

# **Research** Article

# Natural Products as Sources of Antimalarial Drugs: Ethnobotanical and Ethnopharmacological Studies

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Ethnopharmacological Relevance. Malaria is one of the lethal diseases of man, contributing to about 17 million deaths annually, leading to sociocultural, economic, and health influences. Aim of the Study. The study explores the ethnobotanical and ethnopharmacological appraisal of antimalarial plants used by people of Omu Aran, Ogbomoso, Ado Ekiti, and Sagamu communities in Nigeria. Materials and Methods. For this study, relevant information was procured from the inhabitants via a structured questionnaire to procure the general knowledge of antimalarial medicinal plants. Results and Discussion. A total of 90 interviewees (44 men and 46 women) were involved in this survey. A total of 59 medicinal species were identified, which were dispersed in 33 families (Asteraceae (6), Apocynaceae (5), Anacardiaceae, Annonaceae, Fabaceae, Malvaceae, Meliaceae, Poaceae, and Rubiaceae (3 each), Phyllanthaceae (2)) totaling 49% of the cited species. The most cited plants are Azadirachta indica (42), Mangifera indica (38), Carica papaya (28), Cymbopogon citratus (27), Cassia fistula (15), Morinda lucida (14), Anacardium occidentale and Vernonia amygdalina (13 each), Helianthus annuus (11), Enantia chlorantha (10), and Moringa oleifera (9) A total of 105 citations were recorded for the plant parts used (leaf (46), bark (17), fruits (9), root (9), latex (11), stem (11), and inflorescence (2)) while decoction (59%), maceration (25%), infusion (9%), and exudation (7%) were the methods of preparation. Use Values (UVs) of 0.47 to 0.11 were recorded for the frequently used antimalarial plants. The Efficiency Levels (ELs) of 11 different medicinal plants stated by the respondents were Azadirachta indica, Cassia fistula and Morinda lucida (12), Chromolaena odorata (10), Mangifera indica, Enantia chlorantha and Helianthus annuus (8), Cymbopogon citratus (7), Gossypium arboretum (4), Landolphia dulcis (3), and Aloe vera (2) Cocos nucifera, Curcuma longa, Forkia biglobosa, and Musa acuminate are mentioned for the first time in the study area with little or no reported antiplasmodial activities. Conclusion. The study appraised the commonly used antimalarial plants in the study areas. Therefore, commitment to scientifically explore the bioactive compounds, antimalarial potential and toxicological profile of these plants is inevitable as they could lead to novel natural products for effective malaria therapy.

# 1. Introduction

Malaria is one of the communal diseases of man contributing to stern sociocultural, economic, and health influences in humid, middle-income nations, sub-Saharan Africa, Southeast Asia, and South America [1, 2]. It is instigated by *Plasmodium ovale*, *P. malariae*, *P. falciparum*, *P. vivax*, and *P. knowlesi* [3]. The outburst of malarial infections in Africa, the Caribbean, Asia, and South American is symptomatic of *P. falciparum*, the most lethal malaria parasite. The parasite could accumulate in the brain capillaries [4, 5]. Malarial infections in India, Central American, and East Mediterranean could be concomitant to *P. vivax* while *P. ovale* and *P. malariae* are prevalent in Papua New Guinea and sub-Saharan Africa [6].

Malaria epidemic has been enormously high in low socioeconomic empowered regions. In Africa, nearly 19 million cases of malaria infections have been reported accounting to 89% of the global cases and almost 17 million deaths have been published [7]. Also, about 450 thousand African children's deaths have been reported and one-tenth of pregnancy deaths have been concomitant to malaria infections [2, 8]. It affected the morbidity and mortality rate owing to pathogenic resistance to conventional drugs, vector control agents, and human migration [9]. Several factors have been analysed and reported to control malaria infections in Africa. These are climate suitability, dams or reservoirs, migration, and vegetation. According to the report published by The World malaria in 2018, malarial cases have tremendously reduced in relation to the report of 2010. Despite this, between 2015 and 2017, no significant progress was achieved in curbing malaria cases [10]. This trend could be indicative of the widely spread of drug-resistant malaria and the intricacy of parasites' life cycle [11].

Quinoline (QN) derivatives are undoubtedly the commonest antimalarial drugs in Africa. Examples of quinoline antimalarial drugs are quinine, amodiaquine, piperaquine, primaquine, pyronaridine, ferroguine, isoquine, amopyroquine, tertbutylisoquine, mefloquine, tafenoquine, and chloroquine. 4-Aminoquinoline is the most accessible antimalarial pharmacophore used in the last century. In recent times, QN derivatives have been integral component of Artemisinin-based Combination Therapy (ACT) [12]. The discovery of ACT could be considered as the most noteworthy achievement of ethnopharmacological research in the 20th century [13-15], enthused by the use of Artemisia annua L. (Asteraceae). The drug was found effective against all the malarial parasites and led to regulations against quinine-based drugs in Africa. However, despite the predominant achievements of ACT, concerns about the future efficacy of artemisinin have recently been on the rise due to the building-up of resistance by the parasite [7]. This event instigates the unrelenting search for promising antimalarial drugs that are cost-effective, handy, acceptable, and scientifically proven.

Human has used medicinal plants for malaria, cholera, yellow fever, and diabetes treatment [16]. In most African countries, medicinal herbs are viewed as alternative therapies. Medicinal plants have effectively helped in primary health care for the therapy of acute and chronic diseases [17, 18]. They have contributed to the discovery of novel therapeutic agents via isolation, identification, and characterization of secondary metabolites [19]. Secondary metabolites such as flavonoids, stilbenes, coumarins, lignin, tannins, terpenoids, and steroids have been reported as antimalarial compounds [20].

Tropical plants are identified to contain high proportions of natural chemical compounds and a greater diversity than plants from any other biome. Thus, they are potential sources of new medicines [21]. The increased number of drug-resistant strains makes the development of novel antimalarial urgent. The high cost of malaria treatment has left the poor masses of Nigeria heavily reliant on traditional practitioners and medicinal plants for the treatment of the disease. It seems logical to encourage studies on plants from these regions, especially since the major proportions of malaria attributable deaths occur in sub-Saharan African regions. Although several compounds had achieved success at treating malaria diseases, the emerging threats of drug resistance by some plasmodium species call for the development of new molecules with novel bioactive features. The study explores the ethnobotanical and ethnopharmacological appraisal of antimalarial plants used by people of Omu Aran, Ogbomoso, Ado Ekiti, and Sagamu communities in Nigeria. Hence, the search for novel natural antimalarial molecules in selected plant sources via ethnobotanical and ethnopharmacological investigation is clearly justified.

### 2. Methodology

2.1. Geographical Description of the Study Area. The study area comprises four states, namely, Kwara (Omu Aran), Oyo (Ogbomoso), Ekiti (Ado Ekiti), and Ogun (Sagamu) in Nigeria located on 8°08'N (5°06'E), 8°08'N (4°15'E), 7°37'16"N (5°13'17"E), and 6°50'N (3°39'E), respectively. The study areas are located in two important geopolitical zones, that is, Omu Aran (North central), Ogbomoso, Sagamu, and Ado Ekiti (Southwest) of Nigeria (Figure 1) The inhabitants are majorly from the Yoruba ethnic group. The study area falls into the category of state with most prevalence of malaria in Nigeria according to MIS report.

2.2. Typical Vegetation of the Study Area. Ado Ekiti and Sagamu fall in the rain forest region, characterized by temperature of 21° to 28°C, high humidity, and two distinct seasons, rainy season from April to October and dry season from November to March with mean annual rainfall of 1320 mm. Ogbomoso and Omu Aran fall in the savanna region, characterized by temperature of 21° to 33°C with heavy rainfall between April and October. The humidity is high (51.1%) with mean annual rainfall of 1885 mm. The study sites are opulently rich in evergreen floras and this promotes the use of local herbs for diseases prevention and cure.

2.3. Selection of the Informants. For this study, relevant information and data were procured from selected people in the study area via interview using structured questionnaire to procure relevant knowledge of antimalarial plants used in the vicinity. The questions were structured in a simple way and interpreted to selected respondents selected by nomination method after verbal authorization and approval by the chiefs in the study areas. In a particular study area, the leaders suggested prominent people with vast experience in herbal medicines or practitioners of herbal medicines. For reliability and reproducibility, respondents that accepted to be interviewed were briefed on the significance and objectives of the study. A disclaimer was presented to the interviewees that the views, ideas, and opinions expressed belong solely to the interviewers, and not necessarily to any committee or individual. While conducting the research, researchers were honest but not too detailed in briefing the respondents what he or she needed to do. Conducting the survey involved series of activities. These include establishing cordial relationship with respondents, selecting easy ways of interacting, observation, and recording the findings.

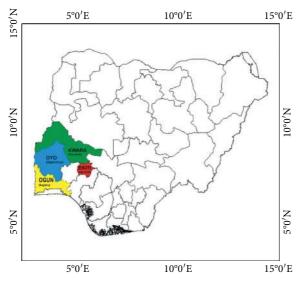


FIGURE 1: Map of Nigeria showing the study area.

Respondents selected must meet the following criteria: (1) they should be indigenous people of Yoruba; (2) they are sound and knowledgeable in phytotherapy; (3) they are accessible to medicinal plants; (4) they must have used herbs for treating malaria; (5) they are approachable and organized.

2.4. Structured Questionnaire. The structured questionnaire was designed according to the technique of Olorunnisola et al. [22] and Sarquis et al. [23] with slight modification. The moderated questionnaire entails information on respondent biodata, commonly used antimalarial medicinal plants, plant parts frequently used, the most effective herbs from the respondents list, mode of preparation, and common side effects of antimalarial plants.

2.5. Data Collection. The study was piloted for 6 months, from March to August 2019. The mode of data collection was through one-on-one interviews, public discussion, and observation. The interviews were conducted mostly in Yoruba (native) language. The respondents gave the native names of plants and showed the interviewers the available plant samples. Information on the questionnaires was supplied on the spot of interview, and several observations and discussions were conducted prior to completing and cross-checking of the information provided.

2.6. Data Analysis. The antimalarial medicinal plants itemized by the respondents were structured according to the scientific, common, and local names, family, plant part used, and mode of preparation. The malarial diseases' symptoms and probable health effects or body reactions were reported. Data were statistically analysed in percentages using Graphpad Prism software (version 6.0) The comparative significance of a plant species for its ethnopharmacological activity was evaluated with the Index of Use Value (UV) and efficiency level (EL).

denotes the therapeutic importance of each medicinal plant species. It is calculated by  $UV = \Sigma Ui/n$ , where Ui is the total number of times plant species is cited and *n* is the total number of respondents interviewed. UV element helps evaluate plant species frequently mentioned for antimalaria. A high UV denotes plant mentioned mostly by respondents and low for sparingly mentioned [23].

2.6.2. Efficiency Level (EL). It is a qualitative index that signifies the efficacy of a single plant species from the list of plants given as a response by the interviewees. EL is calculated by CL = Ui, where Ui is the total number of times a particular plant species is mentioned as the most effective from the list of plant species level. EL indicates plant species showing the most effective therapeutic potentials. A high EL denotes the most efficacious plant.

#### 3. Results and Discussion

3.1. The Demographic Details of the Informants. A total of 90 interviewees (44 men and 46 women) were involved in this ethnobotanical and ethnopharmacological survey. Demographic details of the interviewees are listed in Table 1. The respective age distribution and the level of education of the respondents are shown in Figure 2.

3.2. The Effectiveness of the Medicinal Plants. In this study, 57 respondents (63%) strongly agreed and 26 respondents (29%) agreed that malaria is curable using medicinal herbs while 7 respondents (8%) were neutral. This denotes the local belief in phytotherapy of malaria. The study site has rich vegetation diversity ranging from creeping plant to shrubs and trees. A large number of these plants are used by the inhabitants in malaria therapy due to persistent spread of malaria in these regions.

3.3. Indigenous Notion of the Study Area on Malaria. The common symptoms of malaria and side effects of antimalarial plants according to the native knowledge of Ado Ekiti, Ogbomoso, Omu Aran, and Sagamu people are detailed in Table 2. Yoruba people identify malaria as "iba" and presumed malaria as a common and seasonal disease. From one-on-one interview and observations, malaria prevalence is significantly high during the rainy season in the study areas. According to the respondents, malaria is caused by long-time exposure to rain, cold, hot sun, stress, and mosquito. They believed that these could disrupt the temperature balance in the body.

Likewise, the respondents were screened to procure knowledge of malaria via the common symptoms they experienced (Figure 3) Fever, body pain, fatigue, and headache are the common symptoms in the study area and are related to temperature balance of the body system. The local people believed that it could be caused by excessive heat and longtime exposure to cold environment which forces the body to produce excessive heat. Moreover, they explained that fever

Biodata	Group of informants	No of informants, $n$ (%)
	20-39 years old	49 (54.44)
4 ~~	40-59 years old	22 (24.44)
Age	60-79 years old	15 (16.67)
	>80 years old	04 (4.44)
Sex	Male	44 (48.88)
Sex	Female	46 (51.11)
	Illiterate (none)	16 (17.78)
Education	Primary level	07 (7.78)
Education	Secondary level	23 (25.56)
	Tertiary level	44 (48.89)
Location	Urban	54 (60.00)
Locuiton	Rural	36 (40.00)

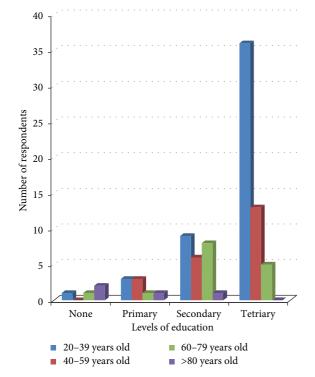


FIGURE 2: Age distribution and level of education of the respondents.

could lead to other symptoms such as headache, fatigue, body pain, and sweating. According to the respondents, probable ways of preventing malaria include reduction in exposure to rain (cold areas) or sun (hot areas), avoidance of mosquito bites, reduction in workload (stress), constant use of antimalarial herbal drugs, and burning of aromatic antimalarial plants which could pose threats to mosquitoes.

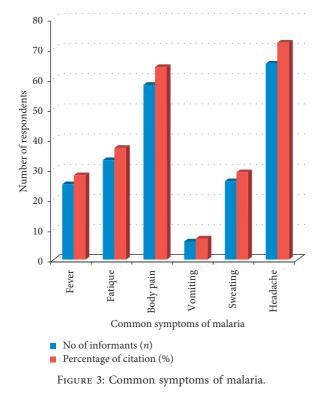
Medicinal plants are universally reported to produce uncharacteristic effects ranging from simple to intricate. The respondents were screened to procure information on common health effects associated with antimalarial herbal drugs. Several reports were obtained, grouped as dizziness, sweating, weakness, frequent urination, itching, and no side effects (Figure 4) However, 15 (70%) respondents cited other effects produced by medicinal plants on their body systems. The respondents believed that these effects are related to the nature of medicinal plants combined, quantity of herbs taken, period when herb is used, temperature of herbal drugs (warm or cold), season drugs are taken, severity of malaria, and body capacity.

3.4. Assortment of Antimalarial Therapeutic Plants. A total of 59 medicinal plants were cited which belong to 33 families. These are Asteraceae (6), Apocynaceae (5), Anacardiaceae, Annonaceae, Fabaceae, Malvaceae, Meliaceae, Poaceae and Rubiaceae (3 each), Phyllanthaceae (2) totaling 48.83% of the sampled species while Asteraceae, Arecaceae, Asphodelaceae, Boraginaceae, Bromeliaceae, Caricaceae, Crassulaceae, Lamiaceae, Lythraceae, Menispermaceae, Moringaceae, Musaceae, Rutaceae, Sapindaceae, Myrtaceae, Solanaceae, Zingiberaceae, Solanaceae, Meliaceae, Theaceae, Labiatae, Hymenocardiacae, and Zingiberaceae accounted for 22.5% of families mentioned once (Table 3) The most cited plants include Azadirachta indica (42), Mangifera indica (38), Carica papaya (28), Cymbopogon citratus (27), Cassia fistula (15), Morinda lucida (14), Anacardium occidentale and Vernonia amagdalina (13 each), Helianthus annuus (11), Enantia chlorantha (10), Moringa oleifera (9), Chromolaena odorata, and Psidium guajava (7 each) The efficacy of a plant species is evidenced in its number of citations, thus, becoming spotlight in pharmacological research leading to the discovery of novel antimalarial drugs. However, we cannot rule out the possibility of cultural factors unrelated to efficacy as having impacted the citation rate.

3.5. Used Medicinal Plant Parts. The commonest used parts cited are leaf (46), bark (17), fruits (9), root (9), latex (11), stem (11), and inflorescence (2) (Figure 5) Many antimalarial herbal drugs are commonly prepared from a single plant part, although they could be prepared from the assortment of two or more plant parts. In this survey, leaf and bark were the most cited plant parts contributing to 255 and 101 of the 480 plant parts cited by the respondents. Leaves are the most commonly used plant parts in Nigeria [24, 25]. This could be due to the simplicity of the collection, site of synthesizing majority of plant secondary metabolites, and diverse bioactive compounds appraised by preliminary phytochemical investigations of leaves [26–28]. Systematic harvest of leaves has little or no influence on plants survival. This explains the frequent utilization of leaves in herbal recipes [29, 30].

3.6. Forms of Herbal Drugs' Preparations for Malaria Therapy. The common herbal drugs' preparations according to the study were categorized as decoction, maceration, infusion, and exudation (Table 3) The most cited methods of preparation are decoction (59%), maceration (25%), infusion (9%), and exudation (7%) (Figure 6) Decoction was cited 99 times; maceration, 65 times; infusion, 35 times; and exudation, 13 times. Decoction is commonly used in herbal recipes because recipe could be stored, could have long-life span, could be taken orally, and could be used as bath. Due to heat treatment, recipe is safe to administer and more metabolites are believed to be extracted. Maceration is also

Common symptoms of malaria	No of informants, $n$ (%)	Health effects of antimalarial herbal drugs	No of informants, $n$ (%)
Fever	25 (28)	Dizziness	16 (18)
Fatigue	33 (37)	Sweating	44 (49)
Body pain	58 (64)	Weakness	22 (6)
Vomiting	6 (7)	Frequent urination	24 (5)
Sweating	26 (29)	Itching	5 (6)
Headache	65 (72)	No side effects	36 (40)



common among the Yorubas. It involves permeation of the plant materials (mostly bark and root) in aqueous (water) or organic (alcohol) solvents.

3.7. Assessment of the Different Indexes. In this study, UVs within 0.47 and 0.11 is appraised as frequently used antimalarial plants by the Yorubas: Azadirachta indica (0.47), Mangifera indica (0.42), Carica papaya (0.31), Cymbopogon citratus (0.3), Cassia fistula (0.17), Morinda lucida (0.16), Anacardium occidentale (0.14), Vernonia amagdalina (0.14), Helianthus annuus (0.12), and Enantia chlorantha (0.11) (Table 3) The most significant plant species are those with high UV and should be compiled for preservation.

The EL appraised the efficacy of a particular plant from the catalogue given by the interviewees. In this study, 11 different medicinal plants were mentioned by the respondents as most efficacious from array of medicinal plants listed. 26 respondents cited *A. indica* and *C. fistula* while *M. lucida* was cited by 12 respondents; *C. odorata*, 10 respondents; *M. indica*, *E. chlorantha*, and *H. annuus*, 8 respondents each; *C. citratus* (7 respondents); *G. arboretum*, 4

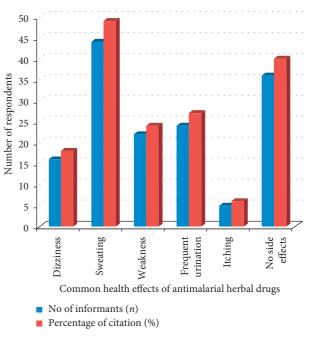


FIGURE 4: Health effects of antimalarial herbal drugs.

respondents; L. dulcis, 3 respondents; and A. vera, 2 respondents.

The *in vitro* and *in vivo* antiplasmodial potency of medicinal plants has been appraised against *P. falciparum*, *P. berghei*, and *P. yoelii*. Some of the plants with exceptional antiplasmodial activities are *P. guajava* [31], *N. latifolia* [32], *C. citratus* [33, 34], *U. chamae* [35], *E. chlorantha* [36, 37], *O. gratissimum* [38], *A. leiocarpus* [39], *P. amarus* [40], *A. indica* [41, 42], *C. odorata* [43, 44], *M. lucida* [45, 46], *V. amygladina* [47], *A. boonei* 44, 48], *A. senegalensis* [48], *A. occidentale* [49, 50], *B. ferruginea* [51], *G. arboretum* [48], *M. oleifera* [39], and *S. jollyanum* [44].

About four plant species are mentioned for the first time as antimalarial medicinal plant. These plants have a low UV indicating that there is little awareness on these plants in the region. The plants are *Cocos nucifera* (0.01), *Curcuma longa* (0.01), *Forkia biglobosa* (0.01), and *Musa acuminate* (0.01).

3.8. Antimalarial Assays of Medicinal Plants. Herbal plants are essential part of biodiversity which have proven to ease and remediate several diseases and infections. In tropical African countries, herbal medicine has been an undisputable therapeutic medium as alternative to conventional medicine [52]. In view of this, therapeutic potentials of medicinal

TABLE 2: The common symptoms of malaria and the health effects of antimalarial herbal drugs.

TABLE 3: The medicinal	plants used as antimalarial in N	igeria (Omu Aran, Ogl	pomoso, Ado Ekiti, and Sagamu).

Botanical name	Local name(s)	Family name	Parts used	Common method of preparation
(1) <i>Acanthospermum hispidum</i> (starburr, goat head)	Dagunro	Asteraceae	Stem, leaves	Decoction, maceration
(2) <i>Ageratum conyzoides</i> (billygoat-weed, goatweed, chickweed, whiteweed)	Imi-esu	Asteraceae	Leaves	Decoction
<ul> <li>(3) Anogeissus schimperi</li> <li>(4) Aloe vera (Aloe)</li> <li>(5) Alstonia boonei (cheese wood, stool wood)</li> </ul>	Ayin Ahon erin Ahun	Combretaceae Asphodelaceae Apocynaceae	Leaves, bark Leaves Bark, root	Decoction, maceration Exudate Decoction, infusion
(6) Anacardium occidentale (cashew)	Kasu	Anacardiaceae	Stem, leaves, bark	Decoction, infusion, maceration
7) Ananas comosus (pineapple)	Eso alade, ope oyinbo	Bromeliaceae	Unripe fruit	Exudate, decoction
8) <i>Annona senegalensis</i> (African custard apple, vild soursop)	Arere	Annonaceae	Root	Infusion, maceration
9) <i>Azadirachta indica</i> (neem, Indian lilac,imtree)	Dogoyaro, eka ebo	Meliaceae	Bark, leaves, root,	Decoction, infusion, maceration,
10) <i>Bridelia exaltata</i> (scrub ironbark, brush ronbark)	Ira, iran oda, ira eju	Phyllanthaceae	Bark	Decoction, maceration
11) <i>Bryophyllum pinnatum</i> (cathedral bells, niracle leaf, life plant)	Abamoda	Crassulaceae	Leaves	Decoction
12) <i>Calotropis procera</i> (sodom apple, rubber push)	Bomu-bomu	Apocynaceae	Leaves, fruit	Decoction, exudate
<ul><li>13) Camellia sinensis (tea bush)</li><li>14) Capsicum frutescens (chili pepper)</li></ul>	Werepe Ata-ijosi, ata-wewe	Theaceae Solanaceae	Leaves Seed/fruit	Decoction Maceration, exudate
15) Carica papaya (pawpaw)	Ibepe	Caricaceae	Fruit, leaves, root	Infusion, maceration
16) <i>Cassia fistula</i> (golden shower, Indian aburnum)	Igi kasia	Fabaceae	Stem, leaves, bark	Decoction, infusion
17) <i>Ceiba pentandra</i> (kapok tree)	Iroko	Malvaceae	Leaves	Decoction
18) <i>Chromolaena odorata</i> (siam weed, devil veed, Christmas bush)	Ewe akintola, awolowo,	Asteraceae	Leaves, stem	Decoction
19) <i>Citrus aurantifolia</i> (lime, key lime, west ndian lime, bartenders lime)	Orombo	Rutaceae	Leaves, fruit	Decoction, exudates
20) <i>Citrus aurantium</i> (sour orange, bigarade orange, bitter orange)	Osan jagan	Rutaceae	Leaves, fruit	Decoction, exudates
21) Citrus limon (lemon)	Osan wewe, ilamuna	Rutaceae	Stem, root, leaves, fruit	Decoction,
22) Citrus paradise (grape)	Ajara	Rutaceae	Fruit	Exudates
23) Cocos nucifera (coconut)	Agbon	Arecaceae	Fruit shell	Decoction, infusion
<ul><li>24) <i>Curcuma longa</i> (turmeric)</li><li>25) <i>Cymbopogon citratus</i> (lemongrass, Malabar</li></ul>	-	Zingiberaceae Poaceae	Fruit Leaves,	Decoction, maceration Decoction
(rass)	koko oba Awopa, dokita igbo, osu			
26) <i>Enantia chlorantha</i> (African yellow wood)	pupa	Annonaceae	Leaves, bark	Decoction, maceration
27) <i>Parkia biglobosa</i> (African locust bean, ggplant)	Igi iru, sumbala	Fabaceae	Leaves, bark	Decoction, maceration
28) Gardenia ternifolia	Oruwon, Gangan	Rubiaceae	Leaves	Decoction
29) <i>Gongronema latifolium</i> (bush buck) 30) <i>Gossypium arboretum</i> (cotton plant)	Arokeke Owu	Apocynaceae Malvaceae	Leaves, bark Leaves	Decoction, maceration Decoction
31) <i>Helianthus annuus</i> (sunflower)	Fufulele, June 12, agunmoniye	Asteraceae	Leaves	Decoction,
32) <i>Heliotropium indicum</i> (Indian heliotrope, urnsole, English combs comb)	Agogo igun, ogbe akuko, akuko omade	Boraginaceae	Stems, leaves, root, bark	Decoction, maceration, infusion
33) Hibiscus sabdariffa (Roselle, carcade)	Zobo	Malvaceae	Flower	Decoction, infusion
34) Hoslunda opposite	Efirin	Labiatae	Leaves	Decoction
35) Hymenocardia acida	Aboopa, orupa	Hymenocardiacae	Leaves	Decoction
36) Khaya grandifoliola (African mahogany)	Oganwo	Meliaceae	Bark	Maceration
37) Lactuca canadensis (Canada lettuce, tall	Yanrin	Asteraceae	Leaves	Decoction
ettuce)				

Botanical name	Local name(s)	Family name	Parts used	Common method of preparation
(39) <i>Lawsonia inermis</i> (Henna, Egyptian privet, cypress shrub)	Laali	Lythraceae	Leaves	Decoction
(40) Lecaniodiscus cupanioide	Akika	Sapindaceae	Leaves	Decoction
(41) Mangifera indica (mango)	Mangoro, oro	Anacardiaceae	Bark, stem, leaves	Decoction, maceration, infusion
(42) Morinda lucida (brimstone-tree)	Oruwo	Rubiaceae	Leaves	Decoction
<ul><li>(43) Moringa oleifera (moringa, drumstick)</li><li>(44) Musa acuminate (banana)</li></ul>	Ewe ile, igbale igi iyanu Ogede	Moringaceae Musaceae	Leaves, bark Leaves	Decoction, maceration Decoction
(45) Nauclea latifolia (African peach)	Egbo igbesi	Rubiaceae	Leaves, root bark	Decoction
(46) <i>Ocimum gratissimum</i> (clove basil, scent plant, African basil)	Efirin, aramogbo	Lamiaceae	Leaves, stem	Decoction
(47) <i>Panicum miliaceum</i> (proso millet, hog millet)	Poporo oka, oka baba	Poaceae	Stem	Decoction, maceration
(48) Parquetina nigrescens	Igi ogbo	Apocynaceae	Leaves	Decoction
(49) <i>Pennisetum purpureum</i> (elephant grass, napier grass, Uganda grass)	Eèsún, eèsún funfun	Poaceae	Leaves	Decoction
(50) Phyllanthus amarus	Eyin olobe	Phyllanthaceae	Leaves	Decoction
(51) Senna alata (candle bush, candletree)	Asunwon oyinbo	Fabaceae	Leaves, flower, fruit	Decoction, maceration
(52) <i>Sorghum bicolor</i> (durra, great millet, jowari)	Poroporo okababa	Poaceae	Stem	Decoction
(53) Sphenocentrum jollyanum	Aduro koko, akerejupon	Menispermaceae	Root	Decoction, maceration
(54) <i>Spondias mombin</i> (yellow mombin, hog plum)	Okika, akika, iyeye	Anacardiaceae	Leaves	Decoction
(55) Swietenia mahagoni (mahogany)		Meliaceae	Bark	Decoction, maceration
(56) <i>Tridax procumbens</i> (coatbuttons, tridax daisy)	Igbalode, muwagun	Asteraceae	Leaves	Decoction
(57) Uvaria chamae (finger root, bush banana)	Eru, eruju, akisan, oko aja	Annonaceae	Stem, leaves, bark	Decoction, maceration
<ul><li>(58) Vernonia amygdalina (bitter leaf)</li><li>(59) Swietenia mahagoni (mahogany)</li></ul>	Onugbo, ewuro	Asteraceae Meliaceae	Leaves, root, Bark	Decoction, maceration Decoction, maceration

TABLE 3: Continued.

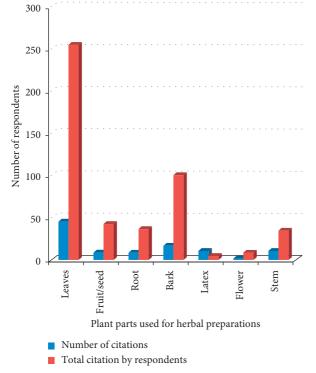
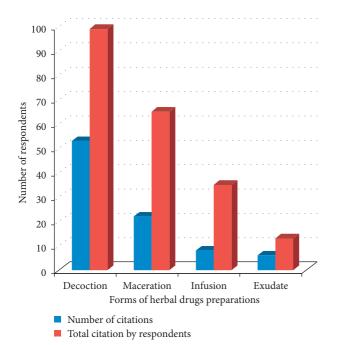
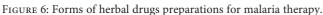


FIGURE 5: Plant parts used for herbal preparations.

plants are appraised against numerous diseases such as malaria, diabetes, cancer, ulcer, hypertension, and viral infections [53]. Generally, pharmacological activities of medicinal herbs could be linked to the existence of secondary metabolites like cardiac glycosides, saponins, tannins, flavonoids, terpenoids, and alkaloids [18]. Several plants have been explored for their antimalarial potency with curative basis exploited from ethnopharmacological beliefs (Table 4) [76].

*Cymbopogon citratus.* Lemongrass (Poaceae) is a perennial grass, evenly distributed in the tropic region, South and Central America, and has an outstanding profile in the folk medicine [17]. The antimalarial potential of aqueous leaf extracts of *C. citratus* assessed on twenty-five Swiss albino mice demonstrated significant prophylactic and chemotherapeutic potency against mice infected with 0.2 ml O<sup>+</sup> human parasitized blood of *P. falciparum* after 72 h. Significant inhibition was observed in parasitaemia level of blood of infected mice [55]. A larvicidal test of geranial, an essential oil in *C. citratus*, was evaluated against *Anopheles funestus* (mature larvae) and *P. falciparum* according to the WHO standard procedure. Prominent activities were recorded at LD<sub>50</sub> (35.5 ppm and 34.6 ppm) after 6 h. Geranial also displayed significant antiplasmodial activity with IC<sub>50</sub>





 $(4.2 \pm 0.5 \text{ lg/mL})$  when assessed by the radioisotopic method. Geranial could serve as effective natural biocides for combating the larvae of malaria vectors [61]. The antiplasmodial activity of aqueous leaf and root extracts of C. citratus (200, 400, and 800 mg/kg) and chloroquine (5 mg/kg) was examined against P. berghei in mice using 4-day suppressive test model at P < 0.05. A dose-dependent suppressive pattern was observed with chloroquine and 800 mg/kg (aqueous root extract) [67]. C. citratus plant displayed significant antimalarial activity than herbal concoction or chloroquine (3200 mg/kg) (control) when used as a prophylactic treatment against CBA/Ca mice with patent P. berghei ANKA or P. chabaudi AS at doses of 1600 and 3200 mg/kg. In addition, the synergetic activity of chloroquine and C. citratus plant exhibited high activity than chloroquine alone against P. berghei. The antimalarial activity of entire C. citratus plant aids inevitable efforts to developing whole plant remedies for the treatment of malaria [65].

Morinda lucida. The antimalarial investigation of partly purified cysteine-stabilised peptide extracts of M. lucida leaf was assessed in vitro against P. falciparum W2 and its activities on certain liver and erythrocyte antioxidant parameters in P. berghei NK65-infected mice. Low activities were observed in *P. falciparum* W2 (IC50: >50 µg/ml); however, in vivo activity against P. berghei led to 51.52% reduction in parasitaemia on 96h after inoculation and considerably decreased (P < 0.05) malondialdehyde concentrations in the liver and erythrocyte at high doses in contrast to untreated controls [60]. N-Hexane and chloroform fractions of M. lucida leaf extract conducted using standard techniques showed significant activities at 0.6 mg/ ml [64]. The antimalarial activities of M. lucida investigated in P. berghei-infected mice exhibited dose-dependent chemosuppression of 39.8-90.5 which show pronounced activities than quinine [58].

Enantia chlorantha. Enantia chlorantha Oliver (or Annickia chlorantha) belongs to Annonaceae family, socalled Awopa, Osu pupa or Dokita igbo, Eru meru, Kakerim, and Erenba-vbogo in Nigeria. It is dense and widely distributed in Nigeria, Angola, Gabon, Cameroon, and Congo [77]. Oral administration of aqueous extract of E. chlorantha inhibited Plasmodium yoelii in mice at 0.2 to 150 mg/ml while ethanolic extract inhibited the parasite at dose of 0.05 to 0.5 mg/g. The ethanolic and aqueous extracts have  $ED_{50}$  values of  $0.34 \text{ mg} \cdot \text{g}^{-1}$  and  $6.9 \text{ mg} \cdot \text{g}^{-1}$  which are schizonticidal in the mode of action. The activities could be linked to the presence of saponins, tannins, simple sugars, and alkaloids [78]. Synergic reactions of E. chlorantha with N. latifolia and A. altilis were reported to display significant antimalarial and prophylactic activities. This justifies the ethnomedical practice of combination of antimalarial herbal therapies in combating acute or chronic malaria [63].

Aloe vera. The methanolic extracts of Aloe vera were assessed in vivo for its antiplasmodial potency against *P. falciparum* strain with 50% inhibition of 32 to 77  $\mu$ g/ml. The anthrone C-glucoside homonataloin isolated inhibited the strains with activity of 13.46 ± 1.36  $\mu$ g/ml (IC<sub>50</sub>); similarly, homonataloin displayed activities of 107.20 ± 4.14  $\mu$ g/ml (IC<sub>50</sub>) [79]. C-glycosylated anthrones, that is, nataloin and 7-hydroxyaloin, two isolated compounds in *Aloe pulcherrima*, displayed significant dose-independent activities on plasmodia strain using 4-day suppressive test. Pronounced activity of 56.2% was observed at 200 mg/kg/day in 48 h, which support the ethnomedical claims of the plant [80].

Carica papaya. The antimalarial property of Carica papaya leaf extracts was screened against P. falciparum 3D7 and Dd2 strains using bioassay-guided fractions and dichloromethane extract. The petroleum ether and chloroform fractions of C. papaya fruit and root assessed in vivo for antimalarial activity against early P. berghei infection in mice displayed pronounced chemosuppressive effect at P < 0.001. Significant activities were observed in petroleum ether fractions (61.78%) compared to 48.11% of chloroform fraction [71]. The synergistic effects displayed by the administration of C. papaya and V. amygdalina in ameliorating plasmodium infection in mice showed significant result at P < 0.05. The oral administration significantly surged the RBC and PCV renaissance when compared to the disease control. This underlined the importance of plants in conventional therapy of malaria infection [68]. Ethanolic leaf extract of C. papaya was appraised on chloroquine-sensitive and chloroquine-resistant strains of P. falciparum. The extracts significantly inhibited the activities of both plasmodium strains with  $IC_{50} = 40.75\%$ , 36.54%, 25.30%, and 18.0% for chloroquine-sensitive and  $IC_{50} = 50.23\%$ , 32.50%, 21.45%, and 23.12% for chloroquine-resistance plasmodium strains [81].

Azadirachta indica. Azadirachta indica extract is appraised to contain bioactive compounds which dictate its potencies against *P. vivax* and *P. falcifarum* [82]. Ethanolic leaf extracts assessed *in vivo* absolutely inhibited *P. berghei* growth, at azadirachtin dosage of 50 mg/kg mouse body

				TABLE 4: The an	TABLE 4: The antimalarial activity of selected medicinal plants.	elected medicinal	plants.		
S/n	Plant name	Plant part used	Country	Plasmodium species treated	Solvent used for extraction	Model	Control	Antiplasmodial activity	Reference
Т	Icacina senegalensis	Leaf	Nigeria	P. berghei	Methanol	Swiss albino mice	Chloroquine	A dose-dependent chemosuppression of the parasites was observed at different dose levels of the extract tested with a considerable mean survival time	[54]
7	Cymbopogon citratus	Leaf	Nigeria	P. falciparum	Aqueous	Swiss albino rats	Chloroquine	Significant decrease of parasitaemia levels was observed in 120 mg/kg body weight treated	[55]
ŝ	Azadirachta indica	Leaf	Ghana	P. berghei	Aqueous and ethanol	BALB/c mice	Distilled water (negative), artemether (positive)	Chemosupression of 69.65, 75.76, 78.32% (ethanol) and 64.42, 70.23, 77.41% (aqueous); artemether (86.77%)	[56]
4	<ul> <li>A. djalonensis, A. indica,</li> <li>C. cajan, C. cujete, L. inermis, L. alata, M. preussii, N. latifolia, O. subscorpioidea, and T.</li> </ul>	Stem bark, leaf, and root	Nigeria	P. berghei	Ethanol and aqueous	Swiss albino mice	Distilled water (negative) and chloroquine (positive)	Optimum activity was recorded on day 4. The activity was highest with water extract of the recipe at 500 mg/kg	[57]
Ŋ	Sometica Alstonia boonei, Curcuma longa	Leaf	Nigeria	P. berghei	Ethanol	Swiss albino mice	Sulphadoxine- pyrimethamine (S- P), and quinine	Chemosuppression of 39.8–90.5, 0.2–74.8, and 34.6–78.4% observed in MLE, ABE, and CLE The extract inhibited P	[58]
9	Azadirachta indica	Leaf	Indonesia	P. falciparum	Ethanol			falciparum on mature schizont stage with $IC_{50}$ of 3.86 $\mu g/ml$ after 32 h incubation	[59]
	Morinda lucida	Leaf	Nigeria	P. berghei	Dichloromethane- methanol	Adult Swiss albino mice	Chloroquine	PPCPE was active against <i>P. berghei</i> NK65 <i>in vivo</i> , with 51.52% reduction in parasitaemia on day 4 after inoculation	[09]
×	Ocimum basilicum, Ocimum canum, and Cymbopogon citratus	Leaf	Cameroon	P. falciparum and mature-stage larvae of Anopheles funestus		Human red blood cells in RPMI 1640 medium	Giemsa-stained blood smear	IC50 = 4.2 ± 0.51 g/mL (C. citratus), 20.6 ± 3.41g/mL (O. canum) and 21 ± 4.61g/mL (O. basilicum)	[61]
6	Azadirachta indica	Leaf	Saudi Arabia	P. berghei	Ethanol	Swiss albino mice	Chloroquine and artemether	Alcoholic extracts displayed no activity, ethanol extracts of neem displayed increased parasitaemia gradually from day 0 (5%, 5.1%, and 7.2%) to day 4, with mean parasitaemia of 53%	[62]
	Maurlas latitalia							Duanhulactic and annative ED of	

[63]

Prophylactic and curative ED<sub>50</sub> of 189.4 and 174.5 mg/kg for *N*. *latifolia* and chemosuppressive ED<sub>50</sub> of 227.2 mg/kg for *A. altilis* 

Pyrimethamine and chloroquine

Berghei-infected mice

Ethanol

P. berghei

Nigeria

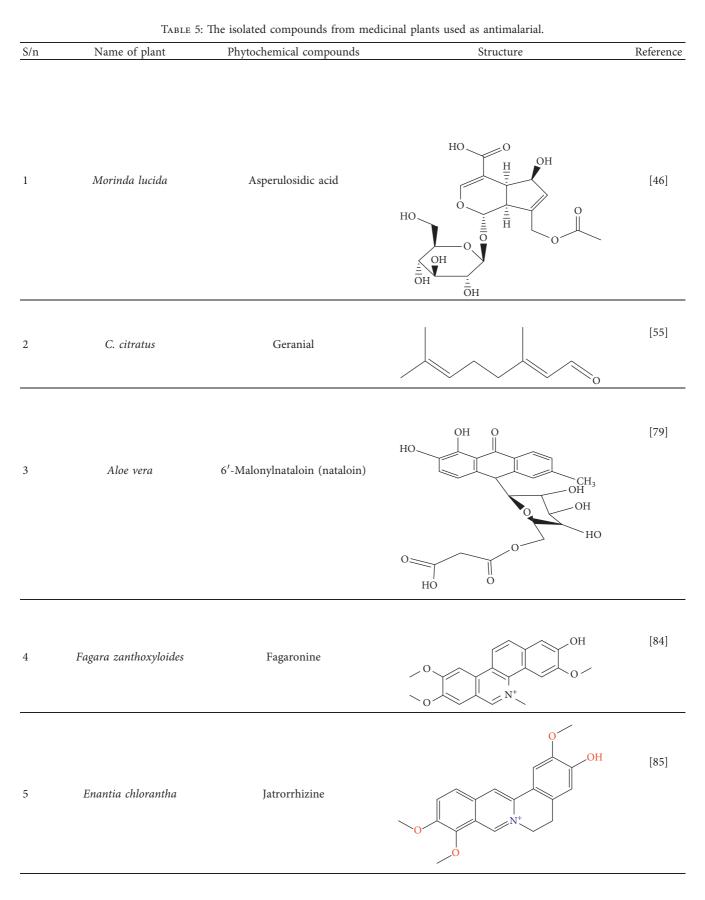
Stem bark, root, leaf

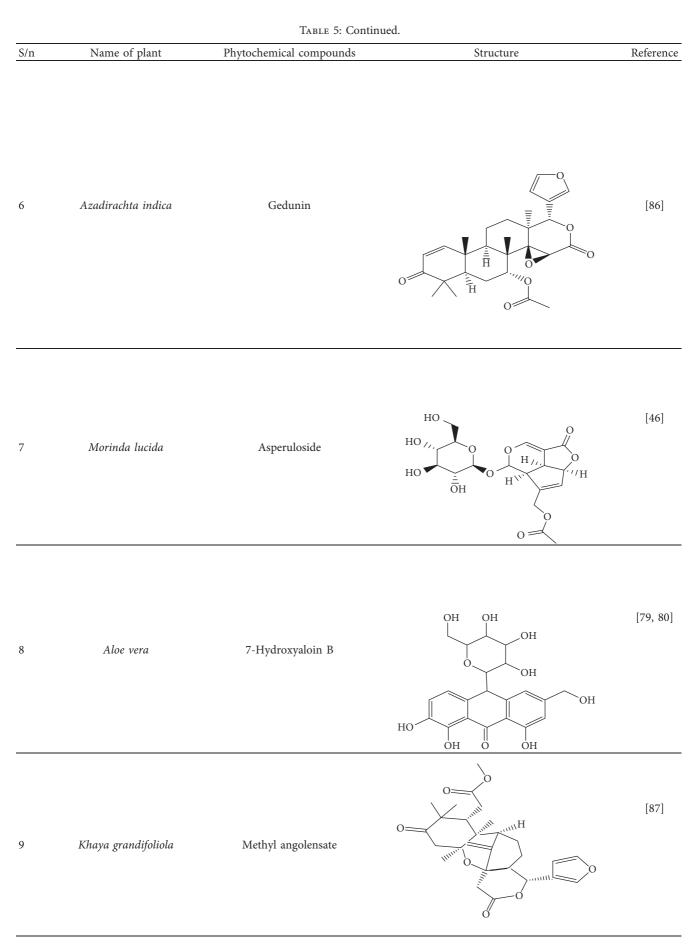
Nauclea latifolia, Artocarpus altilis, Murraya koenigii, and Enantia chlorantha

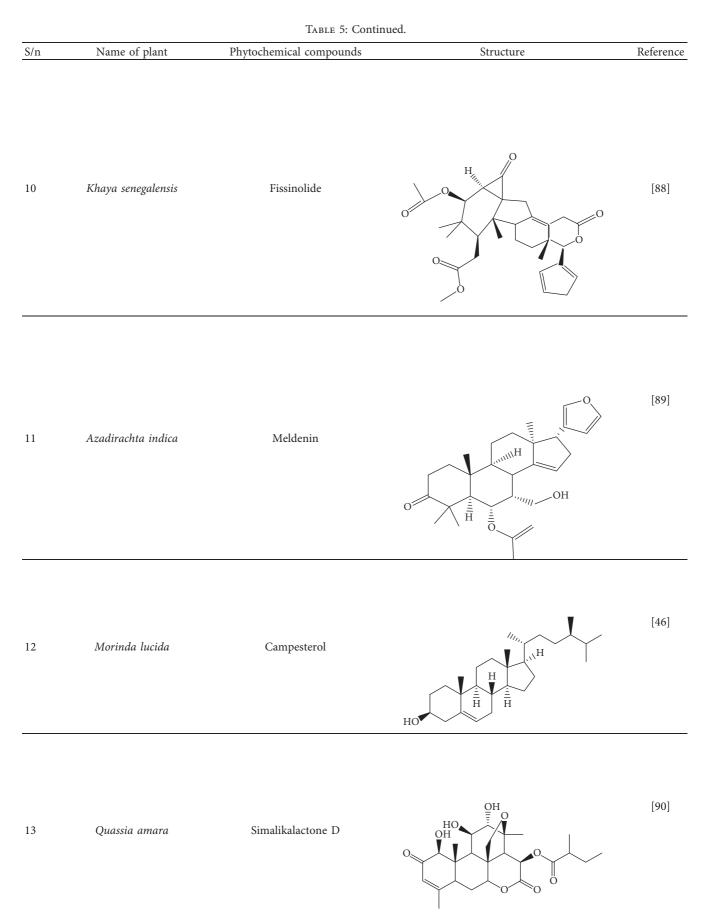
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	ence	4]	2]	5]	[2	8]	[6	[c	[]	[1]
	Reference	[64]	[65]	[66]	[67]	[68]	[69]	[70]	[11]	[[71]
	Antiplasmodial activity	MIC for chloroquine is 0.6 µg/ml, M. lucida is 0.6 mg/ml, and A. Boonei is 0.2 mg/ml	As a proprivacue treatment, une whole plant exhibited higher antimalarial activity than either the herbal infusion or chloroquine	Methanolic extract of leaves showed highest antimalarial activity with IC50 value of $12.17 \mu g/ml$	Ine aqueous leaf extracts have suppressive effect of 20.83%, 55.56%, and 80.56%, root extracts have 50.38%, 77.78%, and 100%	Significant ( $P < 0.05$ ) reduction in the percentage of parasite load between the infected treatment groups and disease control group at day 3	The derived EC <sub>50</sub> (3D7/Dd2, g/mL) are nefang 96.96/55.08, MiB-65.33/34.58, MiL-82.56/40.04, Pg-47.02/25.79, Cp-1188/317.5, Cc-723.3/141s and og-778.5/118.9	Parasite suppression of day 1 (30.3%, 43.4%, and 56.4%), day 2 (32.3%, 51.3%, and 67.4%), day 3 (39.8%, 50.6%, and 64.2%), day 4 (52.6%, 69.4%, and 79.6%) was observed at doses of 100, 200, and	The EC <sub>50</sub> of 0.289 to 1056 $\mu$ g/ml. The antiplasmodial EC <sub>50</sub> of chloroquine was 0.034 $\mu$ g/ml and aloin and aloe-emodin was 67 $\mu$ g/ml and ml and 22 $\mu$ g/ml. respectively	suppression of ol./8% was produced by pet ether fraction of C. papaya fruit rind, chloroform fraction of C. papaya root exhibited (48.11%), methanol fraction produced less effect
	Control	Chloroquine	Chloroquine	Chloroquine	Chloroquine	Halofantrine	Chloroquine and artemisinin	Chloroquine	Chloroquine	Chloroquine
nuea.	Model		CBA/Ca male mice	Infected BALB/ c albino mice	Infected mice	Infected mice	3% hematocrit in human red blood cells	Swiss albino mice		Male Swiss albino mice
1ABLE 4: Continued	Solvent used for extraction	Ethanol		Methanol, ethyl acetate, and chloroform	Aqueous	Aqueous	Aqueous and ethanol		Aqueous	Pet ether, chloroform, and methanol
	Plasmodium species treated	P. falciparum	P. chabaudi AS or P. berghei ANKA	P. falciparum (3D7 strain) and P. berghei (ANKA)	P. berghei	Chloroquine- sensitive <i>P.</i> <i>berghei</i> (Nk65)	P. falciparum	P. berghei	P. falciparum (MRC-2).	P. berghei
	Country	Nigeria	Nigeria	India	Nigeria	Nigeria	Cameroon	Ethiopia	India	Ethiopia
	Plant part used	Leaf, stem bark	Whole plant	Leaf, stem, and flower	Leaf and root	Leaf extracts	Bark and leaf	Leaf	Leaf	Fruit rind and root
	Plant name	Morinda lucida, Artemisia annua	Cymbopogon citratus	Calotropis gigantea	Cymbopogon citratus	Carica papaya and Vernonia amygdalina	Mangifera indica, Psidium guajava, Carica papaya, Cymbopogon citratus, Citrus sinensis, and Ocimum gratissimum	Aloe megalacantha	Aloe vera	Carica papaya
	S/n	11	12	13	14	15	16	17	18	19

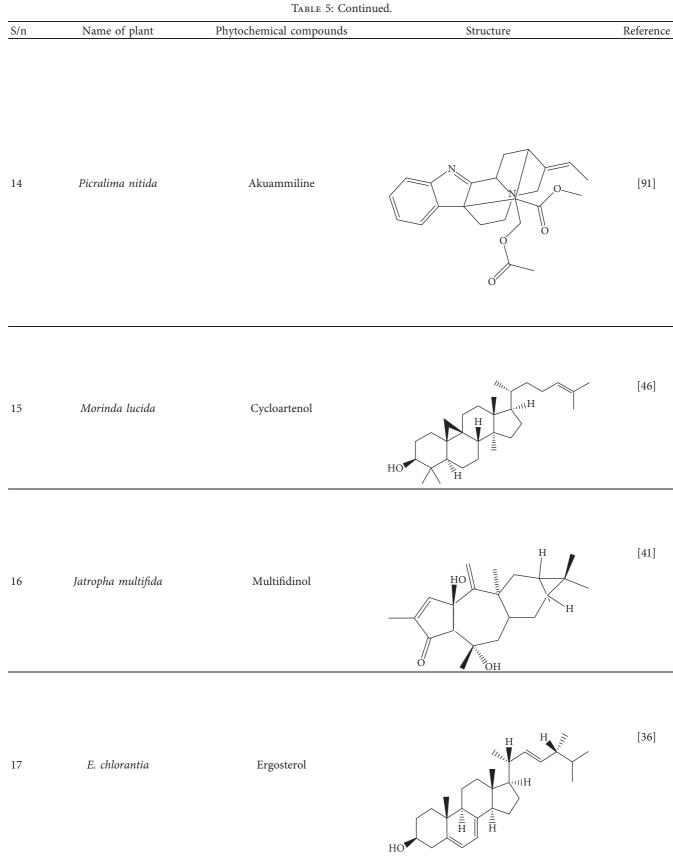
Plant name	Plant part used	Country	Plasmodium species treated	Solvent used for extraction	Model	Control	Antiplasmodial activity	Reference
Mangifera Indica	Leaf	Nigeria	P. Berghei	Aqueous	Infected albino mice	Artesunate	The extract has a dose-dependent reducing effect on the level of parasitaemia	[72]
Stemonocoleus micranthus	Stem bark	Nigeria	P. berghei	Hydromethanol	Swiss albino mice	Chloroquine (positive)	Chemosuppressive effect ranged from 54.14 to 67.73% and 59.41 to 94.51%	[73]
Lawsonia inermis, Tithonia diversifolia, and Chromolaena odorata	Leaf	Nigeria	P. berghei ANKA	Dichloromethane, methanol	Swiss albino mice	Chloroquine and artemisinin	IC <sub>50</sub> of 0.437±0.02 mg/mL and 2.557±0.19 mg/mL against D6 and W2, respectively	[43]
Holarrhena antidysenterica and Azadirachta indica	Leaves, stem, bark	India	P. berghei	Aqueous	Mycoplasma free male Swiss mice	Chloroquine	The parasitaemia increased gradually in all the groups, with the maximum in the control group (day 3–35, day 9–46.98) and minimum in chloroquine arm (day 3–14.06, day 9–19.92)	[41]
Euphorbia hirta and Vernonia amygdalina	Whole plant, leaves	Nigeria	P. berghei	Ethanol	Infected mice	Camosunate, ACT	ACT was slightly potent (>50%) against chloroquine-sensitive <i>P.</i> <i>berghei</i>	[74]
Pseudocedrala kotschyi	Leaf	Nigeria	P. berghei	Ethanol	Swiss Albino mice	Chloroquine	The leaf extract exhibited significant dose-dependent activity against the parasite in the suppressive and curative activity	[75]

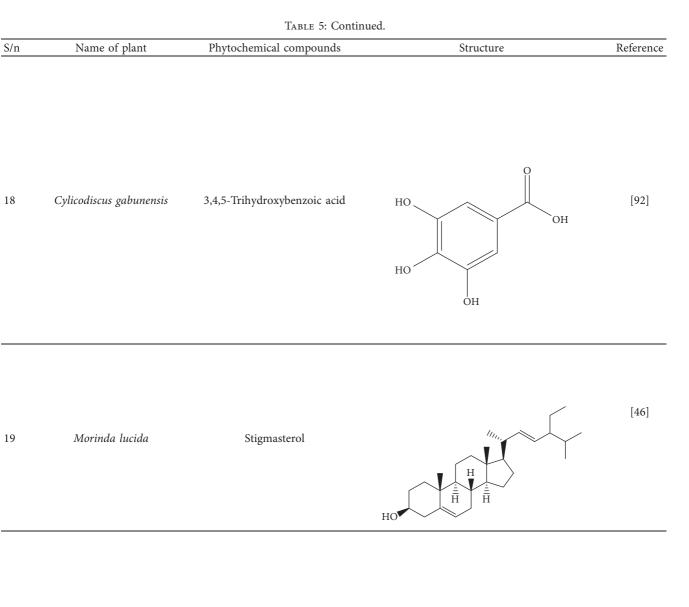


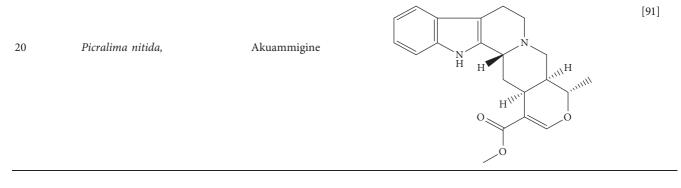


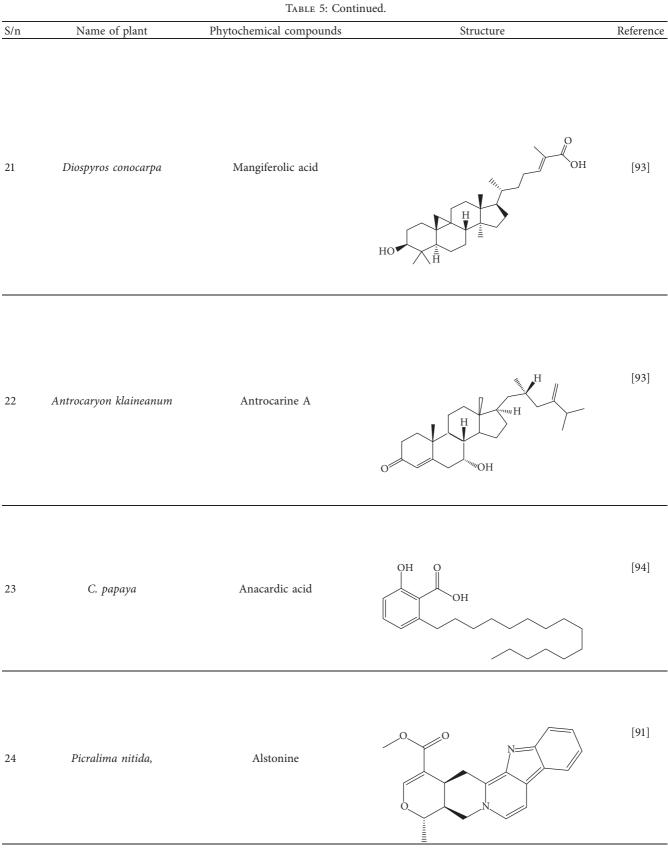


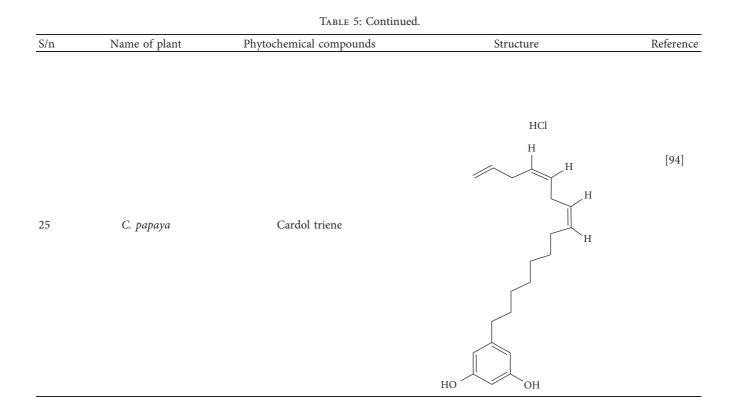
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weight [83]. The *in vivo* antiplasmodial potency of aqueous and ethanolic leaf extracts was examined in *P. berghei*-in-fected BALB/c mice at dosage of 50 to 200 mg/kg/day. Both extracts exhibited significant antiplasmodial potency in a dose-dependent technique which could be due to the active antiplasmodial compounds screened [56].

# 4. Conclusion and Future Prospects

Malaria is a universal civic health peril, and recent drug resistance of the parasite is a persistent concern. This study shows that a highly diverse set of native medicinal herbs is currently used for the management of malaria in Nigeria. Based on the results, there is substantial indication that the traditional use of antimalarial medicinal plants by Yoruba ethnics (studied areas) is driven by important therapeutic agents, which could be elucidated structurally and further established by in vitro or in vivo investigations. In recent times, the growing interest in phytoremediation of malaria led to the isolation and characterization of bioactive compounds in medicinal plants (Table 5) The isolation, characterization, and quantification of these compounds were appraised via chromatographic and spectrophotometric methods. Likewise, different assays such as susceptibility microassay technique [95], four day suppressive test [96], 96-well microtiter plate format SYBR green florescence assay [97], and LDH method [98] are used to appraise the antiplasmodial potential of plant extracts (Table 4).

Several modes of preparation, usage factors, health risks, and countermeasures on the use of antimalarial herbal drugs should be systematically examined through advanced scientific approaches. This will aid in the identification and authentication of therapeutic potency of antimalarial compounds isolated from medicinal herbs, thereby promoting its global relevance as efficacious and safe antimalarial plants in primary health care. Individuals, societies, sociogroups, and governmental and nongovernmental organizations should devise plans which could assist in the conservation of these medicinal plants in order to prevent their extermination and exploitation of indigenous populations, as well as considerations for cultural disruptions should one or more of these plant species become a valuable resource. In the meantime, the outcomes of this study serve as a platform of appraisal for indigenous claims of medicinal plants as effective antimalarial drugs in Nigeria and the world as a whole.

# **Data Availability**

The datasets used and/or analysed during the current study are available in the manuscript and others not included are available from the corresponding author upon request.

# **Conflicts of Interest**

The authors declare that there are no conflicts of interest regarding the submission and publication of this article.

# **Authors' Contributions**

All authors designed the experiment, administered the questionnaires, and analysed and discussed the data obtained.

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