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# ANTIPLASMODIAL ACTIVITIES OF ETHANOL AND ETHYL ACETATE STEM-BARK EXTRACT/FRACTION OF *Blighia sapida* K.D. KOENIG ON MICE INFECTED WITH *Plasmodium berghei*

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## ABSTRACT

Reduction and probably eradication of future occurrence of resistance in malarial parasite demand urgent attention towards the development of alternative antimalarial drugs with new mechanisms of action. In view of this, the study investigated the *in vivo* antiplasmodial activities of ethanol stem-bark extract and ethyl acetate fraction of *Blighia sapida* against *Plasmodium berghei* in mice, to provide scientific support for the ethnomedicinal uses of the plant. Ethanol extract (EE) and ethyl acetate fraction (EAF) of *B. Sapida* stem bark were evaluated for *in vivo* antimalarial activity, using mice model. EE at doses of 250, 500, 1000 mg/kg, and EAF at doses of 125, 250, 500 mg/kg body weight were administered orally. Pyrimethamine, Chloroquine, and Artemether served as positive controls while 0.9% normal saline was given to the negative control group. At doses of 250, 500, and 1000 mg/kg, EE produced chemosuppression of 90.72, 85.62, and 94.06% in prophylactics, 59.33, 75.33, and 82.89% in suppressive and in the curative model on Day 7, 59.46, 59.91, and 56.70% respectively. At doses of 125, 250, and 500 mg/kg, EAF produced chemosuppression of 45.95, 50.74, and 69.12% in prophylactics, 57.97, 66.11, and 81.06 in suppressive and in curative model 71.13, 74.52, and 82.80 % respectively. Results obtained were compared with the standard antimalaria drugs (89.46, 75.37, and 95.54% for pyrimethamine, chloroquine, and artemether, respectively). Results showed that the extract and fraction of *B. Sapida* possessed potent antiplasmodial activities at different doses considered, which supports its use as antimalarial ethnomedicinally.

**Keywords**: Antiplasmodium, curative, extract, *Plasmodium berghei,* prophylactic, suppressive.

## INTRODUCTION

Malaria continues to be a scientifically complex, economically challenging, and life-threatening disease that is prevalent in tropical and sub-tropical regions of the world. It is transmitted to humans by the infected female anopheles mosquito, which is the vector that carries the malaria-causing plasmodium parasite, (Caraballo and King, 2014; World Health Organization [WHO], 2016; Dahalan et al., 2019; Mikailu et.al., 2021).

Malaria affects a large proportion of the population annually around the world (Gething et al., 2012). Among the species, Plasmodium falciparum has been reported to be responsible for the highest lethality, making it a major burden of malaria affliction in Africa. However, Plasmodium vivax is a more abundantly spread species worldwide. It has been observed that there is an increase in the number of individuals with a clinical complication of P. vivax in endemic regions which has been linked to side effects of some antimalarial drugs (Ramos Junior et al., 2010). The high disease burden of malaria has been referred to as one of Africa's major hurdles to socio-economic development (Bhutta et al., 2014). The burden does not just arise from the direct consequence of the disease, but also from the associated economic costs of prevention and treatment as reported by Mabvuto (2014). In 2016, there were 216 million new cases of malaria and 445,000 malaria deaths globally (WHO, 2017). The malaria treatment strategies are to terminate the acute blood infection, clear hypnozoites from the liver, prevent future relapses, cure the clinical symptoms, and prevent the spread of infection (Baird, 2013). Malaria which is a major tropical disease has become increasingly resistant to standard antimalarial drugs. Few studies exist to validate the antimalarial properties of most medicinal plants especially Blighia sapida; hence this study set forth to investigate the antiplasmodial activities of EE and EAF of B. Sapida stem bark.

An ethnobotanical survey has shown that different ailments such as malaria, fever, yellow fever, head lice, dental decay, dysentery, infections of cutaneous, internal hemorrhage, burns, eyes inflammation, constipation, and whitlow have been treated with different parts of B. sapida (Ojo et al., 2018; Sinmisola et al., 2019). All parts of the B. sapida (bark, leaves, capsules, roots, seeds) are usually employed in the treatment of diseases (Simons and Leakey, 2004). B. sapida K. D. Koenig (Family Sapindaceae) is popularly known as "Ackee" (English), "Isin" (Yoruba), "Gwanja kusa" (Hausa), and ''Okpu'' (Ibo) (Aderinola et al., 2007). Oladele and Adewunmi (2008), in their review on medicinal plants used in the management of malaria among the traditional medicine practitioners in South-Western Nigeria, listed Blighia sapida Koenig (Sapindaceae) among other plants. The prophylactic, suppressive, and curative methods are established experimental test models used in determining antiplasmodial activities of any natural products (Alaribe et al., 2021). These models were employed in this study, percentage parasitemia and chemosuppression were also evaluated.

## MATERIALS AND METHODS

### *Plant collection and identification*

Fresh Blighia sapida stem-bark was collected from Sekona-Ede Road, Osun State, Nigeria. The plant material was identified and authenticated at IFE Herbarium (specimen voucher number 17623), by a Botanist at the Department of Botany, Obafemi Awolowo Univer-

sity, Ile-Ife, Nigeria.

***Preparation Plant extract***

The fresh stem bark of B. sapida was cut into tiny pieces after removing the dead cells, air-dried, and milled into powder by an electrical grinding Machine at the Drug Research and Production Unit (DRPU), Faculty of Pharmacy, Obafemi Awolowo University, Ile-Ife. The powdered material (1 kg) was macerated in 70 % (v/v) of ethanol/ water for 72 h at room temperature using the method of Handa et al. (2008) as reported by Adekola et al. (2020). The resulting suspension was filtered and strained with a muslin cloth. The different filtrates were pooled, sieved with white cotton gauze, and filter paper (Whatman No. 1); thereafter, concentrated with a rotary evaporator (Edman High Vacuum Pump) at 40 ºC to yield a residue termed ethanol extract (EE). The resulting extract was weighed, labeled, and stored in the desiccator until required.

***Fractionation of ethanol extract***

The ethanol extract (EE) was partitioned using solvents of varying polarities as described by Geidam et al. (2007). Typically, extract (30 g) was suspended in distilled water (200 mL), shaken thoroughly, and filtered with filter paper (Whatman No. 1). The filtrate was partitioned sequentially with 400mL of each solvent (ethyl acetate and butanol). The mixture was thoroughly shaken, allowed to separate into layers, and separated. The process was repeated for each of the solvent systems several times until the solvent became colorless. The fractions (ethyl acetate fraction [EAF] and butanol fraction [BF]) of the different solvents were concentrated in the rotary evaporator separately. The fractions were weighed, labeled, and kept in desiccators until needed. The EE and EAF were used for the antiplasmodial study because of their bioactivities among other fractions in the in vitro assays carried out.

***Experimental animals***

Healthy adult albino mice (Mus musculus) of either sex, weighing 18-20 g were obtained from the College of Health Sciences, Obafemi Awolowo University, Ile-Ife, Nigeria. The animals were acclimatized to the laboratory conditions for two weeks at the Department of Pharmacology, Faculty of Pharmacy, fed with standard pellet obtained from the Feeds store in Ile-Ife, and had free access to water ad libitum. The principle of laboratory animal care (NIH publication No. 85-23) guidelines and procedures were followed in the study. Animal handling and care complied with international laboratory animal use and care guidelines and the ethical approval for the study (reference number IPH/OAU/12/1332) was obtained from Health Research Ethics Committee, Institute of Public Health, Obafemi Awolowo University, Ile-Ife, Nigeria.

***Acute oral toxicity test***

An acute oral toxicity test was conducted according to Lorke (1983), with slight modifications, using albino mice. The maximum limit dose of 5000 mg /kg was administered to mice for each extract and the mice were observed for mortality 24 h.

***Experimental design***

Chloroquine-resistant Plasmodium berghei (ANKA) obtained from the Institute for Advanced Research and Training (IMRAT) College of Medicine, University of Ibadan, was used to model malaria in the mice. Mice were infected with 0.2 mL of parasitized red blood cells containing about 1.0 x 107 parasites of chloroquine-resistant Plasmodium

berghei (ANKA). Each mouse was inoculated on day one intraperitoneally as reported by Basir et al. (2012). The infected mouse (donors) were monitored for parasite growth. Parasitaemia level was checked every other day and when the level reached about 30%, they were sacrificed and blood was collected into the heparinized bottle by cardiac puncture. Thereafter, inoculums of 0.2ml of parasitized red blood cells containing about $1.0 \times 10^7$ parasites infected red cells were prepared with normal saline. Three experimental test models used were residual infection (prophylactic), early infection (suppressive), and established infection (curative).

***Prophylactic test***

The residual infection (prophylactic) entailed a 3-day treatment of the test animals prior to inoculation with the parasites (Peters, 1965 as modified and reported by Iwalewa et al., 2007 and Orabueze et al., 2020). Five groups of 5 mice were used for each experiment. Three of the groups were administered with 250, 500, 1000 mg/kg EE or 125, 250, 500 mg/kg of EAF. The fourth group received positive control pyrimethamine (1.2 mg/kg). Normal saline (0.2mL) was administered to the negative control groups. Parasitaemia level was assessed 72 h after infection with an inoculum of 0.2mL of parasitized red blood cells containing about $1.0 \times 10^7$ parasites intraperitoneally. Thin smears of blood were prepared from each mouse on a microscope slide. The smears were then fixed with methanol and stained with Giemsa, it was allowed to dry followed by examination and calculation of the percentage of parasitized red blood cells under the microscope.

***Suppressive test***

The four-day suppressive test described by Peters (1965 as modified and reported by Iwalewa et al., 2007) was employed. Injection of inoculums of 0.2mL of parasitized red blood cells containing about $1.0 \times 10^7$ parasites and test substances was started concomitantly. Oral administration of the extract, vehicle, and standard drug was carried out once a day for 4 days. Six groups of 5 mice were used for the experiment. Three of the groups were administered with 250, 500, 1000 mg/kg EE or 125, 250, 500 mg/kg EAF respectively. The fourth and fifth groups received positive control; chloroquine (10 mg/kg) and artemether (25 mg/kg). Normal saline (0.2mL) was administered to the negative control groups. On day 5, thin smears of blood films were prepared from the tail of each mouse on a microscope slide. The smears were then fixed with methanol and stained with Giemsa to examine the parasitized red blood cells under the microscope as described by Abdulelah et al. (2011). The percentage of parasitemia and chemosuppression was calculated according to the method described by Bain (2017) and Bobasa et al. (2018).

$$\%\ \text{parasitemia} = \frac{\text{No of infected erythrocytes (PRBC)}}{\text{Total no of erythrocytes (TRBC)}} \times 100$$

$$\text{Average \% chemosuppression} = \frac{\text{Average \% parasitemia in control} - \text{Average \% parasitemia in treated groups}}{\text{Average \% parasitemia in control}} \times 100$$

***Curative test***

In the case of an established infection test (Curative), oral administration was started 72 h after infection of the animals with inoculums of 0.2mL of parasitized red blood cells containing about 1.0 x 107 parasites (Peters, 1965 as modified and reported by Iwalewa et al., 2007). Once-daily, oral administration of the extract, vehicle, and standard drug was carried out for 5 days. Six groups of 5 mice were used for each experiment. Three of the groups were administered with 250, 500, 1000 mg/kg EE or 125, 250, 500 mg/kg EAF. The fourth and fifth groups received positive control; chloroquine (10 mg/kg) and Artemether (25 mg/kg). Normal saline (0.2mL) was administered to the negative control group. Parasitaemia levels were assessed every other day of treatment and chemosuppression was calculated.

***Data analysis***

The data obtained were analyzed using a one-way analysis of variance (ANOVA) followed by Tukey – Kramer multiple comparisons test using the software Graph pad Prism. The statistical significance was set at $p < 0.05$. Values were expressed as mean ± standard error of the mean (SEM).

## RESULTS

***Acute toxicity test of ethanol extract and ethyl acetate fraction***

There was no death recorded and the animals revealed no signs of toxicity at the maximum dose of 5000 mg/kg for both the extract and its fraction when observed according to the procedure.

***Prophylactic (residual infection) activity***

The result revealed a non-dose dependent activity on the parasitemia level for EE (Table 1) while that of EAF was dose-dependent (Table 2) at $p < 0.05$. The activity of the extract (90.72%) was favorably compared with that of the standard drug (Pyrimethamine) (89.46%) at the lowest dose of 250 mg/kg body weight.

**Table 1: Prophylactic Antiplasmodial Activity of Ethanol Extract of *B. sapida***

| Dose (mg/kg) | Mean % parasitaemia ± SEM | Mean % Chemosuppression |
|---|---|---|
| Negative control (0) | 11.96 ± 4.98 | 0.00 |
| 250 | 1.11 ± 0.34[a,b] | 90.72 |
| 500 | 1.72 ± 0.36[a] | 85.62 |
| 1000 | 0.71 ± 0.25[a] | 94.06 |
| Pyrimethamine (1.2) | 1.26 ± 0.22[a] | 89.46 |

Each value represented the Mean ± SEM, (n = 5) and values with superscript (a) are statistically different from the control while value with superscript (a,b) is not statistically different from the standard drug at $p > 0.05$.

**Table 2: Prophylactic Antiplasmodial Activity of Ethyl Acetate Extract of *B. sapida***

| Dose (mg/kg) | Mean % parasitaemia ± SEM | Mean % Chemosuppression |
|---|---|---|
| Negative control (0) | 2.72 ± 0.15 | 0.00 |
| 250 | 1.47 ± 0.13[a] | 45.95 |
| 500 | 1.34 ± 0.19[a] | 50.74 |
| 1000 | 0.84 ± 0.12[a] | 69.12 |
| Pyrimethamine (1.2) | 1.26 ± 0.22[a] | 89.46 |

Each value represented the Mean ± SEM, (n = 5) and values with superscript (a) are statistically different from the control at $p > 0.05$.

***Four-day suppressive (Early infection) activity***

The result revealed a dose-dependent suppressive activity on the parasitemia level. The activities of both the EE and its fraction were statistically significant compared to control at $p < 0.05$. The EE at the lowest dose of 250 mg/kg displayed 59.33% and 82.89% was estimated at the highest dose of 1000 mg/kg, while the two standard drugs (Chloroquine and Artemether) produced 32.67 and 41.56% respectively (Table 3). The EAF at the lowest dose of 125 mg/kg produced 57.97% chemosuppression when compared with the negative control group while the dose of 250 mg/kg gave 66.11% and at the highest dose of 500 mg/kg, the chemosuppression was increased to 81.06%. The values of the two standard drugs were 32.67 and 83.06% (chloroquine and Artemether respectively). It was observed that Artemether showed the highest percentage chemosuppression value while chloroquine possessed the least chemosuppression (Table 4).

**Table 3: Suppressive Antiplasmodial Activity of Ethanol Extract of *B. sapida***

| Dose (mg/kg) bwt | Mean % parasitaemia ± SEM | Mean % Chemosuppression |
|---|---|---|
| Negative control (0) | 4.50 ± 0.25 | 0.00 |
| 250 | 1.83 ± 0.27[a] | 59.33[a] |
| 500 | 1.11 ± 0.22[a] | 75.33 [a] |
| 1000 | 0.77 ± 0.20[a,b] | 82.89[a,b] |
| Chloroquine **(**10) | 3.03 ± 0.53[a] | 32.67 [a] |
| Artemether (25) | 1.02 ± 0.87 [a] | 83.06 [a] |

Each value represented the Mean ± SEM, (n = 5) and values with superscript (a) are statistically different from the negative control while values with superscript (a,b) are not statistically different from the standard drug (Artemether) at $p > 0.05$.

**Table 4: Suppressive Antiplasmodial Activity of Ethyl Acetate Extract of *B. Sapida***

| Dose (mg/kg) bwt | Mean % parasitemia ± SEM | Mean % Chemosuppression |
|---|---|---|
| Negative control (0) | 6.02 ± 0.64 | 0.00 |
| 125 | 2.53 ± 0.25[a] | 57.97[a] |
| 250 | 2.04 ± 0.38[a] | 66.11 [a] |
| 500 | 1.14 ± 0.18[a,b] | 81.06[a,b] |
| Chloroquine **(**10) | 3.03 ± 0.53[a] | 32.67 [a] |
| Artemether (25) | 1.02 ± 0.87 [a] | 83.06 [a] |

Each value represented the Mean ± SEM, (n = 5) and values with superscript (a) are statistically different from the negative control while values with superscript (a,b) are not statistically different from the standard drug (Artemether) at $p > 0.05$.

***Curative activity (Established infection)***

There was a daily reduction in the parasitemia level in standard drugs and the fraction from (Day 3) to (Day 7) at $P < 0.05$ while there was an increase in parasitemia level of the control group (Normal saline) from day 3 to day 7. However, on day 7, the average percentage chemosuppression of parasitemia by ethanol extract were (59.46, 59.91, and 56.70 ) at doses of 250, 500, and 1000 mg/kg body weight while that of ethyl acetate group displayed (71.13, 74.52, and 82.80 ) at doses of 125, 250, and 500 mg/kg body weight (Table 5) compared to the standard drugs (75.37 and 95.54) at doses of 10 and 25 mg/kg body weight respectively (Tables 6).

**Table 5: Curative antimalarial activity of Ethanol Extract of *B. Sapida***

| Dose (mg/kg) bwt | Mean % Parasitaemia (Mean % Chemosuppression in bracket) | | |
|---|---|---|---|
| Day | Day 3 | Day 5 | Day 7 |
| Negative control (0) | 24.36 ± 0.43 (0.00) | 26.42 ± 0.33 (0.00) | 28.66 ± 0.37 (0.00) |
| 250 | 14.64 ± 0.19 (44.59)[a] | 12.85 ± 0.19 (47.25)[a] | 11.62 ± 0.44 (59.46)[a] |
| 500 | 16.24 ± 0.37 (38.53)[a] | 11.64 ± 0.17 (52.22)[a] | 11.49 ± 0.46 (59.91)[a] |
| 1000 | 15.42 ± 0.18 (41.64)[a] | 12.00 ± 0.18 (50.74)[a] | 12.41 ± 0.38 (56.70)[a] |
| Chloroquine (10) | 2.67 ± 0.46 (52.49)[ab] | 1.40 ± 0.38 (69.83)[ac] | 1.16 ± 0.25 (75.37)[ad] |
| Artemether (25) | 2.00 ± 0.65 (64.41)[ab] | 0.57 ± 0.37 (87.74)[ac] | 0.21 ± 0.99 (95.54)[acd] |

Each value represented the Mean ± SEM, (n = 5) and values with superscript (a) are statistically different from the negative control while values with (ab,ac, ad, acd) are statistically different from extract-treated groups along the column at $p < 0.05$.

**Tables 6: Curative Antiplasmodial Activity of Ethyl Acetate Extract of *B. Sapida***

| Dose (mg/kg) bwt | Mean % Parasitaemia (Mean % Chemosuppression in bracket) | | |
|---|---|---|---|
| Day | Day 3 | Day 5 | Day 7 |
| Negative control (0) | 4.65 ± 0.43 (0.00) | 4.71 ± 0.69 (0.00) | 5.62 ± 0.46 (0.00) |
| 125 | 3.08 ± 0.20 (45.20)[a] | 2.62 ± 0.16 (43.66)[a] | 1.36 ± 0.11 (71.13)[a] |
| 250 | 4.08 ± 0.24 (27.40) [a] | 2.22 ± 0.17 (52.26)[a] | 1.20 ± 0.09 (74.52)[a] |
| 500 | 4.75 ± 0.13 (15.48)[a] | 1.43 ± 0.26 (69.25)[a] | 0.81 ± 0.11 (82.80)[a] |
| Chloroquine (10) | 2.67 ± 0.46 (52.49)[ab] | 1.40 ± 0.38 (69.83)[ac] | 1.16 ± 0.25 (75.37)[ad] |
| Artemether (25) | 2.00 ± 0.65 (64.41)[ab] | 0.57 ± 0.37 (87.74)[ac] | 0.21 ± 0.99 (95.54)[acd] |

Each value represented the Mean ± SEM, (n = 5) and values with superscript (a) are statistically different from the negative control while values with (ab, ac, acd) are statistically different from ethyl acetate treated groups along the column at $p < 0.05$.

## DISCUSSION

Malaria remains a serious global health issue, despite the number of investigations conducted on the disease prevalence, transmission patterns, or treatment (Antonio-Nkondjio et al., 2019). In the 2015 global malaria report, WHO stated that there were 212 million and 429,000 malaria cases and deaths respectively, in which Africa constitutes about 90% (WHO, 2016; Bobasa et al., 2018). The treatment and management of malaria constitute medical issues because of the rate at which the parasites are resistant to the number of available drugs, even combination therapy, uncontrolled reproduction in mosquitoes, and dearth of vaccines (Fenta and Kahaliw, 2019). There is a need for continuous searching for and development of effective new antimalarial drugs.

Prophylactic, four-day suppressive, and curative test models were employed to investigate the effects of both the extract and its EAF on prophylaxis, early and established infections. Percentage inhibition of parasitemia and chemosuppression were compared among the experimental and control groups to determine the antimalarial activity. The extract and its fraction displayed both dose-dependent and non-dose-dependent reduction in the percentage of parasitemia levels in the models used. The findings support the investigation of Oladele and Adewunmi (2008) who classified B. sapida as one of the plants used in the management of malaria in South-Western Nigeria among the traditional medicine practitioners. The antiplasmodial activities of the extract may be due to the presence of alkaloids that are known to be effective against the malaria parasite, and other secondary metabolites in the plant, many of which have been reported to be used as pharmaceuticals (Newman and Cragg, 2012), to possess antiplasmodial effects (Enechi et al., 2019).

The acute toxicity study revealed that oral

administration of Hydro-alcohol extract and the EAF of B. sapida produced no mortality in animals up to the dose of 5000 mg/kg. The rate of feeding was normal, the animals were active, no morphological or behavioral change was observed and no mortality was recorded. The result implies that the LD50 of the extract is above 5000 mg/kg. This method suggests the classification of the extract and its fraction based on the prediction of the dose at which the animals must survive. This is in accordance with Sandu et al. (2012) toxicity scale principle, in which it was stated that any substance with an LD50 value greater than 5000 mg/kg is practically nontoxic.

The extract and EAF of B. sapida demonstrated a statistically significant ($p < 0.05$) inhibition of parasitemia in the three test models, which is an indication of the effectiveness of both the EE and EAF to prevent multiplication and further infection of the parasite on red blood cells. The dose-dependent activity was apparent in the ethyl acetate fraction than the extract but the extract displayed higher prophylactic activity, which could be due to a combination of various secondary metabolites present in the extract.

The extract and EAF exhibited dose-dependent parasitemia chemosuppression activities in the model, and the highest activity was recorded at the maximum dose administered for the extract and fraction. Both the EE and EAF competed favorably with the standard drug (artemether) at their highest doses. The chloroquine possessed the least chemosuppression at ($p < 0.05$). The result corroborates the research work of Ajaiyeoba et al. (2006) who reported the activity of methanol extract of Annona senegalensis to be dose-dependent but unlike the results of Olorunniyi and Morenikeji, (2014) in which the activity of crude aqueous leaf extract of Pyrenacanth astaudtii was non-dose-dependent chemosupression.

Similarly, the results of the curative model showed statistically significant inhibition of parasitemia at $p < 0.05$, in which there was clearance in the parasitemia level in EAF from Day 3 to Day 7 when compared with a negative control group (Normal saline). However, an increase in percentage chemosuppression of the extract-treated groups as well as those of positive control (Chloroquine and Artemether) was observed. For EAF, the average percentage chemosuppression on Day 7 was comparable with the positive control (Chloroquine and Artemether). It was shown that B. sapida exhibited a dose-dependent increase in percentage chemosuppression in the groups treated with EAF (71.1, 74.5, and 82.8%) at doses of 125, 250, and 500 mg/kg, with a similar increase in the standard drugs (Chloroquine and Artemether), treated groups. However, an increase in the level of parasitemia was observed in the untreated control group. This study was in line with those of Iyiola et al. (2011) and Odeghe et al. (2012) in which methanol extract of Anthocleista grandiflora showed a dose-dependent chemosupression. The result is an indication of the effectiveness of this extract in the treatment and management of malaria.

From the values of mean percentage chemosuppression in the three test models considered, EAF demonstrated the highest suppressive and curative antiplasmodial activities. The enhanced activities of this fraction could be deduced from its level of purity by fractionation process compared to EE. Also, phytochemical constituents have been re-

ported to contain an antimalarial property by Kim and David (2013), phytochemicals such as alkaloids, saponins, cardiac glycoside, tannins, flavonoids, terpenoids, and phenolic present in the stem-bark of B.sapida may be responsible for its antimalarial effects.

The prophylactic aspect of this study corroborates the work of Otegbade (2017), in that the EE displayed the highest prophylactic activity against chloroquine-resistant P. berghei parasites but contradicts the same, in the sense that dose-dependent activities were apparent in both prophylactic and suppressive models for EE as well as EAF, non-dose dependent activity was only observed in the curative model for EE. However, the difference observed between the result of this study and that of Otegbade (2017) could be associated with various ways in which different organisms react to treatments as well as the rate at which they metabolize foreign substances. Since the metabolism of any foreign substance could lead to the production of either more active or less active compounds.

## CONCLUSION

This experiment showed that ethanol extract and the fraction of B. Sapida possessed promising antiplasmodial activity against chloroquine-resistant P. berghei parasites, which can serve as justification for its use as an antimalarial in South-Western Nigeria. EAF possessed the highest curative activity, the EE displayed the highest prophylactic while both the EE and EAF are good candidates for suppressive antiplasmodial activities. The displayed antimalarial activity, as well as absence of death and any sign of toxicity in acute toxicity study, affirms its Ethno-botanical use. Hence, there is a need for further study to isolate and characterize the active compound (s) responsible for the observed activity.

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