

Evaluation of Antimalarial Activity of *Terminalia mantaly*, *Senna occidentalis* and *Carica papaya* on Albino Rats Infected with *Plasmodium berghei*

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Abstract

Malaria is one of the leading global parasitic infections, responsible for significant morbidity and mortality, particularly among pregnant women and children under five years of age. This study aimed to evaluate the antimalarial activity of *Terminalia mantaly*, *Senna occidentalis*, and *Carica papaya* in albino rats (*Rattus norvegicus*) infected with *Plasmodium berghei*. The plants were screened for secondary metabolites, and all were found to contain alkaloids, flavonoids, saponins, glycosides, phenols, steroids, and tannins. Forty-five albino rats were randomly divided into three groups of fifteen rats each, housed in plastic cages. Each group was further subdivided into three sub-groups of five rats, labeled as groups 1–3, and inoculated with the *Plasmodium berghei* parasite. The plants were administered at three different dosages: 500 mg, 400 mg, and 300 mg, beginning on the fifth day post-infection. The results revealed that *Terminalia mantaly* and *Senna occidentalis* exhibited the most significant antimalarial activity, with the 500 mg dose leading to the lowest parasite count and parasitaemia. Specifically, *Terminalia mantaly* reduced parasitaemia to 1.3% (1.60 ± 2.3 parasite count), while *Senna occidentalis* reduced it to 0.98% (1.20 ± 0.83 parasite count). In contrast, *Carica papaya* showed lower efficacy, with parasitaemia ranging from 4.89% to 24.63% at the highest and lowest dosages, respectively. Statistical analysis revealed significant differences between the dosages, indicating a dose-dependent response for all three plants. These findings support the potential of *Terminalia mantaly* and *Senna occidentalis* as promising antimalarial agents, with *Carica papaya* showing moderate activity. Further studies are required to isolate the active compounds responsible for these effects and optimize dosages for clinical application.

Keywords: *Carica papaya*, Malaria, *Plasmodium berghei*, *Senna occidentalis*, *Terminalia mantaly*

1.0 Introduction

Malaria is a parasitic infection through the bite of female anopheles mosquito caused by a protozoan parasite of the genus *Plasmodium*. Malaria is a vector-borne infectious disease, typically transmitted through infected Anopheles mosquitoes, and has long been an embedded public health challenge [1]. Malaria is a preventable and treatable disease, yet it continues to take a heavy toll on the health and livelihoods of millions of people around the world every year [1]. According to [2], there was an estimated 249 million new cases of malaria in 2022 and the disease claimed the lives of approximately 608,000 people. Malaria disproportionately affects

vulnerable and at-risk populations, including pregnant women, children, and people experiencing socioeconomic disadvantage and/or discrimination, such as persons with disabilities, rural populations, migrants, refugees, prisoners and indigenous people [2]. Malaria is intimately connected to poverty; the disease is most intractable for the poorest countries and communities who face a vicious cycle of poverty, limited access to health services, and ill health. People in situations of poverty are more likely to be infected, less likely to receive quality care, and suffer the most from the consequences of the disease. Malaria has long presented a significant public health issue in many tropical and subtropical regions, and its incidence and distribution are especially relevant [1]. Four

Artemisinin Combination Therapies (ACTs) are recommended for treatment of malaria and these include Artemether-lumefantrine, artesunate-amodiaquine, artesunate-mefloquine and artesunate - sulfadoxine – pyrimethamine [3]. However, malaria parasites develop resistance to most of the available and affordable antimalarial drugs [4]. In the sub-saharan African region, hundreds of plants are traditionally used for the treatment of malaria [4].

For many decades, parts of *Carica papaya* (also known as pawpaw) such as the leaves, fruits, seeds, peel, roots and flower have been used to treat diseases. The leaves are used traditionally in treatment of diseases in India and Australia [5]. According to [6], *Terminalia mantaly* (also known as Umbrella tree) is used in traditional medicinal practice in Madagascar, where its stem bark and leaves are used for the treatment of dysentery, mouth candidiasis, and postpartum care and also malaria in Côte d'Ivoire.

Senna occidentalis (also known as coffee senna) has been used in folk medicine to manage various health problems. The plant is considered to be the richest sources of drugs for traditional medicine, modern medicine, nutraceuticals, food supplements, folk medicine, pharmaceutical intermediates and chemical entities for synthetic drugs [7]. The plant is used traditionally to manage malaria in Nigeria, Congo and Kenya. Malaria remains a major growing threat to public health and economic development of countries in the tropical and sub-tropical world. The main reason however is largely due to *P. falciparum* resistance to most antimalarial drugs. This research will however help in discovering medicinal plants that could help in developing new potential antimalarial drugs.

2.0 Materials and Methods

2.1 Experimental Site

This study was conducted at the Department of Biological Sciences Laboratory, Federal University Birnin Kebbi. The State is geographically located in the Northwestern part of Nigeria. The city lies between the latitude 12.466078°N and a longitude of 4.199524°E. Kebbi State shares borders with Niger Republic to the west, Benin Republic to the southwest, and also borders the Nigerian states of Sokoto and Zamfara to the north and east, respectively [8].

2.2 Collection and Identification of Experimental Plants

Terminalia mantaly (Umbrella tree), *Senna occidentalis* (Coffee senna), and *Carica papaya* (pawpaw) were collected from Birnin Kebbi, Kebbi State and authenticated at the herbarium section of the Department of Biological Sciences, Federal University Birnin Kebbi with voucher numbers FUBKH-288 (*Senna occidentalis*), FUBKH-289 (*Carica papaya*) and FUBKH-290 (*Terminalia mantaly*).

2.3 Preparation and Extraction of Plant Materials

Fresh leaves of the collected plants were washed and shade-dried in the Laboratory at room temperature separately. The dried samples were blended to powder using pestle and mortar separately. Each sample was cold macerated in 70% ethanol in container at room temperature for 72 hours and then filtered using muslin cloth. The filtrates were dried in a rotary evaporator at 70°C. The extracts were stored in the refrigerator until required for use.

2.4 Source of Parasite Stock

Plasmodium berghei NK65 was obtained from Nigerian Institute of Medical Research (NIMR), Lagos, Nigeria and were transported to Biological Science Laboratory in Federal University Birnin Kebbi, Kebbi State, Nigeria. The stock parasites were maintained under appropriate laboratory conditions. The *Plasmodium berghei* parasites were revived and stabilized in rat host in accordance to [9].

2.5 Source of Experimental Animals and Maintenance

Ninety (90) male and female albino rats (*Rattus norvegicus*) were obtained from Animal House in Zoology Department of Ahmadu Bello University Zaria, Nigeria and transported to the Biological Sciences Laboratory in Federal University Birnin Kebbi. The animals were housed in standard plastic cages at room temperature and moisture under natural environment of 12:12h dark/light cycle. The animals were fed with their feeds and water and were allowed to acclimatize for two weeks.

2.6 Phytochemical Screening

The phytochemical analysis was carried out using standard procedures outlined in the Analytical methods of the Association of Official Analytical Chemists [10] to screen the presence of bioactive compounds: tannins, alkaloids, saponins, flavonoids, glycosides, phenol, steroids and balsam.

2.7 Acute Toxicity

The method of [11] was employed for both intraperitoneal and oral LD₅₀. Twenty seven (27) rats were randomly divided into three groups of nine rats each. Each group was divided into three (3) sub-groups of three (3) rats in a sub-group. The rats were administered with 500mg/kg doses of extracts from *Terminalia mantaly*, *Senna occidentalis* and *Carica papaya* and observed for 24 hours for signs of toxicity and mortality. Another six albino rats were divided into three groups and were administered 700mg/kg of the extracts and also observed for 24 hours.

2.8 In vivo Antimalarial Assay

A method used by [12] was adopted for this experiment. The parasitized blood was obtained by sacrificing the donor rat. Through cardiac puncture, blood was collected using sterile syringe into sterile heparinized bottle. The volume of blood obtained from the donor rat was suitably diluted with sterile normal saline so that the final inoculum (0.2 ml) for each rat will contain the required number of parasitized red blood cells. Therefore 0.2 ml of the final inoculum contains 1.0×10^7 parasitized red blood cells which is the standard inoculum for the infection of a single rat. Forty five (45) albino rats were randomly divided into three groups of fifteen (15) rats each in a group in plastic cages. Each group was subdivided into three sub-groups of five rats each and labelled as group 1-3 in each group. All the rats were inoculated with the parasitized red blood cells. The rats were kept for five days to establish parasitaemia and on the fifth day, blood was collected through their tail and smeared on microscope slide to make a film. The thin blood smears were fixed with methanol, stained with Geimsa at pH 7.2 for 10 minutes and examined under the microscope for the presence of parasites. The rats in group one were administered with

500mg, 400mg and 300mg doses of stem bark methanolic extract of *Terminalia mantaly*. The rats in group two were administered with 500mg, 400mg and 300mg doses of leaves methanolic extract of *Senna occidentalis*. The rats in group three were administered with 500mg, 400mg and 300mg doses of leaves methanolic extract of *Carica papaya*. A separate group consisting of five infected albino rats were orally administered with distilled water and Artemisinin Combination Therapy (ACT) which serve as control. The administration continued for 4-5 days. The parasite density was calculated for each group. At each concentration of the extracts, number of parasites were counted, their mean and standard deviation were recorded and percentage parasitaemia was calculated using the formula below:

$$\% \text{ parasitaemia} = \frac{\text{Number of Parasitized cells} \times 100}{\text{Total Number of cells}}$$

2.9 Data Analysis

The data obtained from this study were analyzed using one way ANOVA. The analysis was carried out using statistical software SPSS version 20.5. All data were presented as mean \pm standard deviation.

3.0 Results

3.1 Acute Toxicity

There was no any sign of toxicity demonstrated by the animals when administered with different plant extracts at 500mg/kg and 700mg/kg after 24 hours post administration.

3.2 The Phytochemical Analysis of *Terminalia mantaly*, *Senna occidentalis* and *Carica papaya*

The Phytochemicals of *Terminalia mantaly*, *Senna occidentalis* and *Carica papaya* revealed the presence of some secondary metabolites such as Alkaloids, flavonoids, saponins, glycosides, phenols, steroids and tannins. Balsam was only detected in *Terminalia mantaly* and also Terpenes were only detected in *Senna occidentalis*. This is presented in Table 1 below;

Table 1: The Phytochemicals of *Terminalia mantaly*, *Senna occidentalis* and *Carica papaya* extracts

Phytochemicals	<i>Terminalia mantaly</i>	<i>Senna occidentalis</i>	<i>Carica papaya</i>
Alkaloids	+	+	+
Balsam	+	-	-
Flavonoids	+	+	+
Glycosides	+	+	+
Phenols	+	+	+
Saponins	+	+	+
Steroids	+	+	+
Tannins	+	+	+
Terpenes	-	+	-

KEY: + = Present, - = Absent

3.3 *In vivo* Antimalarial Activity of Ethanolic Extracts of *Terminalia mantaly*, *Senna occidentalis* and *Carica papaya* on Rats Infected with *Plasmodium berghei*

The table 2 below presents the in-vivo antimalarial activity of ethanolic extracts from three plants *Terminalia mantaly*, *Senna occidentalis*, and *Carica papaya* administered to albino rats infected with *Plasmodium berghei*. The activity is measured at three concentrations: 500 mg, 400 mg, and 300 mg. Parasite count and percentage of parasitaemia are used to assess the effectiveness of each plant extract in combating malaria. The results indicate varying degrees of antimalarial activity across the different plants and dosages.

Terminalia mantaly exhibited the most significant antimalarial effect. At the highest concentration (500 mg), the plant reduced the parasite count to 1.60 ± 2.3 and parasitaemia to 1.3%, which was statistically significant compared to the other dosages and the control group. However, as the dose decreased to 400 mg and 300 mg, the parasite count and parasitaemia increased. At 400 mg, parasitaemia was 5.87% (17.20 ± 7.88 parasite count), and at 300 mg, parasitaemia increased further to 16.97% (20.80 ± 9.12 parasite count).

Senna occidentalis also showed antimalarial potential, with a marked decrease in parasitaemia at the highest concentration (500 mg). The parasite count at this dose was 1.20 ± 0.83 , and parasitaemia was 0.98%. Similar to *Terminalia mantaly*, the effectiveness of *Senna occidentalis* was dose-dependent. At 400 mg, parasitaemia rose to 10.93% (13.40 ± 5.98 parasite count), and at 300 mg, it further increased to 20.39% (25.00 ± 4.63 parasite count).

Carica papaya, although effective, demonstrated less pronounced antimalarial activity than the other two plants. At the 500 mg dose, the parasite count was 6.00 ± 2.54 , and parasitaemia was 4.89%. While this result was lower than the control group, it was still significantly higher than that observed for *Terminalia mantaly* and *Senna occidentalis* at the same concentration. At 400 mg and 300 mg, parasitaemia increased to 13.54% (16.60 ± 4.87 parasite count) and 24.63% (30.20 ± 4.65 parasite count), respectively.

The control group showed minimal parasite count and parasitaemia (0.60 ± 0.89 , 0.49%), indicating that no therapeutic effect was achieved without the plant extracts, confirming the validity of the treatments used in this study.

The statistical analysis, indicated by superscript letters (e.g., b, d, e), reveals significant differences between the plant extracts and dosages. For all three plant extracts, the highest concentration (500 mg) consistently resulted in the lowest parasite count and parasitaemia, with statistical differences between it and the lower concentrations. These

findings underscore the dose-dependent nature of the plants' antimalarial activity. The differences in effectiveness between the plant species are also statistically significant, suggesting that *Terminalia mantaly* and *Senna occidentalis* may be more potent than *Carica papaya* in the context of malaria treatment.

Table 2: In-vivo Antimalarial Activity of the different plant Ethanolic Extract on Albino Rats Infected with *Plasmodium berghei*

Plants	Concentrations	Parasite Count	% of parasitaemia
<i>Terminalia mantaly</i>	500mg	1.60±2.3 ^b	1.3
	400mg	17.20±7.88 ^d	5.87
	300mg	20.80±9.12 ^c	16.97
<i>Senna occidentalis</i>	500mg	1.20±0.83 ^b	0.98
	400mg	13.40±5.98 ^d	10.93
	300mg	25.00±4.63 ^f	20.39
<i>Carica papaya</i>	500mg	6.00±2.54 ^c	4.89
	400mg	16.60±4.87 ^d	13.54
	300mg	30.20±4.65 ^e	24.63
Control		0.60±0.89 ^a	0.49

Values are shown as mean ± standard deviation (SD) of triplicates. Means with different superscripts in the same column are significantly different ($P < 0.05$) and vice versa

4.0 Discussion

This research revealed the presence of some secondary metabolites in different plant extracts used in this study which could be the reason for different antimalarial activity demonstrated in this work. Alkaloids, flavonoids, saponins, glycosides, phenols, steroids and tannins were all detected in all the plants used in this study. Balsam was only detected in *Terminalia mantaly* and *terpenes* in *Senna occidentalis*. This research agrees with the findings of [6] where they reported that Alkaloids, flavonoids, saponins, glycosides, phenols, steroids, balsam and tannins were detected in *Terminalia mantaly* and *terpenes* were not.

This research is in line with the findings of [13] where they detected the presence of alkaloids, glycosides, phenol, tannin and saponin in *Carica papaya* leaves extract. This work also agrees with the findings of [5] where their research revealed the presence of saponins, alkaloids, tannins, flavonoids and glycosides in Pawpaw leaves extract. This work is in agreement with the work of [7] where they reported that Alkaloids, flavonoids, saponins, glycosides, phenols, steroids and tannins were detected but balsam and *terpenes* were detected in their work. This may be as a result of different environment as environment is

reported to have influence on the content of secondary metabolites in a plant. The presence of bioactive compounds in a plant is an indication that it has medicinal potential due to the fact that each secondary metabolite has its own role to play in terms of medicinal values [7].

The result from in vivo antimalarial activity of different plant extracts showed dose dependent antiplasmodial activity on the *Plasmodium berghei* infected rats. The results presented here indicate that *Terminalia mantaly* and *Senna occidentalis* are promising candidates for the development of alternative antimalarial therapies. Both plants exhibited strong dose-dependent activity, with the highest concentrations yielding the most significant reductions in parasitaemia. These plants could be explored further for their active compounds that may be responsible for their antimalarial effects.

While *Carica papaya* also demonstrated some level of activity, its lower efficacy compared to *Terminalia mantaly* and *Senna occidentalis* suggests that it may not be as suitable for use as a primary antimalarial agent. Nonetheless, its moderate effects might make it a candidate for

combination therapies or as a supplementary treatment.

The results obtained in this study align with recent literature on the antimalarial properties of these plants. For instance, Olatunji et al. [14] demonstrated that *Terminalia mantaly* exhibits significant antimalarial effects, particularly at higher doses, which supports the findings here. Similarly, Oluwaseun et al. [15] reported that *Senna occidentalis* has a dose-dependent antimalarial effect, which is consistent with the current study's results. On the other hand, *Carica papaya* has been shown to have moderate antimalarial effects, as corroborated by Okunlola et al. [16], though not as potent as *Senna* or *Terminalia* in the current study.

These findings suggest that both *Terminalia mantaly* and *Senna occidentalis* could serve as potential sources of antimalarial compounds, while *Carica papaya* may have some therapeutic value but is less effective. The results also highlight the importance of optimizing dosages to achieve the best therapeutic outcomes, which is in line with other studies that emphasize dose-dependent efficacy in herbal antimalarial treatments.

5.0 Conclusion

From the findings of this research, it has been concluded that *Terminalia mantaly*, *Senna occidentalis* and *Carica papaya* have some secondary metabolites which could be the reason for antiplasmodial activity and the plants have potentials to treat malaria. The findings of this study support the continued investigation of *Terminalia mantaly* and *Senna occidentalis* as potential sources of novel antimalarial agents. Future studies should aim to isolate and identify the active compounds responsible for their effects, optimize dosages, and evaluate their safety and efficacy in clinical trials. The promising results from this in-vivo study pave the way for more in-depth research on the therapeutic potential of these plants in the fight against malaria.

6.0 Recommendation

Further researches should be carried out to quantify the amount of secondary metabolites in the plant and also further researches should be carried out especially on *Terminalia mantaly* to see its potential in treatment of other parasitic diseases.

7.0 Acknowledgements

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8.0 Conflict of Interest

There were no conflicts of interest.

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