alkaline phosphatase; γ-GT = γ-glutamyl transferase; DB = direct bilirubin; TB = total bilirubin; PT = total proteins; CREA = creatinine; *p < 0.05 = not significant; **p < 0.01 = significant compared to ED; ED = distilled water; Fb 200, 400 and 800 = rats given ethanolic extract of *F. bubu* stem bark harvested at 6 p.m. at doses of 200, 400 and 800 mg/kg respectively.

Table 8. Effects of ethanolic extract of *F. bubu* on some parameters of liver and kidney function in male rats

	ED	Fb 200	Fb 400	Fb 800
ASAT (U/L)	115.90 ± 0.69	115.60 ± 4.14	113.60 ± 2.62	104.00 ± 2.49
ALAT (U/L)	88.67 ± 3.25	85.75 ± 1.52	88.28 ± 2.15	91.39 ± 3.28
PAL (U/L)	70.08 ± 6.00	72.10 ± 10.28	68.57 ± 3.12	64.52 ± 5.84
γ-GT (U/L)	12.38 ± 0.48	12.22 ± 0.39	10.66 ± 0.49	11.24 ± 0.39
BD (mg/dL)	0.17 ± 0.01	0.19 ± 0.01	0.12 ± 0.01	0.19 ± 0.02
BT (mg/dL)	0.69 ± 0.04	0.55 ± 0.11	0.46 ± 0.06	0.64 ± 0.12
PT (mg/dL)	0.65 ± 0.01	0.73 ± 0.01*	0.70 ± 0.01	0.72 ± 0.01*
CREA (mg/dL)	1.33 ± 0.10	1.56 ± 0.08	1.72 ± 0.14	1.64 ± 0.16
UREE (mg/dL)	32.94 ± 2.13	28.25 ± 2.18	26.71 ± 1.97	29.04 ± 2.18

Legend: AST = aspartate aminotransferase; ALT = alanine aminotransferase; ALP = alkaline phosphatase; γ-GT = γ-glutamyl transferase; DB = direct bilirubin; TB = total bilirubin; PT = total proteins; CREA = creatinine; *p < 0.05 = not significant; **p < 0.01 = significant compared to ED; ED = distilled water; Fb 200, 400 and 800 = rats given ethanolic extract of *F. bubu* stem bark harvested at 6 p.m. at doses of 200, 400 and 800 mg/kg respectively.

Table 9. Effects of ethanolic extract of *F. bubu* on some hematological parameters in female rats

	ED	Fb 200	Fb 400	Fb 800
GR (10^3/µL)	7.44 ± 0.45	7.60 ± 0.11	7.54 ± 0.47	7.74 ± 0.41
HGB (g/dL)	14.17 ± 0.62	14.13 ± 0.75	14.07 ± 0.20	14.10 ± 1.04
HTC (%)	46.64 ± 0.22	44.37 ± 0.55	42.72 ± 1.18	42.07 ± 0.66
GB (10^6/µL)	7.74 ± 0.32	7.85 ± 0.42	7.91 ± 0.15	7.96 ± 0.57
VGM (fL)	61.67 ± 2.19	59.00 ± 1.53	60.33 ± 0.88	59.67 ± 0.78
Lym (10^3/µL)	6.90 ± 0.14	6.42 ± 1.15	6.85 ± 0.11	6.27 ± 0.30
GRA (10^3/µL)	0.93 ± 0.07	0.92 ± 0.03	0.96 ± 0.03	0.90 ± 0.03
CCMH (g/dL)	33.57 ± 0.43	33.20 ± 0.42	33.70 ± 0.53	33.03 ± 0.24
TCMH (g/dL)	18.53 ± 0.49	18.43 ± 0.41	18.40 ± 0.36	18.37 ± 0.26
PLT (10^3/µL)	448.50 ± 5.49	441.50 ± 7.79	419.50 ± 11.26*	422.50 ± 2.02*
VPM (fL)	7.20 ± 0.23	7.27 ± 0.19	7.17 ± 0.22	7.13 ± 0.44

Legend: RBC = red blood cells; HGB = hemoglobin; HCT = hematocrit; WBC = white blood cells; MCV = mean corpuscular volume; Lym = lymphocytes; GRA = granulocytes; MCHC = mean corpuscular hemoglobin concentration; MCH = mean corpuscular hemoglobin; PLT = blood platelets; MPV = mean platelet volume; *p < 0.05 = not significant, **p < 0.01 = significant; ED = distilled water; Fb 200, 400 and 800 = rats receiving ethanolic extract of *F. bubu* stem bark harvested at 6 p.m.at doses of 200, 400 and 800 mg/kg respectively.

Table 10. Effects of ethanolic extract of *F. bubu* on some hematological parameters in male rats

	ED	Fb 200	Fb 400	Fb 800
GR (10^3/µL)	7.76 ± 0.15	7.58 ± 0.25	7.72 ± 0.40	7.54 ± 0.14
HGB (g/dL)	15.30 ± 0.21	15.03 ± 0.65	14.37 ± 0.57	14.67 ± 0.20
HTC (%)	46.36 ± 0.65	43.36 ± 0.55	43.12 ± 1.06	45.19 ± 0.95
GB (10^6/µL)	7.53 ± 0.23	7.42 ± 0.17	7.97 ± 0.34	8.07 ± 0.89
VGM (fL)	60.67 ± 1.20	57.00 ± 0.58	62.00 ± 1.53	60.33 ± 0.67
Lym (10^3/µL)	6.04 ± 0.27	5.93 ± 0.84	6.07 ± 0.32	6.21 ± 0.47
GRA (10^3/µL)	1.09 ± 0.05	1.08 ± 0.05	1.06 ± 0.22	1.08 ± 0.13
CCMH (g/dL)	31.90 ± 0.31	31.13 ± 0.72	32.03 ± 0.32	31.50 ± 0.12
TCMH (g/dL)	18.90 ± 0.47	18.57 ± 0.09	18.57 ± 0.27	18.47 ± 0.07
PLT (10^3/µL)	357.70 ± 5.36	426.50 ± 3.75***	431.00 ± 3.46***	396.50 ± 2.02***
VPM (fL)	7.40 ± 0.06	7.27 ± 0.18	7.33 ± 0.33	7.37 ± 0.19

Legend: RBC = red blood cells; HGB = hemoglobin; HCT = hematocrit; WBC = white blood cells; MCV = mean corpuscular volume; Lym = lymphocytes; GRA = granulocytes; MCHC = mean corpuscular hemoglobin concentration; MCH = mean corpuscular hemoglobin; PLT = blood platelets; MPV = mean platelet volume; *p < 0.05 = not significant, **p < 0.01 = significant; ED = distilled water; Fb 200, 400 and 800 = rats receiving ethanolic extract of *F. bubu* stem bark harvested at 6 p.m.at doses of 200, 400 and 800 mg/kg respectively.

Conclusion

This study demonstrated that extracts of *Ficus bubu* Warb., especially the stem bark, have promising antiplasmodial and anthelmintic activities, while remaining safe in acute and subacute toxicity models. The stem bark extract exhibited the highest efficacy against *P. falciparum* strains 3D7 and Dd2, as well as strong larvicidal activity against *Taenia solium* L3 larvae. Toxicological evaluations confirmed that the extracts are well tolerated, with no significant adverse effects observed in rats. These results suggest that *F. bubu* Warb. could serve as a potential source of bioactive molecules for the development of new antimalarial and anthelmintic agents. Further phytochemical and pharmacological investigations are warranted to isolate the active constituents and explore their mechanisms of action.

Abbreviations

10L1Fb: Leaves extract of *Ficus bubu* harvested at 6 a.m.
10R2Fb: Roots extract of *Ficus bubu* harvested at 12 noon
10B3Fb: Stem bark extract of *Ficus bubu* harvested at 6 p.m.
CQ: chloroquine
ART: artemisinin
SEM: Standard Error Mean
TC: Total cholesterol
LDH: lactate dehydrogenase
HDL-C: High density lipoproteins cholesterol
TG: Triglycerides
ED: normal control rats given distilled water
AST: Aspartate Aminotransférase
ALT: Alanine Aminotransférase
ALP: alkaline phosphatase
γ-GT: γ-glutamyl transferase
DB: direct bilirubin
TB: total bilirubin
PT: proteins
CREA: creatinine
RBC: red blood cells
HGB: hemoglobin
HCT: hematocrit
WBC: white blood cells
MCV: mean corpuscular volume
Lym: lymphocytes
GRA: granulocytes
MCHC: mean corpuscular hemoglobin concentration
MCH: mean corpuscular hemoglobin
PLT: blood platelets
MPV: mean platelet volume

Authors' Contribution

JEMT and ECEM designed the study and supervised the work; EEK conducted the experiments and drafted the first manuscript; GMMEL and SEN corrected the first version of the manuscript; LA and ELN analyzed the results and plotted the IC_{50} curves; all authors read and approved the final manuscript.

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Conflict of interest

The authors declare no conflict of interest

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