Infection and Drug Resistance

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REVIEW

The Potentials of *Ageratum conyzoides* and Other Plants from *Asteraceae* as an Antiplasmodial and Insecticidal for Malaria Vector: An Article Review

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Background: Malaria is a life-threatening disease prevalent in tropical and subtropical regions. Artemisinin combination therapy (ACT) used as an antimalarial treatment has reduced efficacy due to resistance, not only to the parasite but also to the vector. Therefore, it is important to find alternatives to overcome malaria cases through medicinal plants such as *Ageratum conyzoides* and other related plants within *Asteraceae* family.

Purpose: This review summarizes the antimalarial and insecticidal activities of *A. conyzoides* and other plants belonging to *Asteraceae* family.

Data Source: Google Scholar, PubMed, Science Direct, and Springer link.

Study Selection: Online databases were used to retrieve journals using specific keywords combined with Boolean operators. The inclusion criteria were articles with experimental studies either in vivo or in vitro, in English or Indonesian, published after 1st January 2000, and full text available for inclusion in this review.

Data Extraction: The antimalarial activity, insecticidal activity, and structure of the isolated compounds were retrieved from the selected studies.

Data Synthesis: Antimalarial in vitro study showed that the dichloromethane extract was the most widely studied with an IC50 value <10 µg/mL. Among 84 isolated active compounds, 2-hydroxymethyl-non-3-ynoic acid 2-[2,2']-bithiophenyl-5- ethyl ester, a bithienyl compound from the *Tagetes erecta* plant show the smallest IC50 with value 0.01 and 0.02 µg/mL in *Plasmodium falciparum* MRC-pf-2 and MRC-pf-56, respectively. In vivo studies showed that the aqueous extract of *A. conyzoides* showed the best activity, with a 98.8% inhibition percentage using a 100 mg/kg dose of *Plasmodium berghei* (NK65 Strain). (Z)- γ-Bisabolene from *Galinsoga parviflora* showed very good insecticidal activity against *Anopheles stephensi* and *Anopheles subpictus* with LC50 values of 2.04 µg/mL and 4.05 µg/mL.

Conclusion: *A. conyzoides* and other plants of *Asteraceae* family are promising reservoirs of natural compounds that exert antimalarial or insecticidal activity.

Keywords: *Ageratum conyzoides*, *Asteraceae*, antimalarial, *Plasmodium*, insecticidal, *Anopheles*

Introduction

Malaria has been a worldwide disease since 1800, caused by *Plasmodium* species through the vector of *Anopheles* mosquitoes.[1] *Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae*, and *Plasmodium knowlesi* are *Plasmodium* species that commonly infect humans.[2–4] According to World Health Organization (WHO), in 2020, there were around 241 million cases of malaria in the World.[5] Caused by various factors such as geographical location, rainfall, and the number of standing water.[6] As contained in the WHO guidelines for treating and preventing the incidence of malaria, several efforts have been made, including the use of Artemisinin Combination Therapies (ACT) for treating *Plasmodium* infections,

Received: 30 August 2023
Accepted: 26 October 2023
Published: 7 November 2023

Insecticide-Treated mosquito Nets (ITN), Insecticides Residual Spraying (IRS), and Larva Source Management (LSM) for preventing the incidence of malaria by controlling the vector.[7–10]

More than 90% of malaria mortality worldwide was caused by *P. falciparum*, whereas *P. vivax* is the most common.[11] ACT therapies; by combining artemisinin derivatives and another antimalarial drug, are the current first-line therapy for uncomplicated *P. falciparum* and second-line therapy for non-*P. falciparum*. Meanwhile, Quinine derivates are considered the first-line choice for non-*P. falciparum* infection.[12] *Plasmodium* parasites are now reported to be resistant to several ACT drugs due to mutations in the *kelch13* gene reported in the Greater Mekong Subregion (GMS).[13,14] Resistance is also experienced by vectors of malaria and *Anopheles* mosquitoes against insecticides (ITN/IRS) due to mutations of the *L1014S* gene.[15] This phenomenon makes the development of treatment and prevention of malaria continue, which is currently widely reported using natural plant-based ingredients with various secondary metabolite compounds such as flavonoids, terpenoids, and chalcones.[16–18] For example, particular species from *Asteraceae* and *Rubiaceae* family have been known as sources of antimalarial drugs: Quinine isolated from the *Cinchona* tree bark (*Rubiaceae*) and Artemisinin isolated from the leaves and floral buds of *Artemisia annua* (*Asteraceae*).[19] Since the African continent accounted for >90% of all global malaria cases, various herbaceous plants have been used for traditional remedies in this region.[20,21] For example, in Uganda, among the 63 plant families, *Asteraceae* species are the most widely used, accounting for up to 15% of all plant species followed by *Fabaceae* (9%), *Lamiaceae* (8%), *Euphorbiaceae* (6%), and *Mimosaceae* (4%) species.[21] More specifically, aqueous extract of dried leaf of *Ageratum conyzoides*, a member of *Asteraceae* family, has been traditionally used to cure malaria in Nigeria[22] Uganda,[21] and India.[23] Research on the *A. conyzoides* plant from the *Asteraceae* family has also been proven to have antiplasmodial and insecticidal activity against *Anopheles* mosquitoes.[24,25] The potency of *A. conyzoides* is inseparable from the role of its secondary metabolites, such as flavonoids and terpenoids.[26] Additionally, this plant is widely used as a source for the adjuvant.[27] This review aims to obtain information about the potential of *A. conyzoides* and other plants from *Asteraceae* as antiplasmodial and insecticidal from existing studies for better development in the future.

Materials and Methods

This review was conducted using an online database with specific keywords combined with Boolean operators. Studies that met the inclusion criteria in the form of experimental studies (either in vivo or in vitro, articles in English or Indonesian, articles published after 1st January 2000, and full-text articles were included in this review. The exclusion criteria were the articles that only had abstracts available, and other articles that did not correlate with the scope of the discussion in this study.

Articles discussing the potential of *A. conyzoides* as antiplasmodials and insecticides will be extracted from the author, year of publication, species used, plant extraction methods, and results. To add information regarding the potency of *A. conyzoides*, this review also presents a similar study to determine the benefits of plants from the *Asteraceae* family as antiplasmodials and insecticidals, with the hope that they will show good results and be useful for future research on *A. conyzoides*. Limitation of this study are not including meta-analysis and comprehensive statistical analysis.

Results and Discussion

Results of Literature Review

The literature search analysis is shown in Figure 1. Among the articles retrieved from several databases, such as Google Scholar, PubMed, Science Direct, and Springer links (Tables 1 and 2), 62 articles were found that met the inclusion criteria. Fifteen articles discussed the potential of the *A. conyzoides* plant, and the remaining 47 discussed the potential of the *Asteraceae* family plants.

From several studies collected in this review, the results of the *A. conyzoides* plant and its family (*Asteraceae*) have varied as antiplasmodial and insecticidal. A part of the plant that is widely used is the leaves of both *A. conyzoides* and its family (*Asteraceae*). The most widely used extract is the dichloromethane extract. Several active compounds have been identified, there are 23 species of plants in the *Asteraceae* family whose active compound(s) have been defined including *Acmella ciliata, Anacyclus pyrethrum, Artemisia afra jacq., Artemisia gorgonum, Baccharis dracunculifolia D. C, Dicoma anomala subsp. Gerrardii, Dicoma tomentosa, Distephanus angulifolius, Galinsoga parviflora, Helichrysum gymnocephalum, Kleinia odora, Microglossa pyrifolia, Pechuel-loeschea leubnitziae, Pentacalia desiderabilis (Vell.)*

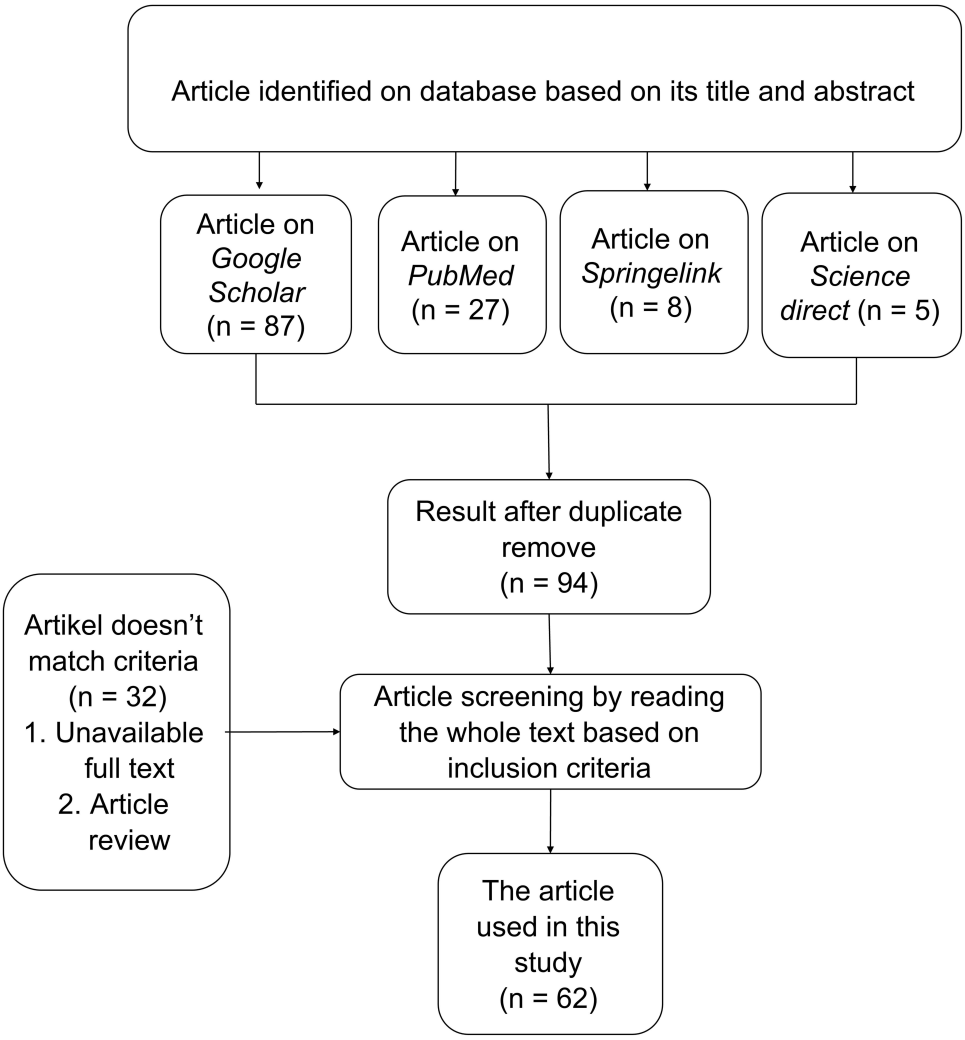

Figure 1 Literature Study Flowchart.

Cuatrec, Sinicio smithioides, Sphaeranthus indicus, Symphyopappus casarettoi, Tagetes erecta, Vernonia guineensis Benth., Vernonia fimbrillifera Less., Vernonia colorata, Xanthium brasilicum Vell, and Ageratum conyzoide.

Traditional Use of *Asteracea* Family as Antimalaria

Since ancient times, certain plants have been recognized to offer therapeutic effects to cure malaria. The use of plants as medicine has grown in popularity since they are more economical, efficient, and safe.[28] The extract is mostly prepared by using single herbal plants (monoteraphy) or from combination of two herbal plants for example *Tamarindus indica* and

Table 1 Keyword and Database Used for *Ageratum conyzoides*

Keyword	Database
("Ageratum conyzoides" OR "Billy goat weed") AND ("Antimalarial" OR "Antiplasmodial" OR "Plasmodium" OR "Anopheles" OR "Insecticidal")	Google Scholar
	PubMed
	Springer Links
	Sciencedirect

Table 2 Keyword and Database Used for *Asteraceae*

Keyword	Database
("Asteraceae") AND ("Antimalarial" OR "Antiplasmodial" OR "Plasmodium" OR "Anopheles" OR "Insecticidal")	Google Scholar
	PubMed
	Springer Links
	Sciencedirect

Mangifera indica.[21,29] The most commonly used plant parts were leaves (67.3%), followed by roots (13.5%), root bark (5.8%), and fruits (5.8%). The herbal medicines were majorly administered orally (86.7%) follow by topical baths (11.1%), and steam baths (2.2%).[20] The most common herbal medicine preparation is water extracts in the form of decoction and infusion or as steam baths.[21] For example traditional remedy preparation of *A. conyzoides* to cure malaria was performed as follows: the water from boiling of *A. conyzoides* leaf was drunk thrice a day for seven days.[21] Besides treating malaria, medicinal herbs from *Asteraceae* also has promising prophylactic use or malaria prevention. The most prevalent technique of preparing plant species for malaria prevention was to dry the plant material and burn it to make smoke, as well as to boil the plant material and consume it as a sauce.[29]

In vitro and in vivo Assay of Antiplasmodial Potency of *Asteraceae* Family

The emergence of drug resistance in *Plasmodium* parasites and unwanted side effects from certain chemical drugs have fueled the search for new plant-derived antimalarials. Consequently, the antimalarial properties of herbal plants have increasingly been reported. Specifically, the antimalarial activity of various extracts, fractions, and active compounds was tested as a starting point to become an alternative that can be used as a potential source of new antimalarial agents in the future.

In vitro and in vivo efficacy tests against *Plasmodium* parasites in vitro or in vivo have been performed on several plants belonging to the *Asteraceae* family (Tables 3 and 4). According to Deharo et al[30] a compound with an IC50 value <5 µg/mL is considered a very effective antimalarial agent based on the results of in vitro tests and is very effective if the in vivo test shows an inhibition percentage >50% at a dose of 100 mg/kg/day.[30] Therefore, 37 plants from the *Asteraceae* family showed antiplasmodial effects that could be tested in the future.

Among the 37 potential plants, the majority of the extract used in this study was dichloromethane extract, and the plants that had the highest activity were *Microglossa pyrifolia* and *Vernonia guineensis Benth* The dichloromethane extract from the leaves showed IC50 values of 1.5, 2.4, 1.8, and 1.6 µg/mL for *P. falciparum* 3D7, W2, Dd2, and Hb3 species, respectively.[52,77] Meanwhile, the results showed little difference from in vivo testing on mice, dichloromethane extract from the whole plant *Anisopappus chinensis* gave medium yield with a suppression percentage of 60% at a dose of 300 mg/kg against *Plasmodium berghei*.[41] However, this cannot be equated considering that the species tested in the two studies are different, no study states that this extract has been tested against *Plasmodium* other than *P. berghei*, therefore research on the effects of dichloromethane extract on mice infected with parasites other than *P. berghei* needs to be carried out.

Studies on the isolation of secondary metabolites from the *Asteraceae* family have also been conducted. In this review, 21 plants of the *Asteraceae* family were investigated for their antiplasmodial activity, as listed in Table 3. Of these 21 plants, there were 78 active antiplasmodial metabolites from various plants. The isolated compounds were very diverse, but the active compound that had the best antiplasmodial activity was 2-hydroxymethyl-non-3-ynoic acid 2-[2,2']-bithiophenyl-5- ethyl ester, a bithienyl compound from the *T. erecta* plant which shows IC50 value 0.01 and 0.02 µg/mL against *P. falciparum* MRC -pf-2 and MRC-pf-56 respectively.[70] In addition, the active compound from the terpenoid group, namely *hautriwaic acid* extracted from the plant *B. dracunculifolia*, also had high activity on *P. falciparum* D6 with IC50 0.8 µg/mL.[47] Other types of terpenoids are also reported to have good effects as antiplasmodial from plants of the *Laminaceae* family.[87]

Table 3 Result for Antiplasmodial and Insecticidal from *Asteraceae* Family

No.	*Asteraceae* Species	Authors (Year)	Target Species	Study Design	Sample Used	Result	Phytochemical Active
1	*Acanthospermum hispidum*	Bero et al (2009)[31]	*Plasmodium falciparum* 3D7 strain	In Vitro	Dichloromethane extract from aerial part	**IC 50**: 7.5 µg/mL	N/A
			Plasmodium falciparum W2 strain	In Vitro	Dichloromethane extract from aerial part	**IC 50**: 4.8 µg/mL	
		Sanon et al (2003)[32]	*Plasmodium falciparum* W2	In Vitro	Alkaloid extract from leaves	**IC 50**: 5.0 µg/mL	N/A
			Plasmodium falciparum D6	In Vitro	Alkaloid extract from leaves	**IC 50**: 4.6 µg/mL	
		Ohashi et al (2018)[33]	*Plasmodium falciparum* 3D7 strain	In Vitro	Ethanol extract from whole plant	**IC50**: >1,000 µg/mL	N/A
2	*Achillea wilhelmsii C. Koch*	Soleimani-Ahmadi et al (2017)[34]	*Anopheles stephensi* (BandarAbass strain)	In Vivo	Leaves-derived: 1. Methanol extract 2. Essential oil extract	% **Mortality**: 320 ppm = 100%; **LC50**: 115.73 160 ppm = 100%; **LC50**: 39.04	N/A
3	*Acmella caulirhiza*	Owuor et al (2012)[35]	*Plasmodium falciparum* (D6) strain	In Vitro	Dichloromethane extract from whole plant	**IC 50**: 9.9 µg/mL	N/A
			Plasmodium falciparum (W2) strain	In Vitro	Dichloromethane extract from whole plant	**IC 50**: 5.2 µg/mL	
4	*Acmella ciliata*	Silveira et al (2016)[36]	*Plasmodium falciparum* (NF54) strain	In Vitro	Subfraction n-Hexane: 1. isobutylamide spilanthol ((2E,6E,8E) -N-isobutyl-2,6,8-decatrienamide 2. N-(2-phenethyl)-2E-en-6,8-nonadiynamide 3. (2E,7Z)-6,9-endoperoxy-N-isobutyl-2,7-decadienamide	**IC 50**: 1. 0.99 µg/mL 2. 22.1 µg/mL 3. 1.29 µg/mL	Alkamide 1. isobutylamide spilanthol ((2E,6E,8E)-N-isobutyl-2,6,8-decatrienamide 2. N-(2-phenethyl)-2E-en-6,8-nonadiynamide 3. (2E,7Z)-6,9-endoperoxy-N-isobutyl-2,7-decadienamide
			Plasmodium falciparum (K1) strain	In Vitro	Subfraction n-Hexane: 1. (2E,7Z)-6,9-endoperoxy-N-isobutyl-2,7-decadienamide	**IC 50**: 1. 0.54 µg/mL	
5	*Acmella oleracea*	Chaniad et al (2022)[19]	*Plasmodium falciparum* (K1) strain	In Vitro	Flower, Leaves, Stem-derived: 1. Ethanol extract 2. Aqueous extract	**IC 50: µg/mL** 21.5 (f); 28.9 (l); 28.2 (s) 47 (f); 110.7 (l); 536.7 (s)	Flavonoid, Terpenoid, Alkaloid, Saponin, Coumarin
6	*Ageratina adenophora*	Rajeswary et al (2014)[37]	*Anopheles stephensi* egg	In Vivo	Leaves-derived: - n-Hexane extract - Benzene extract - chloroform extract - Ethyl acetate extract - Methanol extract	% **Mortality**: 450 ppm = 100% 450 ppm = 100% 375 ppm = 100% 300 ppm = 100% 300 ppm = 100%	N/A

(*Continued*)

https://doi.org/10.2147/IDR.S433328 DovePress

Table 3 (Continued).

No.	*Asteraceae* Species	Authors (Year)	Target Species	Study Design	Sample Used	Result	Phytochemical Active
7	*Ageratum houstonianum Mill.*	Tennyson et al (2012)[38]	*Anopheles stephensi*	In Vivo	Leaves-derived: - n-Hexane extract - Ethyl acetate extract - Methanol extract	**% Repellency activity**: 93.4% 93.4% 91.7%	N/A
8	*Ambrosia maritima L*	Nour AMM et al (2009)[39]	*Plasmodium falciparum* K1 strain	In Vitro	Dichloromethane extract	**IC 50**: 3.08 µg/mL	N/A
9	*Anacyclus pyrethrum*	Althaus et al (2017)[40]	Plasmodium falciparum NF54 strain	In Vitro	1. deca-2E,4E,9-trienoic acid isobutylamide 2. deca-2E,4E-dienoic acid 2-phenylethylamide 3. undeca-2E,4E-dien-8,10-diynoic acid isopentylamide 4. tetradeca-2E,4E,12Z-trien-8,10-diynoic acid isobutylamide 5. dodeca-2E,4E-dien acid 4-hydroxy-2-phenylethylamide	**IC50**: 1. 7.13 µg/mL 2. >5 µg/mL 3. 10.3 µg/mL 4. 7.19 µg/mL 5. 3.18 µg/mL	1. deca-2E,4E,9-trienoic acid isobutylamide 2. deca-2E,4E-dienoic acid 2-phenylethylamide 3. undeca-2E,4E-dien-8,10-diynoic acid isopentylamide 4. tetradeca-2E,4E,12Z-trien-8,10-diynoic acid isobutylamide 5. dodeca-2E,4E-dien acid 4-hydroxy-2-phenylethylamide
10	*Anisopappus chinensis*	Lusakibanza et al (2010)[41]	*Plasmodium falciparum* 3D7	In Vitro	Whole plant-derived: 1. Dichloromethane extract 2. Methanol extract 3. Aqueous extract	**IC 50**: 6.53 µg/mL 8.82 µg/mL 76.51 µg/mL	Flavonoid, terpene, tanin, phenolic acid
			Plasmodium falciparum W2	In Vitro	Whole plant-derived: 1. Dichloromethane extract 2. Methanol extract	**IC 50**: 6.37 µg/mL 12.24 µg/mL	
			Plasmodium berghei	In Vivo	Whole plant-derived: 1. Methanol extract 2. Ethanol extract 3. Dichloromethane extract 4. Aqueous extract	**% Growth inhibition: (300mg/kg)** 80.5% 65.5% 60.8% 85.6%	N/A

11	*Artemisia afra jacq.*	Kraft et al (2003)[42]	*Plasmodium falciparum* PoW	In Vitro	lipophilic extract (petrol ether/ ethylacetate) from aerial part Isolated compound: 1. 7-Metoxyacacetin 2. Acacetin 3.Genkwanin 4. Tamarixetin 5. Apigenin 6 1-desoxy-1α-peroxy-rupicolin A-8-O-acetate 7. Rupicolin A-8-O-acetate 8. Rupicolin B-8-O-acetate 9.11,13-dehydromatricarin 10. 1α,4α-dihydroxybishopsolicepolide 11. 1α,4α-8α-Trihydroxyguaia-2,9,11 (13)-triene-12,6α-olide-8-O-acetate 12. Eudesmaafgraucolid	**IC 50**: 8.9 µg/mL **IC 50**: 1. 4.3 µg/mL 2. 5.5 µg/mL 3. 5.5 µg/mL 4. 33.9 µg/mL 5. 14.6 µg/mL 6. 8.7 µg/mL 7. 12.5 µg/mL 8. 20.1 µg/mL 9. 17.9 µg/mL 10. 8.6 µg/mL 11. 30.9 µg/mL 12. 47.5 µg/mL	– 7-Metoxyacacetin - Acacetin - Genkwanin - 1-desoxy-1α-peroxy-rupicolin A-8-O-acetate - 1α,4α-dihydroxybishopsolicepolide - A-8-O-acetate
			Plasmodium falciparum Dd2	In Vitro	1. lipophilic extract (petrol ether/ ethylacetate) from aerial part 2. Isolated compound: 1. 7-Metoxyacacetin 2. Acacetin 3.Genkwanin 4. Tamarixetin 5. Apigenin 6 1-desoxy-1α-peroxy-rupicolin A-8-O-acetate 7. Rupicolin A-8-O-acetate 8. Rupicolin B-8-O-acetate 9.11,13-dehydromatricarin 10. 1α,4α-dihydroxybishopsolicepolide 11. 1α,4α-8α-Trihydroxyguaia-2,9,11 (13)-triene-12,6α-olide-8-O-acetate 12. Eudesmaafgraucolid	**IC 50**: 15.3 µg/mL **IC 50**: 1 7.0 µg/mL 2. 12.6 µg/mL 3. 8.1 µg/mL 4. 33 µg/mL 5. 25 µg/mL 6. 17.5 µg/mL 7. 10.8 µg/mL 8. 31.8 µg/mL 9. 12.5 µg/mL 10. 11.7 µg/mL 11. 20.4 µg/mL 12. >50 µg/mL	
12	*Artemisia annua*	Cheah et al (2013)[43]	*Anopheles sinensis* larvae	In Vivo	Acetone extract from plant	% **Suppression**: 600 ppm = 99%	N/A
13	*Artemisia gorgonum*	Ortet et al (2011)[44]	*Plasmodium falciparun* FcB1	In Vitro	Isolated flavonoid compound: 1. Eudesmin 2. Magnolin 3. Epimagnolin A 4. Aschantin 5. Kabusin 6. Sesamin 7. Artemetin	**IC 50**: 1. >25 µg/mL 2. 22.7 µg/mL 3. 5.7 µg/mL 4. 5.7 µg/mL 5. 7.67 µg/mL 6. 3.37 µg/mL 7. 3.50 µg/mL	1. Eudesmin 2. Magnolin 3. Epimagnolin 4. Aschantin 5. Kabusin 6. Sesamin 7. Artemetin

(*Continued*)

https://doi.org/10.2147/IDR.S433328 DovePress

Table 3 (Continued).

No.	*Asteraceae* Species	Authors (Year)	Target Species	Study Design	Sample Used	Result	Phytochemical Active
14	Artemisia nilagirica	Panda et al (2018)[45]	*Plasmodium falciparum* (FCR-3 strain)	In Vitro	Extract from leaf: 1. Methanol 2. Chloroform 3. n-hexane 4. Petroleum ether 5. Ethanol 6. Aqueous	**IC 50**: 5.76 µg/mL 7.09 µg/mL 9.88 µg/mL 10.24 µg/mL 11.37 µg/mL 50.15 µg/mL	N/A
		Gogoi et al (2021)[46]	*Plasmodium falciparum* (3D7)	In Vitro	Extract from leaf: 1. Petroleum ether 2. Chloroform 3. Etyl acetate 4. Methanol 5. Hydro alcoholic	**IC 50**: 14.24 µg/mL 11.61 µg/mL 5.22 µg/mL 3.28 µg/mL 3.41 µg/mL	N/A
			Plasmodium falciparum (RKL-9) strains	In Vitro	Extract from leaf: 1. Petroleum ether 2. Chloroform 3. Etyl acetate 4. Methanol 5. Hydro alcoholic	**IC 50**: 18.65 µg/mL 14.51 µg/mL 5.75 µg/mL 3.81 µg/mL 5.51 µg/mL	N/A
15	*Baccharis dracunculifolia D. C*	da Silva Filho et al (2009)[47]	*Plasmodium falciparum* D6 strain	In Vitro	Extract: 1. Hydroalcoholic green propolis extract 2. Dichloromethane extract isolated compound: 1. Ursolic acid 2. 2α-hydroxy-ursolic acid 3. Uvaol 4. Ermanin 5. Hautriwaic acid lactone 6. Clerodane diterpene 7. Viscidone	**IC 50**: 1. 25 µg/mL 2. 20 µg/mL **IC 50**: 1. 1 µg/mL 2. 3.2 µg/mL 3. 3.3 µg/mL 4. 2.6 µg/mL 5. 0.8 µg/mL 6. 3.0 µg/mL 7. 1.9 µg/mL	1. 2α-hydroxy-ursolic acid 2. uvaol 3. ermanin 4. Hautriwaic acid lactone 5. clerodane diterpene 6. viscidone
			Plasmodium falciparum W2 strain	In Vitro	Extract: 1. Hydroalcoholic green propolis extract 2. Dichloromethane extract isolated compound: 1. 2α-hydroxy-ursolic acid 2. Uvaol 3. Ermanin 4. Hautriwaic acid lactone 5. Clerodane diterpene 6. Viscidone	**IC 50**: 1. 13 µg/mL 2. 13 µg/mL **IC 50**: 1. 3.0 µg/mL 2. 1.9 µg/mL 3. 2.2 µg/mL 4. 2.2 µg/mL 5. 2.6 µg/mL 6. 2.3 µg/mL	

16	*Bidens pilosa L.*	Andrade-Neto et al (2004)[48]	*Plasmodium berghei* strain NK-65,	In Vivo	Ethanol extract from root	**% Inhibition**: 1000 mg/kg = 60%	Flavonoid
			Plasmodium falciparum clone W2	In Vitro	Ethanol extract from root	**IC 50**: 12.6 µg/mL	
			Plasmodium falciparum clone D6	In Vitro	Ethanol extract from root	**IC 50**: 10.4 µg/mL	
			Isolate BHz	In Vitro	Ethanol extract from root	**IC 50**: 17 µg/mL	
		Nadia et al (2020)[49]	*Plasmodium berghei* ANKA strain	In Vivo	1. Ethyl acetate extract 2. Fraction 12	**% Suppression**: 250 mg/kg = 79.20% 125 mg/kg = 100%	N/A
		Lacroix et al (2011)[50]	*Plasmodium falciparum* FcB1	In Vitro	Ethyl acetate extract	**IC 50**: 45.8 µg/mL	N/A
17	*Blumea aurita (L. f.) DC*	Nour et al (2009)[39]	P*lasmodium falciparum* K1 strain	In Vitro	Dichloromethane extract	**IC 50**: 2.8 µg/mL	N/A
18	*Blumea balsamifera*	Chaniad et al (2022)[19]	*Plasmodium falciparum* (K1) strain	In Vitro	Leaves & Stem-derived: 1. Ethanol extract 2. Aqueous extract	**IC 50**: 9.7 µg/mL (l); 35.5 µg/mL (s) 30 µg/mL (l); 206 µg/mL (s)	Oleamide, α-amyrin, β-eudesmol, 3,3a epoxydicyclopenta [a,d]cyclo octan-4.beta.-ol, and 9,10a-dimethyl-6-methylene-3.beta.-isopropyl-, sakuranin, quercetin, pilloin, 5,7-dihydroxy, 30,40,50-trimethoxyflavone, retusin and 7,30-dimethylquercetin
19	*Blumea lacera*	Singh et al (2014)[51]	*Anopheles stephensi* Liston	In Vivo	Petroleum extract from leaf	**% Repellency activity**: 2% doses: 84.6% 4% doses: 91.4% 6% doses: 97.0%	N/A
20	*Chromolaena odotarum*	Chaniad et al (2022)[19]	*Plasmodium falciparum* (K1) strain	In Vitro	Leaves & Stem-derived: 1. Ethanol extract 2. Aqueous extract	**IC 50**: 42.8 µg/mL (l); 112.3 µg/mL (s) 137.3 µg/mL (l); 488.9 µg/mL (s)	Flavonoid, Terpenoid, Alkaloid, Tanin, Saponin, Coumarin
21	*Chrysanthemum morifolium*	Chaniad et al (2022)[19]	*Plasmodium falciparum* (K1) strain	In Vitro	Flower, Leaves, Stem-derived: 1. Ethanol extract 2. Aqueous extract	**IC 50: µg/mL** 54.4 (f); 27.6 (l); 107.5 (s) 110.2 (f); 97.7 (l); 503.3 (s)	Flavonoid, Terpenoid, Alkaloid, Tanin, Saponin, Coumarin
22	*Conyza aegyptiaca (L.) Ait.*	Nour et al (2009)[39]	*Plasmodium falciparum* K1 strain	In Vitro	Dichloromethane extract	**IC 50**: 3.59 µg/mL	N/A
		Muganga et al (2010)[52]	*Plasmodium falciparum* 3D7	In Vitro	Extraction from leave: 1. Methanol extract 2. Dichloromethane extract	**IC 50**: 22.7 µg/mL 36.8 µg/mL	N/A
			Plasmodium falciparum W2	In Vitro	Methanol extract from leave	**IC 50**: 24.66 µg/mL	N/A

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Table 3 (Continued).

No.	*Asteraceae* Species	Authors (Year)	Target Species	Study Design	Sample Used	Result	Phytochemical Active
23	*Cosmos sulphureus*	Chaniad et al (2022)[19]	*Plasmodium falciparum* (K1) strain	In Vitro	Ethanol extract from flowers	**IC 50**: 41.2 µg/mL (flowers)	Flavonoid, Terpenoid, Alkaloid, Tanin, Saponin, Coumarin
			Plasmodium falciparum (K1) strain	In Vitro	Aqueous extract from flowers	**IC 50**: 515.3 µg/mL (flowers)	
24	*Crassocephalum vitellinum*	Lacroix et al (2011)[50]	*Plasmodium falciparum* FcB2	In Vitro	Ethyl acetate extract from leave	**IC 50**: 40.6 µg/mL	N/A
25	*Dicoma anomala subsp. gerrardii*	Becker et al (2011)[53]	*Plasmodium falciparum* D10 strain	In Vitro	Plant root isolated compound: 1. sesquiterpene lactone dehydrobrachylaenolide.	**IC 50**: 1. 0.455 µg/mL	Dehydrobrachylaenolide
			Plasmodium falciparum K1 strain	In Vitro	Plant root isolated compound: 1. sesquiterpene lactone dehydrobrachylaenolide.	**IC 50**: 1. 1 µg/mL	
26	*Dicoma tomentosa*	Jansen et al (2012)[54]	*Plasmodium falciparum* 3D7	In Vitro	Crude extract whole plant: 1. Petroleum ether 2. Hexane 3. Dichloromethane 4. Diethyl ether 5. Ethyl acetate 6. Methanol isolated compound: 1. urospermal A-15-O-acetate	**IC 50**: 1. 23.2 µg/mL 2. 18.7 µg/mL 3. 3.4 µg/mL 4. 3.9 µg/mL 5. 4.4 µg/mL 6. 5.8 µg/mL **IC 50**: 1. 0.92 µg/mL	Urospermal A-15-O-acetate
			Plasmodium falciparum W2	In Vitro	Crude extract whole plant: 1. Petroleum ether 2. Hexane 3. Dichloromethane 4. Diethyl ether 5. Ethyl acetate 6. Methanol isolated compound: 1. urospermal A-15-O-acetate	**IC 50**: 1. 21.2 µg/mL 2. 17.7 µg/mL 3. 1.9 µg/mL 4. 4.8 µg/mL 5. 4.6 µg/mL 6. 3.0 µg/mL **IC 50**: 1. 0.77 µg/mL	
27	*Distephanus angulifolius*	Pedersen et al (2009)[55]	*Plasmodium falciparum* D10 strain	In Vitro	Isolated compound sesquiterpene lactone: 1. Vernangulide A 2. Vernangulide B 3. Vernodalol 4. Vernodalin	**IC 50**: 1. 0.764 µg/mL 2. 0.626 µg/mL 3. 1.513 µg/mL 4. 0.635 µg/mL	- Vernangulide A [(6S,7R,8S)-14-acetoxy-8-[2-hydroxymethylacrylat]-15-helianga-1(10),4,11(13)-trien-15-al-6,12-olid] - Vernangulide B [(5R,6R,7R,8S,10S)-14-acetoxy-8-[2-hydroxymethylacrylat]-elema-1,3,11(13)-trien-15-al-6,12-olid] - vernodalol - vernodalin
			Plasmodium falciparum W2 strain		Isolated compound sesquiterpene lactone: 1. Vernangulide A 2. Vernangulide B 3. Vernodalol 4. Vernodalin	**IC 50**: 1. 1.302 µg/mL 2. 0.848 µg/mL 3. 1.956 µg/mL 4. 0.974 µg/mL	

28	*Echinops kebericho*	Toma et al (2015)[56]	*Plasmodium falciparum* ANKA strain	In Vivo	Methanol extract from root	**LD 50**: >5000 mg/kg **% Suppression**: 57.29%	N/A
		Biruksew et al (2018)[57]	*Plasmodium falciparum* ANKA strain	In Vivo	70% methanol rhizome extracts	**% Inhibition**: 250 mg/kg = 22% 500 mg/kg = 34% 1000 mg/kg = 49%	N/A
29	*Eclipta prostrata*	Rajakumar et al (2015)[58]	*Plasmodium falciparum* (Nk 65) strain	In Vivo	1. Aqueous leave extract 2. Palladium acetate 3. Synthesize palladium nanoparticle	**% Inhibition: (150 mg/kg)** 38.34% 58.32% 78.13%	N/A
30	*Francoeuria crispa (Forssk.) Cass.*	Nour et al (2009)[39]	*Plasmodium falciparum* K1 strain	In Vitro	Dichloromethane extract	**IC 50**: 4.66 µg/mL	N/A
31	*Galinsoga parviflora*	Govindarajan et al (2018)[59]	*Anopheles stephensi*	In Vivo	1. Essential oil from leave extract Isolated compound: 1. (Z)-γ-bisabolene compound	**LC 50**: 31.04 µg/mL (EO), 2.04 µg/mL **% Motrality**: 75 µg/mL~100% (EO), 5 µg/mL~100%	(Z)-γ-bisabolene
			Anopheles subpictus	In Vivo	1. Essential oil from leave extract Isolated compound: 1. (Z)-γ-bisabolene compound	**LC 50**: 45.55 µg/mL (EO), 4.50 µg/mL **% Motrality**: 100 µg/mL~97,3% (EO), 10 µg/mL~98%	(Z)-γ-bisabolene
32	*Gerbera jamesonii*	Chaniad et al (2022)[19]	*Plasmodium falciparum* (K1) strain	In Vitro	Flowers & Stem-derived: 1. Ethanol extract 2. Aqueous extract	**IC 50**: 112.4 µg/mL (f); 123.3 µg/mL (s) 207.8 µg/mL (f); 479.4 µg/mL (s)	Flavonoid, Terpenoid, Alkaloid, Tanin, Saponin
33	*Helichrysum declinatum (L. f.) Less*	Nour et al (2009)[39]	*Plasmodium falciparum* K1 strain	In Vitro	Dichloromethane extract	**IC 50**: 7.6 µg/mL	N/A
34	*Helichrysum gymnocephalum*	Ranaivoarisoa et al (2020)[60]	*Plasmodium falciparum* FCM29	In Vitro	1. Crude ethanol extract 2. Hexane extract 3. Dichloromethane extract 4. Aqueous fraction Isolated compound: 1. Pinocembrin 2. 3-O-Acetylpinobanksin 3. 5,7-Dihydroxyisoflavone	**IC 50**: 1. 39 µg/mL 2. 38.35 µg/mL 3. 8.81 µg/mL 4. 46.24 µg/mL **IC 50**: 1. 26.308 µg/mL 2. 4.905 µg/mL 3. 18.999 µg/mL	- Pinocembrin - 3-O-Acetylpinobanksin - 5,7-Dihydroxyisoflavone

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Table 3 (Continued).

No.	*Asteraceae* Species	Authors (Year)	Target Species	Study Design	Sample Used	Result	Phytochemical Active
35	*Kleinia odora*	Al Musayeib et al (2013)[61]	*Plasmodium falciparum* K1	In Vitro	1. Petroleum ether extract: 2. Chloroform extract Isolated compound: 1. Ursolic acid 2. Urs-12-ene-3β,16β-diol 3. 3β 11α-dihydroxy urs-12-ene 4. 3-Hydroxy-13,28-epoxyurs-11-en-28-one	**IC 50**: 1. 8.6 µg/mL 2. 8.2 µg/mL **IC 50**: 1. 13.068 µg/mL 2. 4.132 µg/mL 3. 10.182 µg/mL 4. >28.928 µg/mL	- Ursolic acid - Urs-12-ene-3β,16β-diol - 3β 11α-dihydroxy urs-12-ene - 3-Hydroxy-13,28-epoxyurs-11-en-28-one
36	*Launea taraxacifolia (wild)*	Nour et al (2009)[39]	*Plasmodium falciparum* K1 strain	In Vitro	Dichloromethane extract	**IC 50**: 16.39 µg/mL	N/A
37	*Leonotis nepetifolia*	Lacroix et al (2011)[50]	*Plasmodium falciparum* FcB3	In Vitro	Ethyl acetate extract from leave	**IC 50**: 27.0 µg/mL	N/A
38	*Microglossa pyrifolia*	Kohler et al (2002)[62]	*Plasmodium falciparum* PoW	In Vitro	Extract: 1. Ethyl ether extract isolated compound: 1. Linoleic acid (octadeca-9,12-dienoic acid) 2. E-Phytol 3. Benzyl 2,6-dimethoxybenzoate 4. 13-Hydroxy-octadeca-9Z,11E,15Z-trienoic acid 5. 6E-Geranylgeraniol-19-oic-acid	**IC 50**: 10.5 µg/mL **IC 50**: 1. 6.1 µg/mL 2. 2.5 µg/mL 3. 9.0 µg/mL 4. 6.7 µg/mL 5. 4.3 µg/mL	2. Linoleic acid (octadeca-9,12-dienoic acid) 3. E-Phytol 4. Benzyl 2,6-dimethoxybenzoate 5. 13-Hydroxy-octadeca-9Z,11E,15Z-trienoic acid 6. 6E-Geranylgeraniol-19-oic-acid
			Plasmodium falciparum Dd2	In Vitro	Extract: 1. Ethyl ether extract isolated compound: 1. Linoleic acid (octadeca-9,12-dienoic acid) 2. E-Phytol 3. Benzyl 2,6-dimethoxybenzoate 4. 13-Hydroxy-octadeca-9Z,11E,15Z-trienoic acid 5. 6E-Geranylgeraniol-19-oic-acid	**IC 50**: 1. 13.1 µg/mL 2. 8.7 µg/mL 3. 3.4 µg/mL 4. >25 µg/mL 5. 13.7 µg/mL 6. 5.2 µg/mL	
		Muganga et al (2010)[52]	*Plasmodium falciparum* 3D7	In Vitro	Extraction from leave: 1. Methanol extract 2. Dichloromethane extract	**IC 50**: 4.2 µg/mL 1.5 µg/mL	N/A
			Plasmodium falciparum W2	In Vitro	Dichloromethane extract from leave	**IC 50**: 2.4 µg/mL	N/A
39	*Pechuel-loeschea leubnitziae*	Kadhila et al (2020)[63]	*Plasmodium falciparum* strain (3D7)	In Vitro	Extract: 1. Dichloromethane extract Isolated compound 1. xerantholide	**IC 50**: 1. 7.24 µg/m **IC 50**: 1. 2.42 µg/mL or 2.29 µg/mL	- Npk1 F70-77 - Npk1 F78-90
40	*Pentacalia desiderabilis (Vell.) Cuatrec*	Morais et al (2012)[64]	Plasmodium falciparum K1 strain	In Vitro	Plant leaf isolated compound: 1. Jacaronone	**IC 50**: 1. 7.82 µg/mL	Jacarone

41	*Pluchea dioscoridis (L.) DC*	Nour et al (2009)[39]	*Plasmodium falciparum* K1 strain	In Vitro	Dichloromethane extract	**IC 50**: 31.59 µg/mL	N/A
42	*Praxelis clematidea*	Chaniad et al (2022)[19]	*Plasmodium falciparum* (K1) strain	In Vitro	Leaves & Stem- derived: 1. Ethanol extract 2. Aqueous extract	**IC 50**: 173.8 µg/mL (l); 12.8 µg/mL (s) 417.3 µg/mL (l); 308.3 µg/mL (s)	Flavonoid, Terpenoid, Alkaloid, Tanin, Saponin
43	*Psiadia amygdalina*	Ledoux et al (2018)[65]	*Plasmodium falciparum* 3D7 strain	In Vitro	Leaves & bark-derived: 1. Ethyl acetate	**IC 50**: >50 µg/mL (leaves) 16.61 µg/mL (bark)	N/A
44	*Psiadia bovini*	Ledoux et al (2018)[65]	*Plasmodium falciparum* 3D7 strain	In Vitro	Leaves & bark-derived: 1. Ethyl acetate	**IC 50**: 23.69 µg/mL (leaves) >50 µg/mL (bark)	N/A
45	*Psiadia dentata*	Ledoux et al (2018)[65]	*Plasmodium falciparum* 3D7 strain	In Vitro	Leaves & bark-derived: 1. Ethyl acetate	**IC 50**: 22.99 µg/mL (leaves) >50 µg/mL (bark)	N/A
46	*Psiadia retusa*	Ledoux et al (2018)[65]	*Plasmodium falciparum* 3D7 strain	In Vitro	Leaves & bark-derived: 1. Ethyl acetate	**IC 50**: 12.09 µg/mL (leaves) >50 µg/mL (bark)	N/A
47	*Pulicaria undulata (L.) C. A. Mey*	Nour et al (2009)[39]	*Plasmodium falciparum* K1 strain	In Vitro	Dichloromethane extract	**IC 50**: 3.87 µg/mL	N/A
48	*Sinicio smithioides*	Mollinedo et al (2016)[66]	*Plasmodium falciparum*	In Vitro	Extract from plant: 1. Petroleum ether extract 2. Dichloromethane extract 3. Ethyl acetate 4. Hydroethanolic Isolated compound 1. 9-oxoeuryopsin	**IC 50**: 1. < 1.0 µg/mL 2. > 2.0 µg/mL 3. > 2.0 µg/mL 4. > 2.0 µg/mL **IC 50**: 1. 1.2 µg/mL	9-oxoeuryopsin
49	*Solanecio mannii*	Muganga et al (2010)[52]	*Plasmodium falciparum* 3D7	In Vitro	Extraction from leave: 1. Methanol extract 2. Dichloromethane extract	**IC 50**: 21.6 µg/mL 18.2 µg/mL	N/A
			Plasmodium falciparum W2	In Vitro	Extraction from leave: 1. Methanol extract 2. Dichloromethane extract	**IC 50**: 26.2 µg/mL 12.7 µg/mL	N/A

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Table 3 (Continued).

No.	*Asteraceae* Species	Authors (Year)	Target Species	Study Design	Sample Used	Result	Phytochemical Active
50	*Sphaeranthus indicus*	Sangsopha et al (2016)[67]	*Plasmodium falciparum* K1 strain	In Vitro	Sesquiterpene isolated compound: 1. Indicusalactone 2. (-)-oxyfrullanolide 3. (-)-frullanolide 4. 7-hydroxyfrullanolide 5. Squalene 6. 3,5-di-O-caffeoylquinic acid methyl ester 7. 3,4-di-O-caffeoylquinic acid methyl ester	**IC 50**: 1. 2.87 µg/mL 2. 3.82 µg/mL 3. 6.47 µg/mL 4. 2.49 µg/mL 5. 2.32 µg/mL 6. 2.39 µg/mL 7. 2.90 µg/mL	- indicusalactone - (-)-enantiomer - (-)-frullanolide - 7-hydroxyfrullanolide (- squalene - 3,5-di-O-caffeoylquinic acid methyl ester - 3,4-di-O-caffeoylquinic acid methyl ester
51	*Symphyopappus casarettoi*	Zani et al (2020)[68]	*Plasmodium falciparum* W2 strain	In Vitro	1. Ethanol extract 2. Fr-A 3. Fr-B 4. BP-181-6 Isolated compound: 1. Caryatin BP204	**IC 50**: 1. 4.8 µg/mL 2. 2.5 µg/mL 3. 26 µg/mL 4. 7.2 µg/mL **IC 50**: 1. 2.5 µg/mL	N/A
52	*Synedrella nodiflora*	Chaniad et al (2022)[19]	*Plasmodium falciparum* (K1) strain	In Vitro	Leaves & Stem- derived: 1. Ethanol extract 2. Aqueous extract	**IC 50**: 37.8 µg/mL (l); 142.2 µg/mL (s) 153.9 µg/mL (l); 539.9 µg/mL (s)	N/A
		Chaniad et al (2021)[69]	*Plasmodium berghei* var. Anka I strain	In Vivo	Ethanol extract from leaves	% **Suppression**: 200 mg/kg = 38.57% 400 mg/kg = 57.67% 600 mg/kg = 62.65%	N/A

53	*Tagetes erecta*	Chaniad et al (2022)[19]	*Plasmodium falciparum* (K1) strain	In Vitro	Flowers, Leaves, Stem- derived: 1. Ethanol extract 2. Aqueous extract	**IC 50: µg/mL** 32.8 (f); 70.6 (l); 86.6 (s) 35.6 (f); 229.5 (l); 450.9 (s)	Flavonoid, Terpenoid, Alkaloid, Tanin, Saponin, Coumarin
		Chaniad et al (2021)[69]	*Plasmodium berghei* var. Anka I strain	In Vivo	Aqueous extract from flower	**% Suppression**: 200 mg/kg = 26.33% 400 mg/kg = 50.82% 600 mg/kg = 65.65%	N/A
		Gupta et al (2010)[70]	*Plasmodium falciparum* strain (MRC-pf-2)	In Vitro	Plant extract from root: 1. Petroleum ether 2. Chloroform 3. Ethyl acetate 4. Methanol 5. Aqueous Isolated compound: 1. 2-hydroxymethyl-non-3-ynoic acid 2-[2,2']-bithiophenyl-5-ethyl ester	**IC 50**: 1. 0.22 µg/mL 2. 0.05 µg/mL 3. 0.02 µg/mL 4. 0.09 µg/mL 5. 0.31 µg/mL **IC 50**: 1. 0.01 µg/mL	N/A
			Plasmodium falciparum strain (MRC-pf-56)	In Vitro	Plant extract from root: 1. Petroleum ether 2. Chloroform 3. Ethyl acetate 4. Methanol 5. Aqueous Isolated compound: 1. 2-hydroxymethyl-non-3-ynoic acid 2-[2,2']-bithiophenyl-5-ethyl ester	**IC 50**: 1. 0.37 µg/mL 2. 0.09 µg/mL 3. 0.07 µg/mL 4. 0.15 µg/mL 5. 0.49 µg/mL **IC 50**: 1. 0.02 µg/mL	
54	*Tithonia diversifolia*	Elufioye et al (2004)[71]	*Plasmodium berghei* var. Anka I strain	In Vivo	Ethanol extract from aerial part	**% Suppression**: 200 mg/kg = 54%	N/A
		Nour et al (2009)[39]	*Plasmodium falciparum* K1 strain	In Vitro	Dichloromethane extract	**IC 50**: 6.1 µg/mL	N/A
		Ajayi et al (2020)[72]	*Plasmodium berghei* ANKA strain	In Vivo	Aqueous extract from leaves	**% Suppression**: 200 mg/kg = 64.3% 400 mg/kg = 65.78%	N/A
55	*Tridax procumbens*	Chaniad et al (2022)[19]	*Plasmodium falciparum* (K1) strain	In Vitro	Leaves & Stem- derived: 1. Ethanol extract 2. Aqueous extract	**IC 50**: 57.9 µg/mL (l); 52.6 µg/mL (s) 461.6 µg/mL (l); 775.4 µg/mL (s)	Flavonoid, Terpenoid, Alkaloid, Tanin, Saponin
		Nour et al (2009)[39]	*Plasmodium falciparum* (K1) strain	In Vitro	Dichloromethane extract	**IC 50**: 4.13 µg/mL	N/A
56	*Tagetes minuta*	Lacroix et al (2011)[50]	*Plasmodium falciparum* FcB4	In Vitro	Ethyl acetate extract from leave	**IC 50**: 61.0 µg/mL	N/A

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https://doi.org/10.2147/IDR.S433328 DovePress

Table 3 (Continued).

No.	*Asteraceae* Species	Authors (Year)	Target Species	Study Design	Sample Used	Result	Phytochemical Active
57	*Vernonia amygdalina Del.*	Quartey et al (2020)[73]	*Plasmodium berghei* NK 65	In Vivo	Hydroethanolic stem bark extract	**% Suppression**: 100 mg/kg = 20.30% 200 mg/kg = 38.34% 400 mg/kg = 54.11% 600 mg/kg = 81.80%	Tannins, glycoside, saponin, alkaloid, flavonoid, terpenoids
		Ajayi et al (2020)[72]	*Plasmodium berghei* ANKA strain	In Vivo	Aqueous extract from leaves	**% Suppression**: 200 mg/kg = 63.92% 400 mg/kg = 75.13%	
		Lacroix et al (2011)[50]	*Plasmodium falciparum* FcB5	In Vitro	Ethyl acetate extract from leave	**IC 50**: 97.8 µg/mL	N/A
		Obbo et al (2019)[74]	*Plasmodium falciparum* K1 strain	In Vitro	Extract from leave: 1. Petroleum ether 2. Methanol	**IC 50**: >30 µg/mL >30 µg/mL	N/A
58	*Vernonia cinerea*	Chaniad et al (2022)[19]	*Plasmodium falciparum* (K1) strain	In Vitro	Ethanol extract from leaves & stem	**IC 50**: 30.4 µg/mL (leaves) 143.4 µg/mL (stem)	Flavonoid, Terpenoid, Alkaloid, Tanin, Saponin
					Aqueous extract from leaves & stem	**IC 50**: 63.0 µg/mL (leaves) 917.1 µg/mL (stem)	
		Soma et al (2017)[75]	*Plasmodium falciparum* (K1) strain	In Vitro	Whole plant extract: 1. Dichloromethane 2. Methanol 3. Water methanol 4. Alkaloid extracts	**IC 50**: 1. 5.85 µg/mL 2. 21.08 µg/mL 3. 41.56 µg/mL 4. 2.56 µg/mL	Alkaloid, triterpens
			Plasmodium falciparum (3D7) strain	In Vitro	Whole plant extract: 1. Dichloromethane 2. Methanol 3. Water methanol 4. Alkaloid extracts	**IC 50**: 1. 8.42 µg/mL 2. 26.43 µg/mL 3. >50 µg/mL 4. 4.35 µg/mL	
		Sourabie et al (2018)[76]	*Plasmodium berghei* ANKA strain	In Vivo	Extract from plant: 1. crude 80% methanolic extract 2. hydromethanolic extract 3. Aqueous extract	**% Suppression**: 500 mg/kg = 43.1% 500 mg/kg = 40.6% 500 mg/kg = 3.2%	Alkaloids, triterpenes and sterols, anthracenosids, tannins, saponins

59	*Vernonia guineensis Benth.*	Toyang et al (2013)[77]	*Plasmodium falciparum* Dd2	In Vitro	1. Crude extract from leaf and root: 1. Dichloromethane 2.Methanol 3. Aqueous 2. Isolated compound: 1.Vernopicrin 2. Vernomelitensin 3. Sucrose ester	**IC 50**: 1. 1.8 µg/mL (leaf) and 3.1 µg/mL (root) 2. 3.9 µg/mL (leaf) and 29.9 µg/mL (root) 3.11.3 µg/mL (leaf) and 26.1 µg/mL (root) **IC 50**: 1. 0.8 µg/mL 2. 0.5 µg/mL 3.1.4 µg/mL	Sesquiterpene lactones: - Vernopicrin - Vernomelitensin - Sucrose ester
			Plasmodium falciparum Hb3	In Vitro	1. Crude extract from leaf and root: 1. Dichloromethane 2.Methanol 3. Aqueous 2. Isolated compound: 1.Vernopicrin 2. Vernomelitensin 3. Sucrose ester	**IC 50**: 1. 1.6 µg/mL (leaf) and 3.2 µg/mL (root) 2. 2.0 µg/mL (leaf) and 27.0 µg/mL (root) 3. 9.5 µg/mL (leaf) and 27.2 µg/mL (root) **IC 50**: 1. 0.6 µg/mL 2. 0.4 µg/mL 3.1.6 µg/mL	
60	*Vernonia fimbrillifera Less.*	Bordignon et al (2018)[78]	*Plasmodium falciparum* (3D7) strain	In Vitro	Isolated compound from Dichloromethane fraction: 1. s 8-(4'-hydroxymethacrylate)-dehydromelitensin 2. onopordopicrin 3. 8α-[4'-hydroxymethacryloyloxy]-4-epi-sonchucarpolide	**IC 50**: 1. 2.96 µg/mL 2. 3.37 µg/mL 3. 3.27 µg/mL	Sesquiterpene lactones 1. s 8-(4'-hydroxymethacrylate)-dehydromelitensin 2. onopordopicrin 3. 8α-[4'-hydroxymethacryloyloxy]-4-epi-sonchucarpolide
		Ledoux et al (2018)[65]	*Plasmodium falciparum* 3D7 strain	In Vitro	Leaves & bark-derived: 1. Ethyl acetate	**IC 50**: 5.9 µg/mL (leaves) >50 µg/mL (bark)	N/A
61	*Vernonia colorata*	Kraft et al (2003)[42]	*Plasmodium falciparum* PoW	In Vitro	1. lipophilic extract (petrol ether/ethyl acetate) from aerial part 2. Isolated compound: 1. vernodalol 2.11β,13-dihydrovernodalin 3. 11β,13-dihydrovernolide	**IC 50**: 12.1 µg/mL **IC 50**: 1. 4.0 µg/mL 2. 2.3 µg/mL 3. >50 µg/mL	- vernodalol - 11β,13-dihydrovernodalin
			Plasmodium falciparum Dd2	In Vitro	1. lipophilic extract (petrol ether/ethyl acetate) from aerial part 2. Isolated compound: 1. vernodalol 2.11β,13-dihydrovernodalin 3. 11β,13-dihydrovernolide	**IC 50**: 17.8 µg/mL **IC 50**: 1. 4.8 µg/mL 2. 1.1 µg/mL 3. 37.3 µg/mL	

(*Continued*)

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Table 3 (Continued).

No.	*Asteraceae* Species	Authors (Year)	Target Species	Study Design	Sample Used	Result	Phytochemical Active
62	*Xanthium brasilicum Vell*	Nour et al (2009)[39]	*Plasmodium falciparum* K1 strain	In Vitro	Extract from plant: 1. Hexane extract 2. Dichloromethane extract 3. Ethyl acetate extract isolated compound: 1. 8-Epixanthatin 2. 8-Epixanthatin 1β,5β-epoxide 3. Xanthipungolide 4. Pungiolide A 5. Pungiolide B	**IC 50**: 4.33 µg/mL 2.41 µg/mL 4.78 µg/mL 1. 1.93 µg/mL 2. 1.71 µg/mL 3. >20 µg/mL 4. 2.52 µg/mL 5. 3.42 µg/mL	Isolated compound: - 8-Epixanthatin - 8-Epixanthatin 1β,5β-epoxide - Pungiolide A - Pungiolide B
63	*Zinnia violacea*	Chaniad et al (2022)[19]	*Plasmodium falciparum* (K1) strain	In Vitro	Flowers, Leaves, Stem, Pollen-derived: 1. Ethanol extract 2. Aqueous extract	**IC 50: µg/mL** 112.5 (f); 22.4(l); 111.3(s); 87.8(p) 428.7(f); 197(l); 823.7 (s); 202.8(p)	Flavonoid, Terpenoid, Alkaloid, Tanin, Saponin, Coumarin

Table 4 Result for Antiplasmodial and Insecticidal from *Ageratum conyzoides*

No.	Authors (Year)	Target Species	Study Design	Sample Used	Result	Phytochemical Active	Additional Information
1	Ukwe et al (2010)[22]	*Plasmodium berghei* (NK65 strain)	In Vivo	Leaves-derived: 1. Aqueous extract 2. n-Hexane fraction 3. Chloroform fraction 4. Methanol fraction	**LD 50: >**5000 mg/kg **%Inhibition**: 100 mg/kg = 70.46% 100 mg/kg = 52.17% 400 mg/kg = 52.61% 200 mg/kg = 56.52%	Flavonoid, Alkaloid	N/A
2	Owuor et al (2012)[35]	*Plasmodium falciparum* (D6) strain	In Vitro	Dichloromethane extract from whole plant	**IC 50**: 2.1 µg/mL	N/A	N/A
		Plasmodium falciparum (W2) strain	In Vitro	Dichloromethane extract from whole plant	**IC 50**: 3.4 µg/mL	N/A	N/A
3	Ifijen et al (2019)[79]	*Plasmodium berghei* strain ANKA (PbANKA)	In Vivo	Methanol extract from leaves	**LD 50**: >1000 mg/kg **%Inhibition**: 100 mg/kg = 61%	Terpenoids, Flavonoids, Alkaloids, Steroids and Chromene.	The extract shows no toxicity
4	Abdullah et al (2011)[80]	*Plasmodium falciparum* strain FCB	In Vitro	Plant-derived: 1. Dichloromethane extract 2. Methanol extract	**IC 50**: 9.95 g/mL 25.48 g/mL	N/A	N/A
5	Ukwe et al (2010)[22]	*Plasmodium berghei* (NK65 Strain)	In Vivo	Aqueous extract from leaves	**%Suppression**: 100 mg/kg = 98.80%	N/A	The first research is a combination with conventional malaria drugs, but toxicity tests and the mechanism of the compounds need to be carried out to see their efficacy and safety
6	Muema et al (2016)[81]	*Anopheles gambiae s.s* larvae instar III	In Vivo	Methanol extract from leaves	**LC 50**: 232 ppm **%Mortality**: 250 ppm = 64%	Alkaloids, Aglycone Flavonoids, Triterpenoids, Tannins and Coumarins	The mechanism of the extract on larval development is described
		Anopheles arabiensis larvae instar III	In Vivo	Methanol extract from leaves	**LC 50**: 406 ppm **%Mortality**: 500 ppm = 60%		

(*Continued*)

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Table 4 (Continued).

No.	Authors (Year)	Target Species	Study Design	Sample Used	Result	Phytochemical Active	Additional Information
7	Chaniad et al (2022)[19]	*Plasmodium falciparum* (K1) strain	In Vitro	Leaves & stem-derived: 1. Aqueous extract 2. Ethanol extract	**IC 50**: 78.4 µg/mL (L); 196.7 µg/mL (S) 31.4 µg/mL (L); 99.7 µg/mL (S)	Flavonoid, Terpenoid, Alkaloid	N/A
8	do Ce´u de Madureira et al (2002)[82]	*Plasmodium falciparum* (3D7) strain & *Plasmodium falciparum* (Dd2) strain	In Vitro	Aerial part-derived: 1. Ethanol extract 2. Petroleum fraction 3. Dichloromethane fraction 4. Ethyl acetate fraction	**IC 50**: 150 µg/mL 110 µg/mL 55 µg/mL 220 µg/mL	N/A	The first extraction experiment of *Ageratum* for its antiplasmodial properties
		Plasmodium berghei ANKA strain (PbANKA)	In Vivo	Ethanol extract	**IC 50**: 130 µg/mL		
9	Joshi et al (2016)[83]	*Plasmodium falciparum* (K1 strain)	In Vitro	Ethanol extract from whole plant	**IC 50**: 72.4 µg/mL	Chromenes, benzofurans, flavonoids, farnesene, derivatives daucanolides, triterpenoids, sterols	N/A
10	Jonville et al (2011)[84]	*Plasmodium falciparum* (3D7) strain	In Vitro	Aerial part-derived: 1. Methanol extract 2. Dichloromethane extract	**IC 50**: >50 µg/mL >50 µg/mL	N/A	N/A
11	Arya et al (2011)[85]	*Anopheles stephensi* larvae instar II	In Vivo	Crude extract from plant	**%Mortality**: 300 ppm = 62% **LC 50**: 238 ppm	N/A	N/A
		Anopheles stephensi larvae instar IV	In Vivo	Crude extract from plant	**%Mortality**: 300 ppm = 65% **LC 50**: 228,5 ppm		

12	Adelaja et al (2022)[25]	*Anopheles gambiae s.s.* Kisumu Susceptible Strain (KSS)	In Vivo	Extract plant oil from leaves	**%Mortality**: 0.1 mg/mL = 77% 0.3 mg/mL = 100%	D-limonene terpene	The active compound has been isolated and has a very good effect
13	Nour et al (2010)[24]	*Plasmodium falciparum* (K1) strain	In vitro	Aerial parts-derived: 1. n-Hexane extract 2. Dichloromethane extract 3. Ethyl acetate extract Isolated compound: 1. 5,6,7,8,5-pentamethoxy-3,4-methylenedioxyflavone (eupalestine) 2. 5,6,7,5-tetramethoxy3,4-methylenedioxyflavone 3. - 5,6,7,8,3',4',5'-heptamethoxyflavone (5'-methoxynobiletine,) 4. 5,6,7,3,4,5-hexamethoxyflavone 5. 4-hydroxy-5,6,7,3,5-pentamethoxyflavone (ageconyflavone C) 6. encecalol methyl ether	**IC 50**: 1. 7.1 µg/mL 2. 7.9 µg/mL 3. 15.6 µg/mL **IC 50**: 1. 4.57 µg/mL 2. 4.26 µg/mL 3. >5 µg/mL 4. 2.99 µg/mL 5. 3.59 µg/mL 6. >5 µg/mL	– 5,6,7,8,5-pentamethoxy-3,4-methylenedioxyflavone (eupalestine) - 5,6,7,5-tetramethoxy3,4-methylenedioxyflavone - 5,6,7,8,3',4',5'-heptamethoxyflavone (5'-methoxynobiletine,) - 5,6,7,3,4,5-hexamethoxyflavone - 4-hydroxy-5,6,7,3,5-pentamethoxyflavone (ageconyflavone C) - encecalol methyl ether	The active compound has been isolated and has a very good effect
14	Nour et al (2009)[39]	*Plasmodium falciparum* (K1) strain	In vitro	Dichloromethane extract from plant	**IC 50**: 7.95 µg/mL	N/A	N/A
15	Ramasamy et al (2021)[86]	*Anopheles stephensi* larvae 4th instar	In vitro	Petroleum ether extract from leave	**LC50**: 108 ppm **% Mortality**: 200 ppm = 93%	N/A	N/A

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Insecticidal Activity from *Asteraceae* Family

Table 3 shows that the *Asteraceae* family; not only shows its activity against *Plasmodium*, but also has the potential insecticidal activity against malaria vector, *Anopheles*. Although there are only a few studies mention its activity, in this review the majority of the results that have been tested on *Anopheles* produce good results.

Six studies discussed insecticidal activity, and the extract or active compound showed promising results. The methanol extract and essential oil from the *Achillea wilhelmsii* plant resulted in 100% mortality for *Anopheles stephensi* from both extractions. However, with different doses of 320 ppm and 160 ppm, with LC50 values of 115.73 ppm and 39.04 ppm respectively, indicating that the essential oil from this plant is more potent against *Anopheles*, as seen from the results, the essential oil has 3 times the activity of methanol extract.[34]

More advanced research has shown that the active compound from the *Galinsoga parviflora* plant tested by in vivo method against *A. stephensi* and *Anopheles subpictus* vectors showed excellent LC50 values of 2.04 µg/mL and 4.05 µg/mL for the active compound in the form of *(Z)-γ- bisabolene*, indicating that this compound is even more active than the essential oils tested on this plant, which only showed LC50 values of 31.04 µg/mL and 45.55 µg/mL respectively.[59] This compound also has better larvicidal activity compared to essential oils from plants from other areas where malaria is prevalent: *Juniperus virginiana* with LC50 10.75–9.06 µg/mL (*Anopheles gambiae), Pelargonium roseum* with LC50 13.63–8.98 µg/mL (*A. gambiae*)[88] and *Lantana camara* with LC50 7.73 µg/mL (*A. gambiae* Susceptible strain (Kisumu)) and 25.63 µg/mL (*A. gambiae* Field strain (VK7)).[89] *(Z)-γ-Bisabolene* is a monocyclic sesquiterpene hydrocarbon belonging to the bisabolene type, which is found in several evoluted plant families such as *Lamiaceae* that have good results against *Anopheles*.[90] However, research on this compound needs to be reviewed considering there has been no further research about its toxicity test.

In addition to testing the larvae and eggs of the *Anopheles* vector, studies on *Ageratum houstonianum* and *Blumea lacera* have also tested the effectiveness of the adult vector as a repellent. The study used n-hexane and petroleum extracts from leaves, and the results showed that these two plants were good repellents with results of 93.4%[38] and 97%,[3] respectively, as shown in Table 3. In the *A. houstonianum* experiment, the plant extract was mixed with coconut oil, which is also believed to ward off several species of mosquitoes, resulting in good efficacy as well, but in *B. lacera* extract it was tried without any mixture but produced low efficacy (1 hour).[3,38] Most of the plant-based repellents are shown to repel mosquitoes, but their effect lasts from few minutes to some hours since their active ingredients tend to be highly volatile, so although they are effective repellents for a short period after application, they rapidly evaporate, leaving the user unprotected.[90] Therefore, in the future research coconut oil or compounds can be used as a mixture to inhibit evaporation.

A. conyzoides, a Medicinal Plant with Potential Antimalarial Activity

A. conyzoides is a plant belonging to the *Asteraceae* family with a height that can reach 100 cm and is characterized by the growth of flowers at the ends of the stems. This plant is also known as billy goat weed.[91] Comes in tropical America, Southeast Asia, South China, India, and West Africa.[26] The stems and leaves are covered with fine white hairs, and the leaves are conical in shape and reach 7.5 cm in length, the flowers are sometimes found purplish-blue or white. *A. conyzoides* can sometimes be found in yards, rice fields, and mountains, and can thrive anywhere.[92] This plant has been traditionally used to treat many diseases, such as skin diseases, inflammation, diarrhea, and malaria.[93]

In this study, the 15 articles listed in Table 4 discuss the efficacy tests of these plants both in vitro and in vivo. Eleven of these studies tested the effect of this plant on *Plasmodium*, and the remaining four discussed the effect of this plant on the *Anopheles* malaria vector. There were 4 out of 5 studies testing dichloromethane extract on *Plasmodium* which produced good and moderate results.[30] It was stated that the values obtained from the in vitro test results of the three studies were 2.1, 3.4, 9.95, and 7.9 µg/mL which were tested on *Plasmodium* parasite types D6, W2, FCB, and K1. In addition to the dichloromethane extract, research from Nour et al[24] also suggested active compounds from the flavonoid group that produced positive activity as antiplasmodials, which were tested against *Plasmodium* K1 with results of 4.57, 4.26, 2.99 and 3.59 µg/ mL. In addition, research from Ukwe et al[22] tested the aqueous extract from the leaves of this plant combined with malaria drugs, such as artesunate and chloroquine, to produce excellent values with a suppression

percentage reaching 100% at a dose of 100 mg/kg on *P. berghei*. The results of this study are remarkably similar to those of previous studies on various antimalarial herb-drug interactions, which showed the potential effect of herbs on the antimalarial action of some common medications.[94] Besides that, methanol extract and n-hexane were also reported to have a good effect on *Plasmodium* from in vivo test results. However, the dichloromethane extraction that is mostly carried out on both *A. conyzoides* and their families (*Asteraceae*) requires further research regarding its efficacy in test animals, considering that this extract produces many good scores in tests on *A. conyzoide*s and their families.

The insecticidal potency of *A. conyzoides* was reported to be derived from the petroleum extract of its leaves, which resulted in a 93% mortality rate of *A. stephensi* larvae. This extract was reported to have a moderate antiplasmodial effect in the *Asteraceae* family, as shown in Table 3. However, testing its vector has also been reported to be successful as a repellent from the *B. lacera* plant, as described previously. Further research by Adelaja et al[25] showed that the isolation of the active compound from the terpenoid group in an oil extract dose of 0.3 mg/mL resulted in 100% mortality against *A. gambiae*.[25] These results could rival the positive control of deltamethrin which is a common spray insecticide used for malaria vectors.

In the research included in this review, extracts were taken from plants, both from the *Asteraceae* family and *A. conyzoides* itself; the majority came from dichloromethane extracts, although there were several studies that stated that the results were not as good, all of these could not be separated from the part of the plant used for extraction and from the tested *Plasmodium* species.

The antimalarial activity of *A. conyzoides* and its family (*Asteraceae*) is closely related to the presence of secondary metabolites, as seen in the majority of studies in Tables 3 and 4, showing that the phytochemicals that play a role include flavonoids and terpenoids. The mechanism of action of flavonoids as antimalarials is by inhibiting fatty acid biosynthesis, inhibiting the entry of L-glutamine, and targeting important functional biomolecules such as enzymes and DNA in plasmodium.[95] Whereas the terpenoid group with the sesquiterpene lactone type inhibits the process of sporogonic development in gametogenesis and/or macrogamete fertilization. Another mechanism of the terpenoid group is the inhibition of protein synthesis in cells, which inhibits parasite growth.[96]

Antimalaria an Insecticidal Natural Compounds Isolated from *Asteraceae*

In vitro antimalarial activities of the compounds were classified into four categories: high (IC50 < 5 µg/mL), promising (5 < IC50 < 15 µg/mL), moderate (15 < IC50 < 50 µg/mL), and inactive (IC50 > 50 µg/mL).[97] Based on the summary in Tables 3 and 4, the natural compounds from *Asteraceae* (including *A. conyzoides*) were classified based on their IC50 values. Among 84 compounds, there were 50 compounds with high antimalarial activity (Figure 2) (59.52%), 26 with promising antimalarial activity (Figure 3) (30.95%), 15 with moderate antimalarial activity (Figure 4) (17.86%), and only two with inactive antimalarial activity (Figure 5) (2.38%). Therefore, plants from the *Asteraceae* family are excellent reservoirs for antimalarial drugs of natural origin. Among the compounds with high antimalarial activity, 2-hydroxy-methyl-non-3-ynoic acid 2-[2,2']-bithiophenyl-5-ethyl ester exhibited the best antimalarial activity with an IC50 0.01–0.02 µg/mL (10–20 ng/mL). This compound has better antimalarial activity than the established antimalarial drug, chloroquine (IC50 232.65 ng/mL[98]), and has comparable IC50 with artemisinin (with ic50 1.5–7.5 ng/mL[99]). Resistance to chloroquine and artemisinin is the main obstacle to global malaria elimination/eradication programs.[100] The discovery of natural antimalarial drugs provides new hope for combating the emergence of antimalarial drug resistance worldwide. Furthermore, the structures of these natural compounds listed in Figures 2–5 could also be used as reference backbones for novel antimalarial drug synthesis, docking studies of various enzymes to reveal the mechanism of action of each compound, or to estimate ADMET (adsorption, distribution, metabolism, excretion, and toxicity) parameters before in vivo testing.

The larvicidal activity of a compound against the *Anopheles* mosquito is classified into six categories: extremely active (LC50<1 µg/mL), highly active (1 µg/mL <LC50 <5 µg/mL), active (5 µg/mL<LC50 <50 µg/mL), moderately active (50 µg/mL <LC50 <100 µg/mL), slightly active (100 µg/mL <LC50 <200 µg/mL), and inactive (LC50 >200 µg/mL).[101] Among natural compounds isolated from *Asteraceae* family, (Z)-γ-bisabolene from the essential oil of *G. parviflora* (Figure 6) exerts high larvicidal activity with LC50 values of 2.04 µg/mL and 4.05 µg/mL against *A. stephensi* and *A. subpictus* vectors.[59] This compound might be a novel insecticide of natural origin with low toxicity because

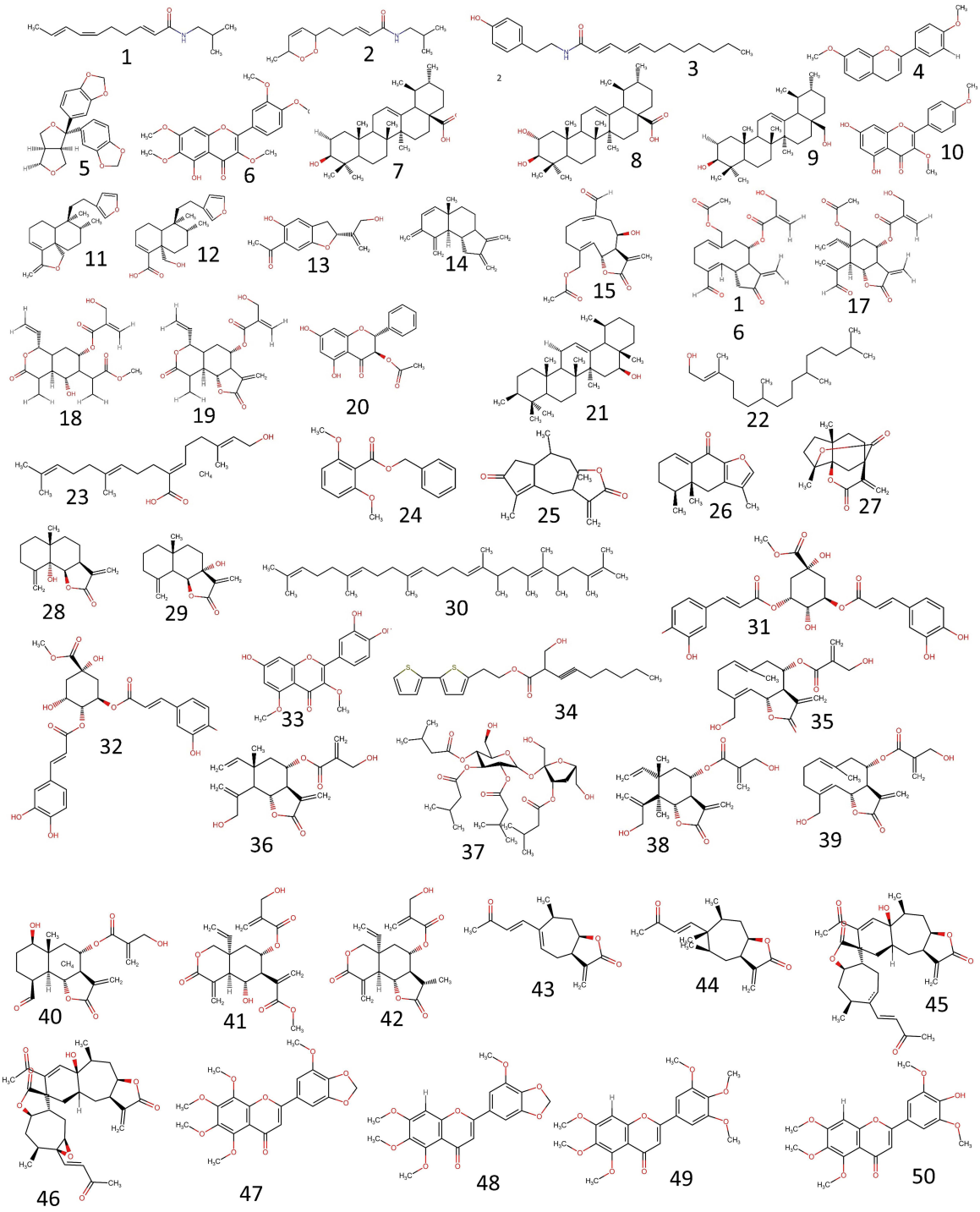

Figure 2 Natural Compounds Isolated from Asteraceae with High Antimalaria Activity. 1: isobutylamide spilanthol ((2E,6E,8E) -N-isobutyl-2,6,8-decatrienamide, 2: (2E,7Z)-6,9-endoperoxy- N-isobutyl-2,7-decadienamide,[36] 3: dodeca-2E,4E-dien acid 4-hydroxy-2-phenylethylamide,[40] 4: 7-Metoxyacacetin,[42] 5: Sesamin, 6: Artemetin,[44] 7: Ursolic acid, 8, 2α-hydroxy-ursolic acid, 9: Uvaol, 10: Ermanin, 11: Hautriwaic acid lactone, 12: Clerodane diterpene, 13: Viscidone,[47] 14: sesquiterpene lactone dehydrobrachylaenolide,[53] 15: urospermal A-15-O-acetate,[54] 16: Vernangulide A, 17: Vernangulide B, 18: Vernodalol, 19: Vernodalin,[55] 20: 3-O-Acetylpinobanksin,[60] 21: Urs-12-ene-3β,16β-diol,[61] 22: E-Phytol, 23: 6E-Geranylgeraniol-19-oic-acid, 24: Benzyl 2.6-dimethoxybenzoate,[62] 25: xerantholide,[63] 26: 9-oxoeuryopsin,[66] 27: Indicusalactone, 28: (-)-oxyfrullanolide, 29: 7-hydroxyfrullanolide, 30: Squalene, 31: 3,5-di-O-caffeoylquinic acid methyl ester,[67] 32: 3.4-di-O-caffeoylquinic acid methyl ester, 33: Caryatin BP204,[68] 34: 2-hydroxymethyl-non-3-ynoic acid 2-[2,2']-bithiophenyl-5-ethyl ester,[70] 35: Vernopicrin, 36: Vernomelitensi), 37: Sucrose ester,[77] 38: s 8-(4'-hydroxymethacrylate)-dehydromelitensin, 39: onopordopicrin, 40: 8α-[4'-hydroxymethacryloyloxy]-4-epi-sonchucarpolide,[78] 41: vernodalol, 42: 11β,13-dihydrovernodalin,[42] 43: 8-Epixanthatin, 44: 8-Epixanthatin 1β,5β-epoxide, 45: Pungiolide A, 46: Pungiolide B,[39] 47: 5,6,7,8,5-pentamethoxy-3,4-methylenedioxyflavone (eupalestine), 48: 5,6,7,5-tetramethoxy3,4-methylenedioxyflavone, 49: 5,6,7,3,4,5-hexamethoxyflavone, 50: 4-hydroxy-5,6,7,3,5-pentamethoxyflavone (ageconyflavone C).[24]

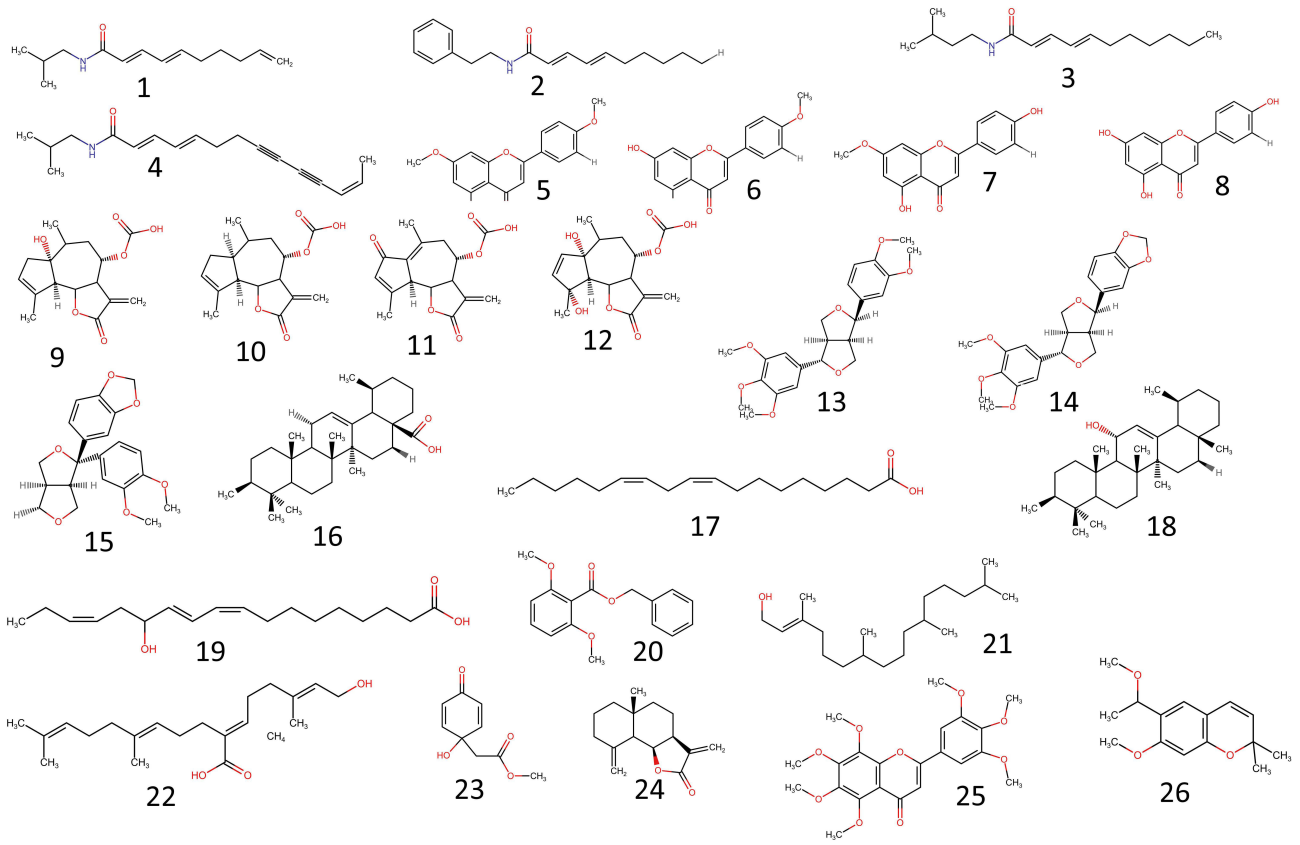

Figure 3 Natural Compounds Isolated from Asteraceae with Promising Antimalaria Activity. 1: deca-2E,4E,9-trienoic acid isobutylamide, 2: deca-2E,4E-dienoic acid 2-phenylethylamide, 3: undeca-2E,4E-dien-8,10-diynoic acid isopentylamide, 4: tetradeca-2E,4E,12Z-trien-8,10-diynoic acid isobutylamide,[40] 5: 7-Metoxyacacetin, 6: Acacetin, 7: Genkwanin, 8: Apigenin, 9: 1-desoxy-1α-peroxy-rupicolin A-8-O-acetate, 10: Rupicolin A-8-O-acetate, 11: 11,13-dehydromatricarin, 12: 1α,4α-dihydroxybishopsolicepolide.[42] 13: Epimagnolin A, 14: Aschantin, 15: Kabusin,[44] 16: Ursolic acid, 17: 3β 11α-dihydroxy urs-12-ene,[61] 18: Linoleic acid (octadeca-9,12-dienoic acid), 19: Benzyl 2.6-dimethoxybenzoate, 20: 13-Hydroxy-octadeca-9Z,11E,15Z-trienoic acid, 21: E-Phytol, 22: 6E-Geranylgeraniol-19-oic-acid,[62] 23: Jacaronone,[64] 24: (-)-frullanolide,[67] 25: 5,6,7,8,3',4',5'-heptamethoxyflavone (5'-methoxynobiletine,), 26: encecalol methyl ether.[24]

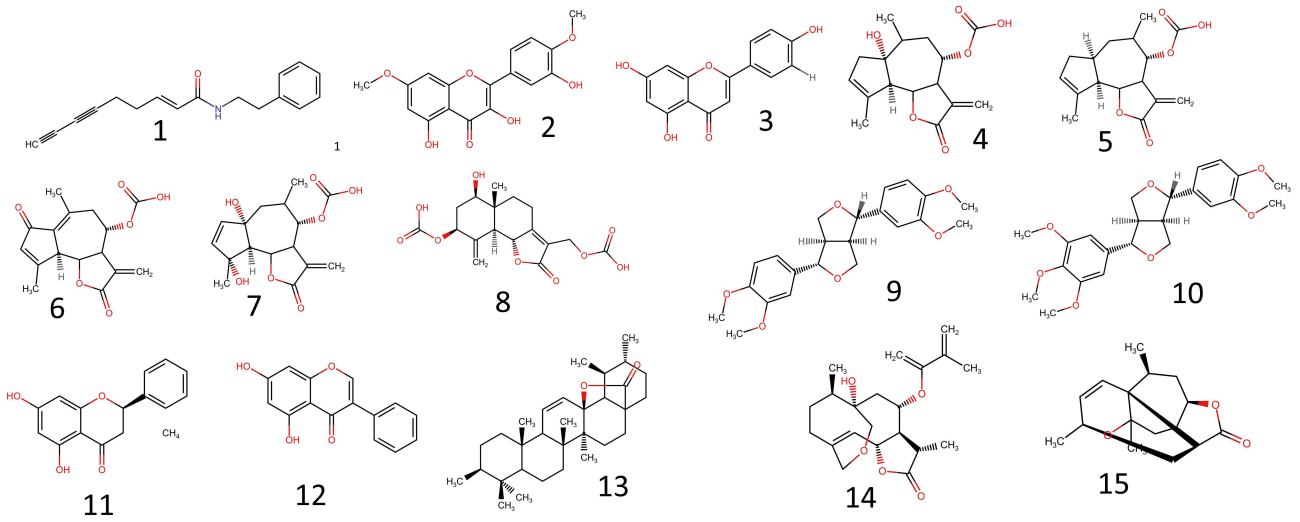

Figure 4 Natural Compounds Isolated from Asteraceae with Moderate Antimalaria Activity. 1: N-(2-phenethyl)-2E-en-6,8- nonadiynamide,[36] 2: Tamarixetin, 3: Apigenin, 4: 1-desoxy-1α-peroxy-rupicolin A-8-O-acetate, 5: Rupicolin B-8-O-acetate, 6: 11,13-dehydromatricarin, 7: 1α,4α-8α-Trihydroxyguaia-2,9,11(13)-triene-12,6α-olide-8-O-acetate, 8: Eudesmaafgraucolid,[42] 9: Eudesmin, 10, Magnolin,[44] 11: Pinocembrin, 12: 5,7-Dihydroxyisoflavone,[60] 13: 3-Hydroxy-13,28-epoxyurs-11-en-28-one,[61] 14: 11β,13-dihydrovernolide,[42] 15: Xanthipungolide.[39]

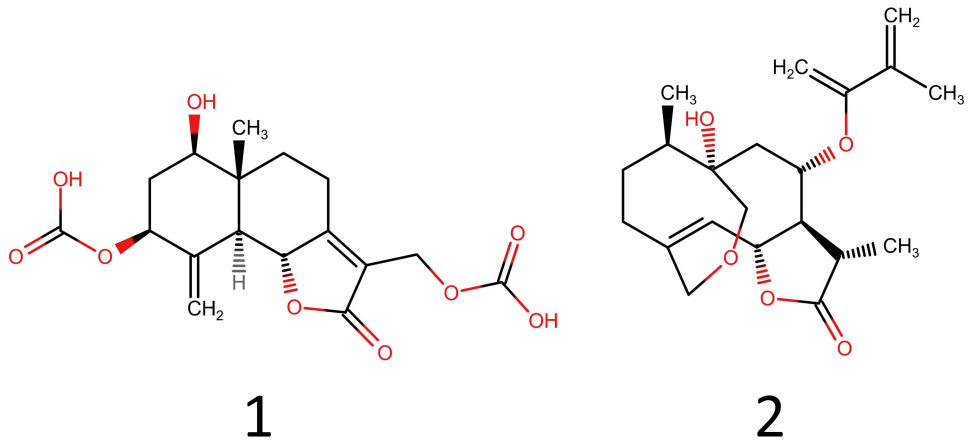

Figure 5 Natural Compounds Isolated from Asteraceae with Inactive Antimalaria Activity. 1: Eudesmaafgraucolid, 2: 11β,13-dihydrovernolide.[42]

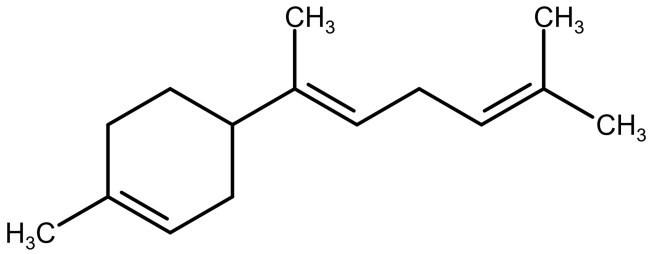

Figure 6 Z-γ-bisabolene from the essential oil of *Galinsoga parviflora* (*Asteraceae*) with insecticidal activity.[59]

established synthetic compounds, such as permethrin or deltamethrin, usually pose potential hazards to humans and the environment because of their high toxicity and may lead to resistance development.[102,103]

Conclusion

There are 64 plant species with antimalarial or insecticidal activities were included in this study. For the antimalarial in vitro study, the dichloromethane extract was the most widely studied, with most of the extracts showing high and moderate activity (IC50 value <10 µg/mL). There are 84 compounds isolated from 22 plant species, 59.52% of compounds have high antimalarial activity, of which 2-hydroxymethyl-non-3-ynoic acid 2-[2,2']-bithiophenyl-5- ethyl ester from *T. erecta* showed the best activity with IC50 value 0.01 of 0.02 µg/mL against *P. falciparum* MRC-pf-2 and MRC-pf-56 respectively, this compound has comparable IC50 with established antimalaria drug artemisinin (0.0015 and 0.0075 µg/mL). The in vivo antimalarial study showed that the aqueous extract of *A. conyzoides* showed the best activity, with a 100 mg/kg dose exerting 98.8% inhibition against *P. berghei* (NK65 Strain). In contrast, in a study on insecticidal activity, (Z)- γ-bisabolene from *G. parviflora* showed excellent activity against *A. stephensi* and *A. subpictus* with LC50 values of 2.04 µg/mL and 4.05 µg/mL. In conclusion, *A. conyzoides* and other plants from the *Asteraceae* family are promising reservoirs for natural compounds that exhibit antimalarial or insecticidal activity.

Acknowledgments

The authors acknowledge the support of the Faculty of Medicine Universitas Padjadjaran, particularly the supervising team, and the support of the Directorate of Research, Community Service, and Innovation Universitas Padjadjaran.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Garcia LS. Malaria. *Clin Lab Med*. 2010;30(1):93–129. doi:10.1016/j.cll.2009.10.001
2. Wångdahl A, Wyss K, Saduddin D, et al. Severity of Plasmodium falciparum and non-falciparum malaria in travelers and migrants: a nationwide observational study over 2 decades in Sweden. *J Infect Dis*. 2019;220(8):1335–1345. doi:10.1093/infdis/jiz292
3. Singh B, Kim Sung L, Matusop A, et al. A large focus of naturally acquired Plasmodium knowlesi infections in human beings. *Lancet*. 2004;363(9414):1017–1024. doi:10.1016/s0140-6736(04)15836-4
4. Yusof R, Lau YL, Mahmud R, et al. High proportion of knowlesi malaria in recent malaria cases in Malaysia. *Malar J*. 2014;13:168. doi:10.1186/1475-2875-13-168
5. WHO. World malaria report 2021. ; 2021 https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2021 Accessed 5 July 2022.
6. Kimbi H, Nana Y, Sumbele I, et al. Environmental factors and preventive methods against malaria parasite prevalence in Rural Bomaka and Urban Molyko, Southwest Cameroon. *J Bacteriol Parasitol*. 2013;4. doi:10.4172/2155-9597.1000162
7. Tse EG, Korsik M, Todd MH. The past, present and future of anti-malarial medicines. *Malar J*. 2019;18(1):93. doi:10.1186/s12936-019-2724-z
8. WHO. WHO Guidelines for malaria; 2021. Available from: https://www.who.int/publications/i/item/guidelines-for-malaria. Accessed 5 July 2022.
9. WHO. Malaria. 2021 . Available from: https://www.who.int/news-room/fact-sheets/detail/malaria. Accessed 10 July 2023.
10. Killeen GF, Masalu JP, Chinula D, et al. Control of malaria vector mosquitoes by insecticide-treated combinations of window screens and eave baffles. *Emerg Infect Dis*. 2017;23(5):782–789. doi:10.3201/eid2305.160662
11. Alemayehu A. Biology and epidemiology of Plasmodium falciparum and Plasmodium vivax gametocyte carriage: implication for malaria control and elimination. *Parasite Epidemiol Control*. 2023;21:e00295. doi:10.1016/j.parepi.2023.e00295
12. Virginia DM, Shegokar R, Pathak Y. Malaria – current Treatment Options. In: Shegokar R, Pathak Y, editors. *Malarial Drug Delivery Systems: Advances in Treatment of Infectious Diseases*. Springer International Publishing; 2023:71–89.
13. Roberts L. Drug-resistant malaria advances in Mekong. *Science*. 2017;358(6360):155–156. doi:10.1126/science.358.6360.155
14. WHO Artemisinin resistance and artemisinin-based combination therapy efficacy . ; 2019 https://www.who.int/docs/default-source/documents/publications/gmp/who-cds-gmp-2019-17-eng.pdf?ua=1 Accessed 10 July 2022 :.
15. Kawada H, Dida GO, Ohashi K, et al. Multimodal pyrethroid resistance in malaria vectors, Anopheles gambiae s.s., Anopheles arabiensis, and Anopheles funestus s.s. in Western Kenya. *PLoS One*. 2011;6(8):e22574. doi:10.1371/journal.pone.0022574
16. Kaur R, Kaur H. Plant derived antimalarial agents. *J Med Plants Stud*. 2017;5:346–363.
17. Kirandeep K, Meenakshi J, Tarandeep K, Rahul J. Antimalarials from nature. *Bioorg Med Chem*. 2009;17(9):3229–3256. doi:10.1016/j.bmc.2009.02.050
18. Obidike Ezenyi I, Salawu O. *Approaches, Challenges and Prospects of Antimalarial Drug Discovery from Plant Sources*. IntechOpen; 2016.
19. Chaniad P, Phuwajaroanpong A, Techarang T, Viriyavejakul P, Chukaew A, Punsawad C. Antiplasmodial activity and cytotoxicity of plant extracts from the Asteraceae and Rubiaceae families. *Heliyon*. 2022;8(1):e08848. doi:10.1016/j.heliyon.2022.e08848
20. Tabuti JRS, Obakiro SB, Nabatanzi A, et al. Medicinal plants used for treatment of malaria by indigenous communities of Tororo District, Eastern Uganda. *Trop Med Health*. 2023;51(1):34. doi:10.1186/s41182-023-00526-8
21. Okello D, Kang Y. Exploring Antimalarial Herbal Plants across Communities in Uganda Based on Electronic Data. *Evid Based Complement Alternat Med*. 2019;2019:3057180. doi:10.1155/2019/3057180
22. Ukwe V, Epueke E, Ekwunife O, Akunne T, Christian A, Ubaka C. Antimalarial activity of aqueous extract and fractions of leaves of Ageratum conyzoides in mice infected with Plasmodium berghei. *Int J Pharm Sci*. 2010;2:33–38.
23. Kamaraj C, Ragavendran C, Kumar RCS, et al. Antiparasitic potential of asteraceae plants: a comprehensive review on therapeutic and mechanistic aspects for biocompatible drug discovery. *Phytomed Plus*. 2022;2(4):100377. doi:10.1016/j.phyplu.2022.100377
24. Nour AM, Khalid SA, Kaiser M, Brun R, Abdalla WE, Schmidt TJ. The antiprotozoal activity of methylated flavonoids from Ageratum conyzoides L. *J Ethnopharmacol*. 2010;129(1):127–130. doi:10.1016/j.jep.2010.02.015
25. Adelaja O, Oduola A, Omotayo A, Obembe A, Adeogun A. Spatial toxicity of selected insecticidal plant oils against Anopheles gambiae Giles (Diptera: culicidae); 2022. doi:10.21203/rs.3.rs-1334833/v1
26. Amadi B, Majesty D, Nnabugwu A. Chemical profiles of leaf, stem, root and flower of Ageratum conyzoides. *Asian J Plant Sci Res*. 2012;2:428–432.
27. Supandi, Eka SaputraSE YH, Anwar C, et al. Potential of reclamation area of coal mining sites in medical field. *Int J Adv Res Eng Technol*. 2020;11(8):714–720.
28. Budiarti M, Maruzy A, Mujahid R, et al. The use of antimalarial plants as traditional treatment in Papua Island, Indonesia. *Heliyon*. 2020;6(12):e05562. doi:10.1016/j.heliyon.2020.e05562
29. Anywar G, Van't Klooster CIEA, Byamukama R, et al. Medicinal plants used in the treatment and prevention of Malaria in Cegere Sub-County, Northern Uganda. *Ethnobot Res Appl*. 2016;14:505–516. doi:10.17348/era.14.0.505-516
30. Deharo E, Bourdy G, Quenevo C, Muñoz V, Ruiz G, Sauvain M. A search for natural bioactive compounds in Bolivia through a multidisciplinary approach. Part V. Evaluation of the antimalarial activity of plants used by the Tacana Indians. *J Ethnopharmacol*. 2001;77(1):91–98. doi:10.1016/s0378-8741(01)00270-7
31. Bero J, Ganfon H, Jonville MC, et al. In vitro antiplasmodial activity of plants used in Benin in traditional medicine to treat malaria. *J Ethnopharmacol*. 2009;122(3):439–444. doi:10.1016/j.jep.2009.02.004
32. Sanon S, Azas N, Gasquet M, et al. Antiplasmodial activity of alkaloid extracts from Pavetta crassipes (K. Schum) and Acanthospermum hispidum (DC), two plants used in traditional medicine in Burkina Faso. *Parasitol Res*. 2003;90(4):314–317. doi:10.1007/s00436-003-0859-9

33. Ohashi M, Amoa-Bosompem M, Kwofie KD, et al. In vitro antiprotozoan activity and mechanisms of action of selected Ghanaian medicinal plants against Trypanosoma, Leishmania, and Plasmodium parasites. *Phytother Res*. 2018;32(8):1617–1630. doi:10.1002/ptr.6093
34. Soleimani-Ahmadi M, Abtahi SM, Madani A, et al. Phytochemical profile and mosquito larvicidal activity of the essential oil from aerial parts of Satureja bachtiarica Bunge against malaria and lymphatic filariasis vectors. *J Essent Oil Bear Plants*. 2017;20(2):328–336. doi:10.1080/0972060X.2017.1305919
35. Owuor BO, Ochanda JO, Kokwaro JO, et al. In vitro antiplasmodial activity of selected Luo and Kuria medicinal plants. *J Ethnopharmacol*. 2012;144(3):779–781. doi:10.1016/j.jep.2012.09.045
36. Silveira N, Saar J, Santos AD, et al. A new alkamide with an Endoperoxide Structure from Acmella ciliata (Asteraceae) and Its in Vitro Antiplasmodial Activity. *Molecules*. 2016;21(6):765 doi:10.3390/molecules21060765.
37. Rajeswary M, Govindarajan M, Murugan K, et al. Ovicidal efficacy of Ageratina Adenophora (Family: Asteraceae) against Anopheles Stephensi (Diptera: culicidae). *Int J Pure Appl Zool*. 2014;2:168.
38. Tennyson S, Ravindran J, Eapen A, William J. Repellent activity of Ageratum houstonianum Mill. (Asteraceae) leaf extracts against Anopheles stephensi, Aedes aegypti and Culex quinquefasciatus (Diptera: culicidae). *Asian Pac J Trop Dis*. 2012;2(6):478–480. doi:10.1016/S2222-1808(12)60104-2
39. Nour AM, Khalid SA, Kaiser M, Brun R, Abdallah WE, Schmidt TJ. The antiprotozoal activity of sixteen asteraceae species native to Sudan and bioactivity-guided isolation of xanthanolides from Xanthium brasilicum. *Planta Med*. 2009;75(12):1363–1368. doi:10.1055/s-0029-1185676
40. Althaus JB, Malyszek C, Kaiser M, Brun R, Schmidt TJ. Alkamides from anacyclus pyrethrum L. and their in vitro antiprotozoal activity. *Molecules*. 2017;22(5):796. doi:10.3390/molecules22050796
41. Lusakibanza M, Mesia G, Tona G, et al. In vitro and in vivo antimalarial and cytotoxic activity of five plants used in Congolese traditional medicine. *J Ethnopharmacol*. 2010;129(3):398–402. doi:10.1016/j.jep.2010.04.007
42. Kraft C, Jenett-Siems K, Siems K, et al. In vitro antiplasmodial evaluation of medicinal plants from Zimbabwe. *Phytother Res*. 2003;17(2):123–128. doi:10.1002/ptr.1066
43. Cheah S-X, Tay J-W, Chan L-K, Jaal Z. Larvicidal, oviposition, and ovicidal effects of Artemisia annua (Asterales: asteraceae) against Aedes aegypti, Anopheles sinensis, and Culex quinquefasciatus (Diptera: culicidae). *Parasitol Res*. 2013;112(9):3275–3282. doi:10.1007/s00436-013-3506-0
44. Ortet R, Prado S, Regalado EL, et al. Furfuran lignans and a flavone from Artemisia gorgonum Webb and their in vitro activity against plasmodium falciparum. *J Ethnopharmacol*. 2011;138(2):637–640. doi:10.1016/j.jep.2011.09.039
45. Panda S, Rout JR, Pati P, Ranjit M, Sahoo SL. Antimalarial activity of Artemisia nilagirica against Plasmodium falciparum. *J Parasit Dis*. 2018;42(1):22–27. doi:10.1007/s12639-017-0956-9
46. Gogoi N, Gogoi B, Chetia D. In vitro antimalarial activity evaluation of two ethnomedicinal plants against chloroquine sensitive and resistant strains of plasmodium falciparum. *Clin Phytosci*. 2021;7(1):42. doi:10.1186/s40816-021-00269-1
47. da Silva Filho AA, Resende DO, Fukui MJ, et al. In vitro antileishmanial, antiplasmodial and cytotoxic activities of phenolics and triterpenoids from Baccharis dracunculifolia D. C. (Asteraceae). *Fitoterapia*. 2009;80(8):478–482. doi:10.1016/j.fitote.2009.06.007
48. Andrade-Neto VF, Brandão MG, Oliveira FQ, et al. Antimalarial activity of Bidens pilosa L. (Asteraceae) ethanol extracts from wild plants collected in various localities or plants cultivated in humus soil. *Phytother Res*. 2004;18(8):634–639. doi:10.1002/ptr.1510
49. Nadia NAC, Cédric Y, Raoul SNS, et al. Antimalarial activity of ethyl acetate extract and fraction of Bidens pilosa against plasmodium berghei (ANKA). *J Parasitol Res*. 2020;2020:8832724. doi:10.1155/2020/8832724
50. Lacroix D, Prado S, Kamoga D, et al. Antiplasmodial and cytotoxic activities of medicinal plants traditionally used in the village of Kohima, Uganda. *J Ethnopharmacol*. 2011;133(2):850–855. doi:10.1016/j.jep.2010.11.013
51. Singh SP, Pawan Kumar M. Mosquito repellent action of Blumea lacera (Asteraceae) against Anopheles stephensi and Culex quinquefasciatus. *Int J Mosquito Res*. 2014;1:10–13.
52. Muganga R, Angenot L, Tits M, Frédérich M. Antiplasmodial and cytotoxic activities of Rwandan medicinal plants used in the treatment of malaria. *J Ethnopharmacol*. 2010;128(1):52–57. doi:10.1016/j.jep.2009.12.023
53. Becker JV, van der Merwe MM, van Brummelen AC, et al. In vitro anti-plasmodial activity of Dicoma anomala subsp. gerrardii (Asteraceae): identification of its main active constituent, structure-activity relationship studies and gene expression profiling. *Malar J*. 2011;10:295. doi:10.1186/1475-2875-10-295
54. Jansen O, Tits M, Angenot L, et al. Anti-plasmodial activity of Dicoma tomentosa (Asteraceae) and identification of urospermal A-15-O-acetate as the main active compound. *Malar J*. 2012;11:289. doi:10.1186/1475-2875-11-289
55. Pedersen MM, Chukwujekwu JC, Lategan CA, Staden J, Smith PJ, Staerk D. Antimalarial sesquiterpene lactones from Distephanus angulifolius. *Phytochemistry*. 2009;70(5):601–607. doi:10.1016/j.phytochem.2009.02.005
56. Toma A, Deyno S, Fikru A, Eyado A, Beale A. In vivo antiplasmodial and toxicological effect of crude ethanol extract of Echinops kebericho traditionally used in treatment of malaria in Ethiopia. *Malar J*. 2015;14(1):196. doi:10.1186/s12936-015-0716-1
57. Biruksew A, Zeynudin A, Alemu Y, et al. Zingiber Officinale Roscoe and Echinops Kebericho Mesfin Showed Antiplasmodial Activities against Plasmodium Berghei in a Dose-dependent Manner in Ethiopia. *Ethiop J Health Sci*. 2018;28(5):655–664. doi:10.4314/ejhs.v28i5.17
58. Rajakumar G, Rahuman AA, Chung IM, Kirthi AV, Marimuthu S, Anbarasan K. Antiplasmodial activity of eco-friendly synthesized palladium nanoparticles using Eclipta prostrata extract against Plasmodium berghei in Swiss albino mice. *Parasitol Res*. 2015;114(4):1397–1406. doi:10.1007/s00436-015-4318-1
59. Govindarajan M, Vaseeharan B, Alharbi NS, et al. High efficacy of (Z)-γ-bisabolene from the essential oil of Galinsoga parviflora (Asteraceae) as larvicide and oviposition deterrent against six mosquito vectors. *Environ Sci Pollut Res Int*. 2018;25(11):10555–10566. doi:10.1007/s11356-018-1203-3
60. Ranaivoarisoa R, Ralambonirina S, Randriamialinoro F, Randrianasolo R, Ratsimbason M, Ranarivelo L Discoveries and Innovations in Chemistry, Bioactivity, and Applications African Natural Plant Products, Volume III (Washington, D.C.: American Chemical Society)1361 ; 2020:171–178.
61. Al Musayeib NM, Mothana RA, Gamal AA, Al-Massarani SM, Maes L. In vitro antiprotozoal activity of triterpenoid constituents of Kleinia odora growing in Saudi Arabia. *Molecules*. 2013;18(8):9207–9218. doi:10.3390/molecules18089207

62. Köhler I, Jenett-Siems K, Kraft C, et al. Herbal remedies traditionally used against malaria in Ghana: bioassay-guided fractionation of Microglossa pyrifolia (Asteraceae). *Z Naturforsch C J Biosci*. 2002;57(11–12):1022–1027. doi:10.1515/znc-2002-11-1212
63. Kadhila NP, Sekhoacha M, Tselanyane M, Chinsembu KC, Molefe-Khamanga DM. Determination of the antiplasmodial activity, cytotoxicity and active compound of Pechuel-loeschea leubnitziae O. Hoffm. (Asteraceae) of Namibia. *SN Appl Sci*. 2020;2(8):1328. doi:10.1007/s42452-020-2926-6
64. Morais TR, Romoff P, Fávero OA, et al. Anti-malarial, anti-trypanosomal, and anti-leishmanial activities of jacaranone isolated from Pentacalia desiderabilis (Vell.) Cuatrec. (Asteraceae). *Parasitol Res*. 2012;110(1):95–101. doi:10.1007/s00436-011-2454-9
65. Ledoux A, Cao M, Jansen O, et al. Antiplasmodial, anti-chikungunya virus and antioxidant activities of 64 endemic plants from the Mascarene Islands. *Int J Antimicrob Agents*. 2018;52(5):622–628. doi:10.1016/j.ijantimicag.2018.07.017
66. Mollinedo P, Vila JL, Arando H, Sauvain M, Deharo E, Bravo JA. Anti-infective assessment of Senecio smithioides (Asteraceae) and isolation of 9-oxoeuryopsin, a furanoeremophilane-type sesquiterpene with antiplasmodial activity. *Nat Prod Res*. 2016;30(22):2594–2597. doi:10.1080/14786419.2015.1115994
67. Sangsopha W, Lekphrom R, Kanokmedhakul S, Kanokmedhakul K. Cytotoxic and antimalarial constituents from aerial parts of Sphaeranthus indicus. *Phytochem Lett*. 2016;17:278–281. doi:10.1016/j.phytol.2016.08.001
68. Zani C, Rachou I, Cruz-Mg O, et al. Isolation of caryatin as an antiplasmodial component of symphyopappus casarettoi (Asteraceae). *Int J Herbal Med*. 2020;8:116–122.
69. Chaniad P, Techarang T, Phuwajaroanpong A, Na-Ek P, Viriyavejakul P, Punsawad C. In vivo antimalarial activity and toxicity study of extracts of tagetes erecta L. and Synedrella nodiflora (L.) Gaertn. from the Asteraceae Family. *Evid Based Complement Alternat Med*. 2021;2021:1270902. doi:10.1155/2021/1270902
70. Gupta P, Vasudeva N. In vitro antiplasmodial and antimicrobial potential of Tagetes erecta roots. *Pharm Biol*. 2010;48(11):1218–1223. doi:10.3109/13880201003695142
71. Elufioye TO, Agbedahunsi JM. Antimalarial activities of Tithonia diversifolia (Asteraceae) and Crossopteryx febrifuga (Rubiaceae) on mice in vivo. *J Ethnopharmacol*. 2004;93(2–3):167–171. doi:10.1016/j.jep.2004.01.009
72. Ajayi C, Elujoba AA, Okella H. In vivo antimalarial activities of five Ugandan medicinal plants on plasmodium berghei in mice. *Eur J Med Plants*. 2020;31:1–13. doi:10.9734/ejmp/2020/v31i1230300
73. Quartey AK, Jibira Y, Forkuo-Donkor A, et al. Hydroethanolic stem bark extract of Vernonia amygdalina Del. (Asteraceae) suppresses yeast-induced pyrexia and Plasmodium berghei malaria in murine models. Journal of Medicinal Plants Research.2020;14(6):258-264. doi:10.5897/JMPR2020.6931
74. Obbo CJD, Kariuki ST, Gathirwa JW, Olaho-Mukani W, Cheplogoi PK, Mwangi EM. In vitro antiplasmodial, antitrypanosomal and antileishmanial activities of selected medicinal plants from Ugandan flora: refocusing into multi-component potentials. *J Ethnopharmacol*. 2019;229:127–136. doi:10.1016/j.jep.2018.09.029
75. Soma A, Sanon S, Gansane A, et al. Antiplasmodial activity of Vernonia cinerea Less (Asteraceae), a plant used in traditional medicine in Burkina Faso to treat malaria. *Afr J Pharm Pharmacol*. 2017;11:87–93. doi:10.5897/AJPP2016.4703
76. Sourabie S, Soma A, Yerbanga RS, et al. In vivo antiplasmodial activity of crude extracts of Vernonia cinerea Less (Asteraceae) against Plasmodium berghei infection in mice in Bobo Dioulasso. *Burkina Faso*. 2018. doi:10.13140/RG.2.2.19053.28648
77. Toyang NJ, Krause MA, Fairhurst RM, Tane P, Bryant J, Verpoorte R. Antiplasmodial activity of sesquiterpene lactones and a sucrose ester from Vernonia guineensis Benth. (Asteraceae). *J Ethnopharmacol*. 2013;147(3):618–621. doi:10.1016/j.jep.2013.03.051
78. Bordignon A, Frédérich M, Ledoux A, et al. In vitro antiplasmodial and cytotoxic activities of sesquiterpene lactones from Vernonia fimbrillifera Less. (Asteraceae). *Nat Prod Res*. 2018;32(12):1463–1466. doi:10.1080/14786419.2017.1350665
79. Ifijen I, Maliki M, Ogbeide O, Omorogbe S, Ikhuoria E. Chemical substances and *in-vivo* antiplasmodial activity of *Ageratum Conyzoides* in *Plasmodium Berghei* infected mice. *J Appl Sci Environ Manag*. 2019;23:1813–1817. doi:10.4314/jasem.v23i10.7
80. Abdullah WO, Unyah N, Hamat R, et al. In vitro antiplasmodial activity and cytotoxicity of ten plants used as traditional medicine in Malaysia. *MJHS*. 2011;9(2):5–8.
81. Muema JM, Njeru SN, Colombier C, Marubu RM. Methanolic extract of Agerantum conyzoides exhibited toxicity and growth disruption activities against Anopheles gambiae sensu stricto and Anopheles arabiensis larvae. *BMC Complement Altern Med*. 2016;16(1):475. doi:10.1186/s12906-016-1464-7
82. Do Céu de Madureira M, Paula Martins A, Gomes M, Paiva J, Proença da Cunha A, Do Rosário V. Antimalarial activity of medicinal plants used in traditional medicine in S. Tomé and Príncipe islands. *J Ethnopharmacol*. 2002;81(1):23–29. doi:10.1016/s0378-8741(02)00005-3
83. Joshi B, Hendrickx S, Magar LB, Parajuli N, Dorny P, Maes L. In vitro antileishmanial and antimalarial activity of selected plants of Nepal. *J Intercult Ethnopharmacol*. 2016;5(4):383–389. doi:10.5455/jice.20160728031236
84. Jonville MC, Kodja H, Strasberg D, et al. Antiplasmodial, anti-inflammatory and cytotoxic activities of various plant extracts from the Mascarene Archipelago. *J Ethnopharmacol*. 2011;136(3):525–531. doi:10.1016/j.jep.2010.06.013
85. Arya Neetu SC, Shakya A, Bharti M, Sahai N. Efficacy of Ageratum conyzoides against the control of mosquitoes. *Ijpsr*. 2011;31:3235–3237 doi:10.13040/IJPSR.0975-8232.
86. Ramasamy V, Karthi S, Ganesan R, et al. Chemical characterization of billy goat weed extracts Ageratum conyzoides (Asteraceae) and their mosquitocidal activity against three blood-sucking pests and their non-toxicity against aquatic predators. *Environ Sci Pollut Res Int*. 2021;28(22):28456–28469. doi:10.1007/s11356-021-12362-6
87. Sungula J, Taba K, Ntumba KI, Theodore K. In vitro antimalarial activity of 11 terpenes isolated from Ocimum gratissimum and Cassia alata Leaves. Screening of their binding affinity with Haemin. *J Plant Stud*. 2012;1:168. doi:10.5539/jps.v1n2p168
88. Yohana R, Chisulumi PS, Kidima W, Tahghighi A, Maleki-Ravasan N, Kweka EJ. Anti-mosquito properties of Pelargonium roseum (Geraniaceae) and Juniperus virginiana (Cupressaceae) essential oils against dominant malaria vectors in Africa. *Malar J*. 2022;21(1):219. doi:10.1186/s12936-022-04220-8
89. Wangrawa DW, Badolo A, Ilboudo Z, et al. Insecticidal activity of local plants essential oils against laboratory and field strains of Anopheles gambiae s. l. (Diptera: culicidae) from Burkina Faso. *J Econ Entomol*. 2018;111(6):2844–2853. doi:10.1093/jee/toy276

90. Morshedloo MR, Craker LE, Salami A, Nazeri V, Sang H, Maggi F. Effect of prolonged water stress on essential oil content, compositions and gene expression patterns of mono- and sesquiterpene synthesis in two oregano (Origanum vulgare L.) subspecies. *Plant Physiol Biochem*. 2017;111:119–128. doi:10.1016/j.plaphy.2016.11.023
91. Maia MF, Moore SJ. Plant-based insect repellents: a review of their efficacy, development and testing. *Malar J*. 2011;10(1):S11. doi:10.1186/1475-2875-10-S1-S11
92. Okunade AL. Ageratum conyzoides L. (Asteraceae). *Fitoterapia*. 2002;73(1):1–16. doi:10.1016/S0367-326X(01)00364-1
93. Kamboj A, Saluja AK. *Ageratum conyzoides* L.: a review on its phytochemical and pharmacological profile. *Int J Green Pharm*. 2008;2(2):59. doi:10.4103/0973-8258.41171
94. Muregi FW, Chhabra SC, Njagi EN, et al. Anti-plasmodial activity of some Kenyan medicinal plant extracts singly and in combination with chloroquine. *Phytother Res*. 2004;18(5):379–384. doi:10.1002/ptr.1439
95. Rudrapal M, Chetia DD. Plant flavonoids as potential source of future antimalarial leads. *Sys Rev Pharm*. 2016;8:13–18. doi:10.5530/srp.2017.1.4
96. Widia Astuti N, Fitrianingsih SP, Suwendar. Studi Literatur Aktivitas Antimalaria Tanaman Afrika (Vernonia amygdalina Del.). *Bandung Confer Series Pharm*. 2022;2(2). doi:10.29313/bcsp.v2i2.4815
97. Laryea MK, Sheringham Borquaye L. Antimalarial, antioxidant, and toxicological evaluation of Extracts of *Celtis africana, Grosseria vignei, Physalis micrantha*, and *Stachytarpheta angustifolia*. *Biochem Res Int*. 2021;2021:9971857. doi:10.1155/2021/9971857
98. Fitriani IN, Sholahudin M, Zikri AT. Analysis of Quantitative Structure-Activity Relationship (QSAR) of 1,8-Napthalymide-4-aminoquinoline derivatives as antimalarial compounds. *Walisongo J Chem*. 2022;5(2):194–201. doi:10.21580/wjcv5i213412
99. Quadros HC, Çapcı A, Herrmann L, et al. Studies of potency and efficacy of an optimized Artemisinin-Quinoline hybrid against multiple stages of the Plasmodium life cycle. *Pharmaceuticals (Basel)*. 2021;14(11):1129. doi:10.3390/ph14111129
100. Hanboonkunupakarn B, Tarning J, Pukrittayakamee S, Chotivanich K. Artemisinin resistance and malaria elimination: where are we now? *Front Pharmacol*. 2022;13. doi:10.3389/fphar.2022.876282
101. Sedaghat MM. Proposed categories of larvicidal activity of natural products derived from plants against Anopheles vector larvae. 2nd International Conference and Exhibition on Pharmacognosy, Phytochemistry & Natural Products; 2014.
102. Muhammed M, Dugassa S, Belina M, Zohdy S, Irish SR, Gebresilassie A. Insecticidal effects of some selected plant extracts against Anopheles stephensi (Culicidae: diptera). *Malar J*. 2022;21(1):295. doi:10.1186/s12936-022-04320-5
103. Tene Fossog B, Kopya E, Ndo C, et al. Water quality and *Anopheles gambiae* larval tolerance to pyrethroids in the cities of Douala and Yaoundé (Cameroon). *J Trop Med*. 2012;2012:429817. doi:10.1155/2012/429817