ANTIPLASMODIAL ACTIVITY AND PHYTOCHEMICAL EVALUATION OF THE STEMS OF *ALBIZIA CORIARIA* AND *FICUS SUR*.

ABSTRACT

Background: Malaria continues to wreak havoc on various populations as a result of the mortality and economic burden associated with the disease. Progress made in the therapeutics of the disease is threatened by the emerging parasite resistance to currently used first line treatment drugs. This has prompted the search for new, effective, and safe antimalarial agents. The use of traditional medicine in the treatment of various types of diseases including malaria is a regular practice seen with many cultures in Ghana. The stem of *Albizia coriaria* and *Ficus sur* are such plants in use with little evidence about their *in vivo* efficacy.

Aim: This study therefore aimed to assess the *in vivo* antiplasmodial potential, and the safety of the hydroethanolic stem extract of *Albizia coriaria* and *Ficus sur*.

Method: Qualitative phytochemical screening was done on the powdered plant material and its extracts using standard methods. Acute toxicity was carried out according to OECD guidelines using the Limit test. *In vivo* antiplasmodial activity of the hydroethanolic extract was assessed using the Peter's 4-day suppressive and Rane's curative test.

Results: The powdered plant samples and their respective hydroethanolic extracts revealed the presence of terpenoids, flavonoids, coumarins among others. The hydroethanolic extract was safe with the lethal dose above 3000 mg/kg. All the extracts significantly ($P < 0.005$) suppressed parasitaemia in the Peter's suppressive and Rane's curative test with *Albizia coriaria* producing the highest suppression of 68.89 and 61.46% in the suppressive and curative test respectively. Whereas the highest suppression of 44.00 and 49.54% was recorded for *F. sur* in the suppressive and curative test respectively.

Conclusion: This study has provided a basis for the traditional use of the stem of *Albizia coriaria* and *Ficus sur* in the treatment of malaria.

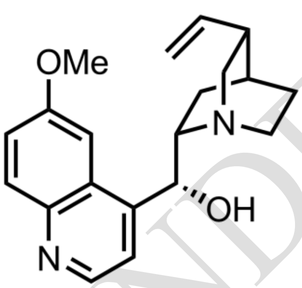
1. INTRODUCTION

The use of plants in the treatment of diseases across various civilizations is well embedded in history (1). Herbs and herbal products are been used extensively in all parts of the world, not only in traditional medicine, but also as a source of valuable substances useful as food, pharmaceuticals and cosmetics (2). Only a small fraction of the over 350000 species of plants in the world have been evaluated pharmacologically and phytochemically. Phytochemical investigations of medicinal plants have revealed various phytoconstituents with varying pharmacological actions, some of which are used clinically. Hence, the plant kingdom can be said to have a massive storehouse of compounds of pharmacological significance that needs to be explored (3). In most cases, information on the potential pharmacological activity is obtained through ethnobotanical survey. One disease, for which ethnobotanical information afforded clinically important drugs for its mitigation is malaria.

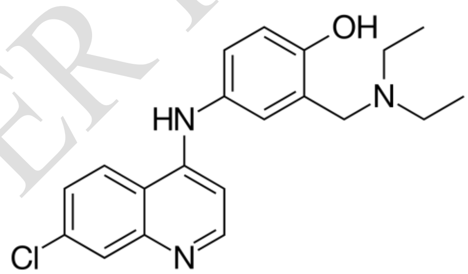
Malaria remains one of the most devastating diseases in the world, especially in developing countries, despite the global efforts targeted at eradicating or controlling the disease. The disease impacts over 500 million people internationally and causes mortality between 1 to 2.5 million people every year, with the most vulnerable groups being pregnant women and children under the age of 5 (1). Different ethnobotanical surveys have identified several plants used in traditional medicine for the treatment of malaria (6). Some of these plants were explored to produce natural, semi-synthetic and synthetic antimalarial drugs for clinical use. For example, from the aminoquinoline alkaloid quinine, isolated from the stem bark of Cinchona species, several antimalarial medications including chloroquine and amodiaquine were produced. Similarly, the leaves of the Chinese plant *Artemisia annua*, yielded several artemisinin derivatives including dihydroartemisinin, artesunate and artemether as antimalarials. The discovery of these agents, using natural products as template for their design, brought malaria on it knees averting needless deaths especially, in sub-Saharan Africa where the impact of the disease is most felt. However, due to the development of resistance by the plasmodium parasite, the efficacy of these antimalarials is on the wane. Chloroquine, for example, was abandoned as first line treatment of malaria about two decades ago upon recommendation by the world health organisation due to tangible proofs of resistance and therapeutic failure (7). Artemisinin-based combination therapies were introduced to mitigate this threat but there are worrying signs of the development of resistance to this first line treatments. To date, however, resistance to quinine is not widespread (8), the first antimalaria compound discovered from plant. Thus, exploration of the efficacy of medicinal plants used in folklore medicine for the treatment of malaria is a rational research approach since majority of secondary metabolites in plants remain underexploited (9).

Malaria is very endemic in Ghana, accounting for 2% and 3% of global cases and deaths respectively (2). Ghana is ranked among eleven other countries, as a high-burden country, accounting for >70% of the global malaria cases and deaths (10). Several Ghanaians use home-based herbal remedies containing for example *Cryptolepis sanguinolenta* root and *Azadirachta indica* leaves, for the management of malaria (10). For most of these homebased medications, there is no scientific data in support of their use and their bioactive ingredients have also not been explored. In this research two of such plants, stem bark of Ficus sur and whole stem of Albizia coriaria used in folklore medicine for the treatment of malaria, were evaluated for their antiplasmodial activities.

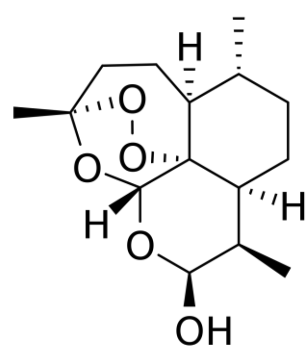
Ficus sur is one of the 750 plant species belonging to the family Moraceae. It occurs from sea-level up to 2500 m altitude, on riverbanks and in riverine forest, but also in upland forest, woodland and wooded grassland. Locally known as ‘Odoma’ (Akan-Twi). A decoction of the bark is used in the treatment of malaria, pain, rheumatism, diarrhoea, oedema in children, infertility and as a galactagogue (11). *Albizia coriaria* is one of about 150 species that belong to the Genus Albizia. This genus is pan tropical, occurring in Asia, Africa, Madagascar, North America and Australia. It is utilized traditionally in the treatment of tape worm infection, stomach trouble, amoebic dysentery and malaria (12). The use of the stem of *Albizia coriaria* and *Ficus sur* in the treatment of malaria has been documented traditional medicine. There is, however, lack of scientific data on the efficacy of the plant extracts. This study therefore aimed to investigate the antiplasmodial activity of the hydroethanolic extract of the two plants and investigate their phytochemical constitution.



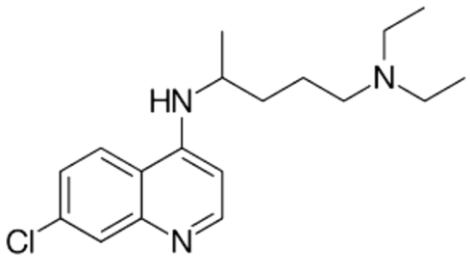
Quinine



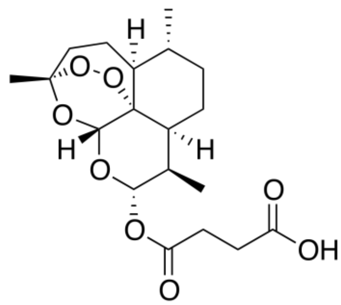
Amodiaquine



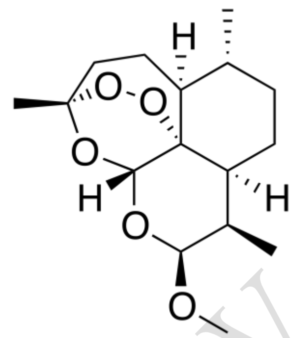
Dihydroartemisinin



Chloroquine



Artesunate



Artemether

Plate 1. Chemical structure of different phytochemicals

2. METHOD

2.1. PLANT MATERIAL COLLECTION AND AUTHENTICATION

The stem bark of *Albizia coriaria* and *Ficus sur* were harvested from Kwahu Asakraka in the Eastern Region of Ghana. The plant materials were authenticated by Prof. Isaac Kingsley Amponsah of the Department of Pharmacognosy, Faculty of Pharmacy and Pharmaceutical Sciences, Kwame Nkrumah University of Sciences and Technology (KNUST). Herbarium specimens of *A. coriaria* and *Ficus sur* were kept in the herbarium of the Department of Herbal medicine with identification (KNUST/HM1/2020/S051) and (KNUST/HM1/2020/S054) respectively.

2.2. PROCESSING OF PLANT MATERIALS AND EXTRACTION

The harvested plant materials were washed under running tap water, chopped into smaller pieces and air dried under shade and ambient temperature (28-35^{o}C) for 14 days. Each dried plant material was coarsely powdered using a mechanical grinder and packed into brown paper bags and kept at the laboratory until required for use. Five hundred grams each of the coarsely powdered stem bark of *Albizia coriaria* and *Ficus sur* were Soxhlet extracted with 70% ethanol. They were concentrated at 50 °C under reduced pressure using the rotary evaporator and subsequently kept in a desiccator.

2.3. BIOASSAYS

2.3.1. Ethical clearance

Animal experimental techniques were carried out after the study received ethical permission from the Committee on Animal Ethics and Research, Department of Pharmacology, Kwame Nkrumah University of Science and Technology (KNUST/Cology/034). Furthermore, guidelines for the Helsinki Declaration for the care of experimental animals were meticulously observed (13).

2.3.2. Acute toxicity

Albizia coriaria and *Ficus sur* have a long history of use in traditional medicine as antimalarial plants without demonstrable toxicity hence the limit test at the single dose of 3000 mg/kg body weight was adopted (14). Swiss albino rats were put into three (3) groups of three (3). Two groups as test groups for each extract with the last group designated as the control group. Animals were starved overnight and given water *ad libitum*. Following the starvation period, rats were weighed and dosed with 3000 mg/kg bodyweight of extract using a gastric tube. Feeding was delayed for another 3 hours after drug administration, during which the rats were individually monitored at 30-minute intervals for the first 1 hour and then on occasionally for the following 24 hours, with specific attention paid to the first 4 hours. Thereafter, observation was made daily for the next 13 days for indicators of toxicity including gross physical and behavioural changes.

2.3.3. Experimental animals

Swiss albino mice and rats were obtained from the Noguchi Memorial Institute for Medical Research (NMIMR), University of Ghana, Legon, Accra. Animals were housed at the animal house of the Department of Pharmacology, KNUST. They were exposed to a 12:12 hours dark-to-light cycle with free access to clean drinking water and pellet diet. All the animals were allowed a week of acclimatization before the experiment (15). All experiments were conducted with regards to the internationally accepted laboratory animal use, care and guidelines.

2.3.4. Parasite inoculation

The ANKA strain of *Plasmodium berghei* was obtained from the KNUST School of Medical Sciences. Healthy mice were infected with the Plasmodium parasite by intraperitoneal injection of 0.2 mL of inoculum (infected blood with the parasitaemia level: 1×10^7 parasitized erythrocytes) as described by Baah et al., (16).

2.3.5. Four-day suppressive antimalarial test

This test was used to evaluate the schizonticide activity of the hydroethanolic extracts against *P. berghei* infected mice (17). Swiss Albino mice were inoculated on the first day (Day 0), intraperitoneally, with 0.2 ml of infected blood. The mice were then divided randomly into eight groups of five mice per group. Six groups (I, II, III, IV, V and VI) were assigned as test groups for the two extracts whereas groups (VII & VIII) were used as control (negative and positive). Three hours after infection 30, 100 and 300 mg/kg/day of hydroalcoholic crude extract of *A. coriaria* and *Ficus sur* were administered to the test groups. Artesunate at the dose of 4 mg/kg/day and an equivalent volume of vehicle (0.2 ml 7% tween 80 solution) were administered to the positive and negative control groups respectively, for four consecutive days (Day 0–3). On the fifth day, (96 h post-infection), thin blood smears were made from the tail of each mouse, fixed with methanol and stained with 10% Giemsa. Parasitaemia was determined by counting the number of parasitized red blood cells out of total red blood cells in five randomly chosen fields of the slide using a light microscope (Leica DM750, Wetzlar-Germany). Percentage parasitaemia was determined as described by Baah et al., (16).

2.3.6. Rane's Curative Test

The curative potential of the hydroethanolic stem extracts of the plants were evaluated as described by Nardos *et al* (18). Seventy-two (72) hours following parasite inoculation, mice were randomly divided into eight groups after the establishment of parasitaemia. Mice were dosed with 30, 100 and 300 mg/kg/day of extract, 4 mg/kg/day of artesunate and 2 ml/day of the vehicle for 4 consecutive days. Thin blood smears were prepared from the tail vein of the mice before treatment and 24 hours following the last treatments to assess parasitaemia. Body weights were taken prior to the start of treatment and on day 7 post-infection. Animals were monitored for survival over 30 days post-infection.

2.4. PHYTOCHEMICAL SCREENING

The hydroethanolic and the dried powdered stem bark of *Albizia coriaria* and *Ficus sur* was subjected to general qualitative phytochemical screening using standard methods (19).

3. RESULTS AND DISCUSSION

3.1. Acute oral toxicity

Administration of the 70% ethanol extract of the stem bark of *Albizia coriaria* and *Ficus sur* at 3000 mg/kg caused no observable physical and behavioural changes for 24 hours. Additionally, no mortality was seen within the 2-week observation period. Hence the LD_{50} the extracts were estimated to be above 3000 mg/kg. The acute toxicity test suggests a good margin of safety. This partially justifies the safety of the extracts. This also supports its long-standing usage in traditional medicine in the treatment of many disorders without evidence of toxicity. It thus corroborates findings from the cytotoxicity assay of *Albizia coriaria* reported by Obakiro et al., (20) where the extract was found to be safe.

3.2. Peter's Suppressive test

In antimalarial research, *in vivo* models are used due to their possible prodrug influence and equipping the body's defences in getting rid of the pathogen (21). The extracts of *Albizia coriaria* and *Ficus sur* demonstrated a significant (P < 0.005) dose-dependent suppression with the highest suppression seen at 300 mg/kg for both extracts. The hydroethanolic extract of *Ficus sur* demonstrated a highest suppression of 44.00% at 100 mg/kg with the highest dose of 300 mg/kg having an inferior suppression of 35.11% (Table 1). *A. coriaria* produced the highest suppression of 68.89% as seen in table 1. At all dosages of the extract, the survival time of mice in the treatment groups were prolonged, with the 300 mg/kg dose

producing the greatest survival time (Table 1). The Peter's 4-day suppressive assay is the preliminary model for assessing the antimalarial activity of potential agents against *P. berghei* (22). *Albizia coriaria* reduced parasitaemia in a dose dependent manner. *In vivo* antiplasmodial activity of *Albizia coriaria* can be classified as having good antiplasmodial activity against *Plasmodium berghei* according to the classification by Muñoz et al., (23). This corroborates earlier reports by Muthaura et al., (24) where the methanolic extracts *of A. coriaria* stem bark demonstrated promising *in vitro* antiplasmodial activity.

Table 1. Effect of the extracts on parasitaemia and survival time of the *P. berghei*-infected mice in the Suppressive test

Dose (mg/kg)		**% Parasitaemia (mean ± SEM)**	**% Suppression**	**MST**
NC		45.00 ± 5.21	-	9.25±2.87
Ficus	300	29.20 ± 0.86^{a2}	35.11	23.19±4.10
	100	25.20 ± 1.66^{a4}	44.00	25.65±2.86
	30	29.80 ± 1.46^{a2}	33.78	17.71±3.25
Albizia	300	14.00 ± 0.71^{a4}	68.89	28.07±2.14
	100	30.95 ± 5.08^{a1}	31.22	20.42±4.65
	30	33.22 ± 0.57^{a1}	26.18	18.30±5.68
ART	4	16.29 ± 2.67^{a4}	63.80	26.22±2.42

Values are presented as Mean±SEM, N = 5, NC = vehicle-treated group, ART = Artesunate. Values are significantly different at ^{1}P < 0.05, ^{2}P < 0.01, ^{4}P < 0.0001, ^{a}compared to the vehicle-treated group, MST = Mean Survival Time.

3.2.1. Effect of the extracts on bodyweight in the Suppressive test

Treatment with *Albizia coriaria* and *Ficus sur* prevented significant decrease in the weight of the mice in the treated groups relative to the vehicle treated group (NC) which showed a reduction (Figure 1). Similarly, there was no significant weight decline in the artesunate-treated group. All the tested extracts prevented the weight loss associated with the infection. Weight loss in malaria infection can lead to exacerbation of the pathology which can lead to the eventual death of the organism (25). Therefore, the extracts' ability to prevent the weight loss may be contributing to the significant levels of survival by the experimental animals compared to the animals in the negative control group. The increase in the survival time of the mice corroborates the decline of the parasitaemia's degenerative consequences in the treated groups.

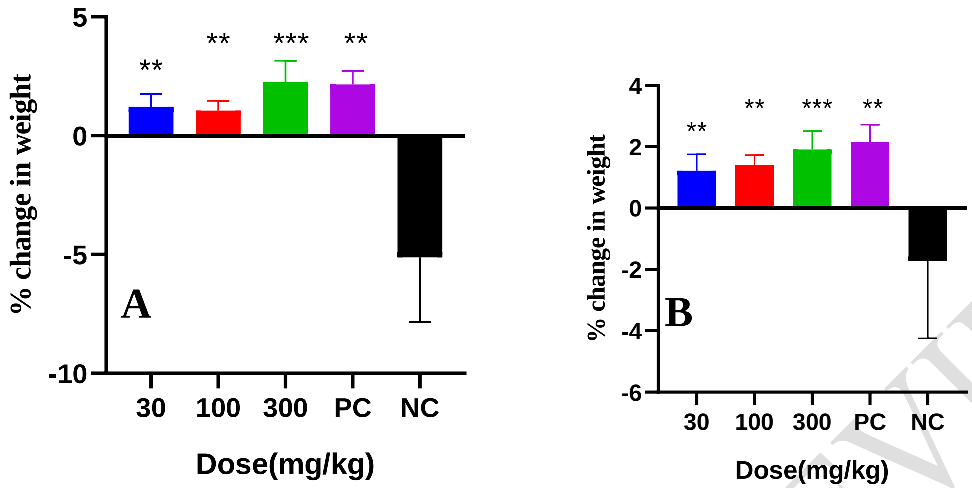


Figure 1. Percentage change in weight of mice infected with *P. berghei* on day 0 and day 4 in the 4-day suppressive assay in *Albizia coriaria* (B), and *Ficus sur* (A) *Values are significantly different at *P* < 0.05, **Values are significantly different at *P* < 0.005, ***Values are significantly different at *P* < 0.0005 compared to Day 0.

3.3. Rane's curative test

The hydro ethanol stem extracts of *Albizia coriaria* and *Ficus sur* caused a significant (*P* < 0.005) decrease in parasitaemia levels on day 7 relative to day 3 at all tested doses. A dose dependent parasitaemia suppression was observed with all the extracts with the highest suppression seen at the highest dose for both extracts. *A. coriaria* produced the highest percentage suppression of 61.46 followed by *F. sur*. Artesunate (25 mg/kg/day) had a superior curative potential (85.25 %) than the extracts at all doses (Table 2). Survival time increased with increase dose for all the tested extracts with the highest doses recording the highest survival time for all the tested extracts. The hydro ethanol extract *Albizia coriaria* recorded the highest survival of 24.05 days.

The curative test evaluates the potential of an agent to clear the parasites in an established infection (26). This is relevant as this mimic the state in which people in endemic areas use these plant medicines in the treatment of malaria. Both extracts demonstrated a dose dependent suppression of parasitaemia. *A. coriaria* extract produced superior activity at the highest dose in the suppressive assay than the curative test. On the other hand, *Ficus sur* produced a superior suppression at the highest dose in the curative study. This suggests *A. coriaria* will be more suited in treating the disease at the early stages of infection whiles *Ficus sur* may be more active in an established infection.

Table 2. Effect of the extracts on parasitaemia and survival time of the *P. berghei*-infected mice in the Curative test

Dose (mg/kg)		**% Parasitaemia (mean ± SEM)**		**% Suppression**	**MST**
		DAY 3	**DAY 7**		
NC		52.00±5.21	56.00±5.21[a]	NS	10.58±4.21
Ficus	300	56.21±3.14	28.26±4.25[a]*	49.54	19.55±7.45*
	100	51.05±5.47	34.28±6.25[a]*	38.79	15.36±4.31*
	30	48.21±6.50	39.24±5.10[a]*	29.93	14.70±6.29*
Albizia	300	53.59±4.35	21.58±3.65[a]*	61.46	24.05±5.33*
	100	55.36±2.15	26.19±2.50[a]*	53.23	20.46±6.10*
	30	49.10±4.88	36.57±7.22[a]*	34.70	17.28±4.36*
ART	25	54.47±3.78	8.26±0.52[a]*	85.25	30.00±0.00*

Values are presented as mean ± SEM, N = 5, NC = vehicle-treated group, ART = Artesunate, NS = No Suppression. Values are significantly different at $P < 0.005$, [a]compared to Day 3, *compared to the vehicle-treated group, MST = Mean Survival Time.

3.3.1. Effect of the extracts on bodyweight in the curative study

Relative to the negative control group, all the extracts were able to prevent the decline in the bodyweight of the treated mice at all tested doses in the curative assay (Figure 2). The extracts also produced a dose dependent increase in the bodyweight of the mice. Even though the 30 mg/kg group of Ficus also recorded a decline in the percentage change in bodyweight, it was still significantly different from the untreated group.

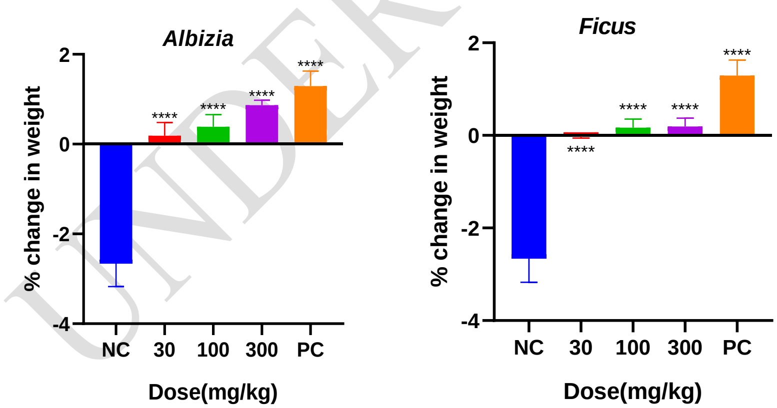


Figure 2. Percentage change in weight of mice infected with *P. berghei* on day 0 and day 4 in the 4-day suppressive assay in *Albizia coriaria* and *Ficus sur.* *Values are significantly different at $P < 0.05$, **Values are significantly different at $P < 0.005$, ***Values are significantly different at $P < 0.0005$ compared to Day 0.

3.4. PRELIMINARY PHYTOCHEMICAL SCREENING

The qualitative phytochemical screening of the powdered plant materials and their respective extracts did not show any differences in the phytochemicals tested as seen in table 3. Alkaloids were not detected in the Ficus. The presence of different phytochemicals in plants is indicative of their many possible therapeutic gains (19). The absence of alkaloids does not support earlier reports by Ishola et al., (27) where alkaloids were detected in the stem bark. Also, the absence of phytosterols does not corroborate earlier reports by Omara et al., (28). This can be attributed to plant related factors such as geographical location, season and time of harvesting. The majority of antimalarial pharmaceuticals have traditionally come from natural phenolic compounds (29). In a previous work by Saloufou *et al*., (30), the bark of *F. sur* exhibited the highest flavonoid content of all the various plant parts. Consequently, the phenolic content of the extracts including the flavonoids may be contributing to the antimalarial activity observed.

Table 3: Phytochemical constituents of bark extracts and powder from *Albizia coriaria,* and *Ficus sur*.

Phytochemical component	FSP	FSE	ACP	ACE
Coumarins	+	+	+	+
Flavonoids	+	+	+	+
Alkaloids	-	-	+	+
saponins	+	+	+	+
triterpenoids	+	+	+	+
phytosterols	+	+	-	-
tannins	+	+	+	+
Reducing sugars	+	+	+	+

4. CONCLUSION

The stem of *Albizia coriaria* and *Ficus sur* demonstrated good antiplasmodial activities in the suppressive assay. This study has provided a basis for the traditional use of the stem of *Albizia coriaria,* and *Ficus sur* in the treatment of malaria.

REFERENCES

1. Moghadamtousi SZ, Fadaeinasab M, Nikzad S, Mohan G, Ali HM, Kadir HA. Annona muricata (Annonaceae): A review of its traditional uses, isolated acetogenins and biological activities [Internet]. Vol. 16, International Journal of Molecular Sciences. MDPI AG; 2015 [cited 2021 Apr 19]. p. 15625–58. Available from: https://pubmed.ncbi.nlm.nih.gov/26184167/
2. Souza CRF, Ramos DN, Rojas DFC, Oliveira WP. Stability Testing and Shelf Live Prediction of a Spouted Bed Dried Phytopharmaceutical Preparation From Maytenus ilicifolia. 2013;91(NOVEMBER):1847–55.
3. Hostettmann K, Wolfender JL, Terreaux C. Modern Screening Techniques for Plant Extracts. Pharm Biol [Internet]. 2001 Jan [cited 2021 Apr 19];39(sup1):18–32. Available from: https://pubmed.ncbi.nlm.nih.gov/21554168/
4. WHO 2019. World Malaria Report. World Health Organization. 2019.
5. World Health Organization. World Malaria Report. Vol. WHO/HTM/GM, World Health. 2020. 238 p.
6. Komlaga G, Agyare C, Dickson RA, Mensah MLK, Annan K, Loiseau PM, et al. Medicinal plants and finished marketed herbal products used in the treatment of malaria in the Ashanti region, Ghana. J Ethnopharmacol. 2015;

7. Asare KK, Boampong JN, Afoakwah R, Ameyaw EO, Sehgal R, Quashie NB. Use of proscribed chloroquine is associated with an increased risk of pfcrt T76 mutation in some parts of Ghana. Malar J [Internet]. 2014 Jun 26 [cited 2024 Mar 9];13(1):1–8. Available from: https://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-13-246

8. Achan J, Talisuna AO, Erhart A, Yeka A, Tibenderana JK, Baliraine FN, et al. Quinine, an old anti-malarial drug in a modern world: Role in the treatment of malaria. Malar J [Internet]. 2011 May 24 [cited 2024 Mar 9];10(1):1–12. Available from: https://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-10-144

9. Keita K, Darkoh C, Okafor F. Secondary plant metabolites as potent drug candidates against antimicrobial-resistant pathogens. Sn Appl Sci [Internet]. 2022 Aug 1 [cited 2024 Mar 9];4(8):209. Available from: /pmc/articles/PMC9264742/

10. Nortey NND, Korsah S, Tagoe M, Apenteng JA, Owusu FA, Oppong J, et al. Herbs Used in Antimalarial Medicines: A Study in the Greater Accra Region of Ghana. Evid Based Complement Alternat Med [Internet]. 2023 Aug 19 [cited 2024 Mar 9];2023:1–8. Available from: https://pubmed.ncbi.nlm.nih.gov/37636997/

11. Burrows JE (John E, Burrows S. Figs of southern & south-central Africa. 2003;379.

12. Koko WS, Galal M, Khalid HS. Fasciolicidal efficacy of Albizia anthelmintica and Balanites aegyptiaca compared with albendazole. J Ethnopharmacol [Internet]. 2000 Jul [cited 2022 Jul 18];71(1–2):247–52. Available from: https://pubmed.ncbi.nlm.nih.gov/10904170/

13. Touitou Y, Portaluppi F, Smolensky MH, Rensing L. Ethical Principles and Standards for the Conduct of Human and Animal Biological Rhythm Research. Chronobiol Int [Internet]. 2004 [cited 2024 Mar 8];21(1):161–70. Available from: https://www.tandfonline.com/doi/abs/10.1081/CBI-120030045

14. Guidelines O, The FOR, Of T. Oecd guidelines for the testing of chemicals. 2008;(October).

15. Mzena T, Swai H, Chacha M. Antimalarial activity of Cucumis metuliferus and Lippia kituiensis against Plasmodium berghei infection in mice. Res Rep Trop Med. 2018;9:81–8.

16. Baah MK, Mensah AY, Asante-Kwatia E, Amponsah IK, Forkuo AD, Harley BK, et al. In Vivo Antiplasmodial Activity of Different Solvent Extracts of Myrianthus libericus Stem Bark and Its Constituents in Plasmodium berghei -Infected Mice. Evidence-based Complement Altern Med. 2020;2020.

17. Peters W, Portus JH, Robinson BL. The chemotherapy of rodent malaria, XXII: The value of drug-resistant strains of P. Berghei in screening for blood schizontocidal activity. Ann Trop Med Parasitol [Internet]. 1975 [cited 2021 May 9];69(2):155–71. Available from: https://pubmed.ncbi.nlm.nih.gov/1098584/

18. Nardos A, Makonnen E. In vivo antiplasmodial activity and toxicological assessment of hydroethanolic crude extract of Ajuga remota. Malar J. 2017;16(1):1–8.

19. Biapa PCN, Agbor GA, Oben JE, Ngogang JY. Phytochemical studies and antioxidant properties of four medicinal plants used in Cameroon. African J Tradit Complement Altern Med. 2007;

20. Obakiro SB, Kiprop A, K'Owino I, Andima M, Owor RO, Chacha R, et al. Phytochemical, Cytotoxicity, and Antimycobacterial Activity Evaluation of Extracts and Compounds from the Stem Bark of Albizia coriaria Welw ex. Oliver. Evidence-based Complement Altern Med. 2022;2022.

21. Waako PJ, Gumede B, Smith P, Folb PI. The in vitro and in vivo antimalarial activity of Cardiospermum halicacabum L. and Momordica foetida Schumch. Et Thonn. J Ethnopharmacol. 2005;

22. Fidock DA, Rosenthal PJ, Croft SL, Brun R, Nwaka S. Antimalarial efficacy screening: effecacy

models for compound screening (Supplemental file). Nat Rev Drug Discov. 2004;3:509–20.

23. Muñoz V, Sauvain M, Bourdy G, Callapa J, Bergeron S, Rojas I, et al. A search for natural bioactive compounds in Bolivia through a multidisciplinary approach. Part I. Evaluation of the antimalarial activity of plants used by the Chacobo Indians. J Ethnopharmacol. 2000;

24. Muthaura CN, Keriko JM, Mutai C, Yenesew A, Gathirwa JW, Irungu BN, et al. Antiplasmodial potential of traditional phytotherapy of some remedies used in treatment of malaria in Meru-Tharaka Nithi County of Kenya. J Ethnopharmacol [Internet]. 2015 Dec 4 [cited 2024 Jan 9];175:315–23. Available from: https://pubmed.ncbi.nlm.nih.gov/26409181/

25. Komlaga G, Forkuo AD, Suleman N, Nkrumah D, Nketia R, Bekoe SO. Antimalarial Property and Acute Toxicity of the Leaves of Theobroma cacao L. Evidence-based Complement Altern Med. 2021;2021.

26. Baah MK, Mensah AY, Asante-Kwatia E, Amponsah IK, Forkuo AD, Harley BK, et al. In Vivo Antiplasmodial Activity of Different Solvent Extracts of Myrianthus libericus Stem Bark and Its Constituents in Plasmodium berghei -Infected Mice . Evidence-Based Complement Altern Med. 2020;2020(April):1–10.

27. Ishola IO, Olayemi SO, Yemitan OK, Ekpemandudiri NK. Mechanisms of anticonvulsant and sedative actions of the ethanolic stem-bark extract of Ficus sur Forssk (Moraceae) in rodents. Pakistan J Biol Sci PJBS [Internet]. 2013 Nov 1 [cited 2022 Jul 18];16(21):1287–94. Available from: https://europepmc.org/article/med/24511736

28. Omara T, Kiprop AK, Kosgei VJ. Albizia coriaria Welw ex Oliver: a review of its ethnobotany, phytochemistry and ethnopharmacology. Adv Tradit Med 2021 [Internet]. 2021 Jul 21 [cited 2022 Jul 18];1–16. Available from: https://link.springer.com/article/10.1007/s13596-021-00600-8

29. Builders M. Antimalarial phenolic compounds in Africa : a review of biomedical and pharmaceutical sciences. Eur J Biomed Pharm Sci. 2020;6(4):6–11.

30. Saloufou KI, Boyode P, Simalou O, Eloh K, Idoh K, Melila M, et al. Chemical composition and antioxidant activities of different parts of Ficus sur. J Herbmed Pharmacol [Internet]. 2018 Jul 2 [cited 2022 Jul 18];7(3):185–92. Available from: http://herbmedpharmacol.com/Article/jhp-1242