Antiplasmodial, antimalarial activities and toxicity of African medicinal plants: a systematic review of literature

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Abstract

Background: Malaria still constitutes a major public health menace, especially in tropical and subtropical countries. Close to half a million people mainly children in Africa, die every year from the disease. With the rising resistance to frontline drugs (artemisinin-based combinations), there is a need to accelerate the discovery and development of newer anti-malarial drugs. A systematic review was conducted to identify the African medicinal plants with significant antiplasmodial and/or anti-malarial activity, toxicity, as well as assessing the variation in their activity between study designs (in vitro and in vivo).

Methods: Key health-related databases including Google Scholar, PubMed, PubMed Central, and Science Direct were searched for relevant literature on the antiplasmodial and anti-malarial activities of African medicinal plants.

Results: In total, 200 research articles were identified, a majority of which were studies conducted in Nigeria. The selected research articles constituted 722 independent experiments evaluating 502 plant species. Of the 722 studies, 81.9%, 12.4%, and 5.5% were in vitro, in vivo, and combined in vitro and in vivo, respectively. The most frequently investigated plant species were Azadirachta indica, Zanthoxylum chalybeum, Picrilia nitida, and Nauclea latifolia meanwhile Fabaceae, Euphorbiaceae, Annonaceae, Rubiaceae, Rutaceae, Meliaceae, and Lamiaceae were the most frequently investigated plant families. Overall, 248 (34.3%), 241 (33.4%), and 233 (32.3%) of the studies reported very good, good, and moderate activity, respectively. Alchornea cordifolia, Flueggea virosa, Cryptolepis sanguinolenta, Zanthoxylum chalybeum, and Maytenus senegalensis gave consistently very good activity across the different studies. In all, only 31 (4.3%) of studies involved pure compounds and these had significantly ($p = 0.044$) higher antiplasmodial activity relative to crude extracts. Out of the 198 plant species tested for toxicity, 52 (26.3%) demonstrated some degree of toxicity, with toxicity most frequently reported with Azadirachta indica and Vernonia amygdalina. These species were equally the most frequently inactive plants reported. The leaves were the most frequently reported toxic part of plants used. Furthermore, toxicity was observed to decrease with increasing antiplasmodial activity.

Conclusions: Although there are many indigenous plants with considerable antiplasmodial and anti-malarial activity, the progress in the development of new anti-malarial drugs from African medicinal plants is still slothful, with only one clinical trial with Cochlospermum planchonii (Bixaceae) conducted to date. There is, therefore, the need to scale up anti-malarial drug discovery in the African region.

Keywords: Malaria, Medicinal plants, Antiplasmodial activity, Antimalarial activity

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Background

Malaria still constitutes a major public health menace, especially in tropical and subtropical countries. Various species of *Plasmodium*, transmitted through the bite of an infected female *Anopheles* mosquito, cause malaria, including *Plasmodium falciparum*, *Plasmodium malariae*, *Plasmodium ovale*, *Plasmodium vivax*, and *Plasmodium knowlesi*. Among these species, *P. falciparum* is the most virulent, responsible for the highest morbidity and mortality. It is also the predominant species in sub-Saharan Africa (SSA), a region with the highest number of malaria cases and deaths in the world. According to the World Health Organization (WHO), there were 228 million cases, and 405,000 malaria attributed deaths in 2018 [1]. In SSA, children and pregnant women are the most at-risk groups [1–3].

Malaria can be treated using chemotherapy but there is widespread resistance to many of the drugs. The first case of resistance to artesinin was reported in Cambodia in 2006 and has then spread to most of South-East Asia [4, 5]. The safety of chemoprophylaxis is also a major concern; for instance, primaquine, atovaquone, and doxycycline are contraindicated in pregnant women and children [6]. All these shortcomings necessitate the discovery and production of new drugs to treat malaria.

In the past 50 years, natural compounds including plant products, have played an important role in drug discovery and have provided value to the pharmaceutical industry [7]. For instance, therapeutics for various infectious diseases, cancer, and other debilitation diseases caused by metabolic disorders have all benefited from many drug classes that were initially developed based on active compounds from plant sources [8]. Furthermore, quinine and artemisinin, and their synthetic derivatives which are the mainstay of anti-malarial chemotherapy, were also derived from plant sources. In malaria-endemic areas, especially in Africa, many people rely on herbal medicines as the first line of treatment [9]. The common reasons for their preference vary from the cost of standard drugs, availability and accessibility, perceived effectiveness, low side effect, and faith in traditional medicines [10].

Reviews of the antiplasmodial and anti-malarial activities of medicinal plants are needed to drive research into the discovery and production of new anti-malarial drugs. Only a few reviews of the antiplasmodial or anti-malarial activity of medicinal plants have been published in the scientific literature [11–16]. These reviews focused only on studies with high antiplasmodial or anti-malarial activity and hardly report on their toxicity. The purpose of this study was to review medicinal plants with moderate to very good antiplasmodial and anti-malarial activities, as well as assess the variation in the activities between different methods. Furthermore, the toxicity of plant species is highlighted.

Methods

The literature was reviewed in search of scientific articles reporting antiplasmodial activities (IC$_{50}$, ED$_{50}$, LD$_{50}$, and parasite suppression rate) of medicinal plants used in Africa to treat malaria. The current study conforms to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines [17].

Search strategy and selection criteria

Relevant articles were searched in health-related electronic databases including PubMed, PubMed Central, Google Scholar, and ScienceDirect using the keywords: Traditional herbs or Medicinal plants or Antiplasmodial activity or Antimalarial activity or Herbal medicine or *Plasmodium*.

The search was limited to studies published in English or containing at least an abstract written in English until May 2020. The titles and abstracts were subsequently examined by two reviewers, independently (parallel method) to identify articles reporting the antiplasmodial activity of medicinal plants. In the case of any discrepancy in their reports, a third reviewer was brought in to resolve the issue. Relevant papers were equally manually cross-checked to identify further references. The following data were extracted from the selected articles by the reviewers: plant species, plant family, place of collection, parts of the plant used, type of study (whether in vitro, in vivo, or human), the extraction solvent used, IC$_{50}$ or ED$_{50}$ values, parasite suppression rate, isolated compounds, interaction with known malarial drugs (whether synergistic or antagonistic), and toxicity. Articles that did not report antiplasmodial or anti-malarial activity of medicinal plants as well as review articles were excluded. The entire selection process is presented in Fig. 1.

In this study, antiplasmodial activity pertains to studies performed in vitro using different strains of *Plasmodium falciparum*, meanwhile, anti-malarial activity is reserved for in vivo studies performed using mice and various parasite models (including *Plasmodium berghei*, *Plasmodium yoelii*, and *Plasmodium chabaudi*) and reporting parasite suppression rate.

Categorization of antiplasmodial and anti-malarial activities

For in vitro studies, the antiplasmodial activity of an extract was considered very good if IC$_{50}$ < 5 µg/ml, good 5 µg/ml ≤ IC$_{50}$ < 10 µg/ml, and moderate 10 µg/ml ≤ IC$_{50}$ < 20 µg/ml [18]. For in vivo studies, the anti-malarial activity of an extract is considered very good if the suppression is ≥ 50% at 100 mg/kg body weight/day, good if the suppression is ≥ 50% at 250 mg/kg body weight/day, and moderate if the suppression is ≥ 50% at 500 mg/kg body weight/day [18]. Antiplasmodial activities of 20 µg/ml and above for in vitro studies and
anti-malarial ≥ 50% at > 500 mg/kg body weight/day for in vivo studies, were considered inactive.

Risk of bias in individual studies
The level of risk of bias for the study was likely to be high mainly because of differences in the studies and the methods used to determine the antiplasmodial or anti-malarial activity. The stains of Plasmodium used to assess the antiplasmodial or anti-malarial activity of the medicinal plants equally varied between studies. Furthermore, the extraction solvent, as well as the extraction yield of the plants in the different studies, was not the same, which may have accounted for the variation in the antiplasmodial and anti-malarial activities for the same plants but in the different studies.

Results
The PRISMA flowchart (Fig. 1) presents a four-phase study selection process in the present systematic review study. A total of 25,159 titles were identified in the initial search. After the title and abstract screening, 228 full-text
articles were retrieved. Of these, a final 200 articles were identified for the review.

For this review, the evaluation of the individual plant species was considered as an independent study, so it is common for one article to have more than one study depending on the number of plant species evaluated. In all, there were 722 independent studies. Five hundred and ninety-one (81.9%) of the independent studies were in vitro (Table 1), 90 (12.4%) were in vivo (Table 2) and 40 (5.5%) were both in vitro and in vivo (Table 3). There was only one human study (clinical trial) conducted so far (Table 4). The selected research articles were from 31 African countries. Out of the 200 research articles reviewed, most of them were from Nigeria (29.0%), Kenya (24.0%), Ethiopia (6.5%), Cameroon (5.0%), Ivory Coast (5.5%), D.R. Congo (5.0%), and Burkina Faso (3.5%) (Fig. 2). The studies cover the period from 1989 to 2020.

Family and species distribution of plants evaluated
From 722 studies, the most frequent plant families studied included Fabaceae 47 (6.5%), Euphorbiaceae 45 (6.2%), Annonaceae 37 (5.1%), Rubiaceae 37 (5.1%), Rutaceae 37 (5.1%), Meliaceae 30 (4.2%), and Lamiaceae 12 (1.7%). Five hundred and two (502) plant species were investigated in this study. Of them, the most investigated were: Azadirachta indica, Zanthoxylum chalybeum, Picrilima nitida, and Nauclea latifolia. The most frequent parts of the plants tested were the leaves, roots, root bark, stems, and the whole plant. A majority of the studies used the crude extracts of the plants compared to pure compounds (95.7% vs. 4.3%). In descending order, methanol 322 (44.7%), dichloromethane 207 (28.7%), ethanol 103 (14.3%), water 85 (11.7%) and ethyl acetate 62 (8.6%) were the most frequent extraction solvent used.

In vitro and in vivo activities of the plants evaluated
Overall, 248 (34.3%) of the studies reported activity that was very good (IC$_{50}$ values $< 5$ µg/ml or suppression rate of $\geq 50\%$ at 100 mg/kg body weight/day), 241 (33.4%) reported good activity and 233 (32.3%) reported moderate activity. For the in vitro studies, a majority 228 (38.6%) reported very good activity; 206 (34.9%) reported good activity and 187 (31.6%) reported moderate activity. Meanwhile for the in vivo studies, a majority 19 (21.1%) reported moderate activity, 16 (17.8%) reported very good activity and 13 (14.4%) reported good activity. For studies reporting both the in vitro and in vivo activity, a majority of 17 (42.5%) reported only moderate activity, 13 (32.5%) studies reported very good activity and 10 (25.0%) reported good activity. Among the plants with very good activity, only one species demonstrated very good activity both in vitro and in vivo (Table 3).

Among the studies, the most frequent plant species demonstrating very good antiplasmodial activity were: Alchornea cordifolia [3/3, 100%], Flueggea virosa [3/3, 100%], Cryptolepis sanguinolenta [9/4, 75%], Zanthoxylum chalybeum [4/5, 80%] and Maytenus senegalensis [3/6, 50%]. Plant families with the most active species include Rutaceae [13/25, 52.0%], Apocynaceae [13/26, 50%], Celastraceae [7/15, 46.7%], Annonaceae [17/37, 45.9%], Euphorbiaceae [21/48, 43.8%], Combretaceae [7/16, 43.8%], Fabaceae [18/47, 38.3%], Lamiaceae [8/23, 34.8%], Asteraceae [23/69, 33.3%], and Rubiaceae [8/37, 21.6%]. The fractions are derived from the count of studies reporting very good antiplasmodial activity (numerator) divided by the total number of studies that assessed the activity of that plant species (denominator).

Azadirachta indica and Vernonia amygdalina were the most frequently reported inactive species (Additional file 1: Table S1). Furthermore, Fabaceae, Rubiaceae, Euphorbiaceae, and Asteraceae were the plant families containing the most frequently reported inactive plants. A majority of 95.7% (691/722) of the studies used the crude extract of the plants. The antiplasmodial and/or anti-malarial activity was significantly higher ($p = 0.044$) in studies using pure compounds compared to those using crude preparations.

Toxicity of plants evaluated for their antiplasmodial and anti-malarial activity
Out of the 198 plants evaluated in toxicity assays, 52 (26.3%) were found to demonstrate some degree of toxicity. The most frequently reported plants with toxicity were Azadirachta indica and Vernonia amygdalina. Plant families harboring the most toxic species were Lamiaceae, Anacardiaceae, Moraceae, Meliaceae, Asteraceae, and Fabaceae. Approximately 33% of the plants tested demonstrated some toxicity in vitro and 26.7% had some degree of toxicity in vivo. Among plants with very good, good, and moderate antimalarial activity, 17.8%, 28.3%, and 35.4% had some degree of toxicity, respectively. The leaf was the plant part with the most frequently reported toxicity. Albino mice and Vero E6 cells were the most commonly used assays for the assessment of the toxicity of the plants.

Discussion
Resistance to the frontline anti-malarial drugs is increasing and is now a global concern. With this rising rate of resistance, there is a need to accelerate research into the discovery and development of new anti-malarial drugs. Unfortunately, from this study, it is evident that the progress into the discovery of a new anti-malarial drug in
Table 1  In vitro antiplasmodial activity of African medicinal plants

| Plant species                      | Plant family      | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | IC50 or ED50 or LD50 | Strain of Plasmodium Tested | Toxicity (value; assay) |
|-----------------------------------|-------------------|------------------|--------------------|--------------------|--------------------------|-----------------------|---------------------------|---------------------------|
| Dicoma anomala subsp. Gerrardii   | Compositae       | South Africa     | Whole plant        | Methanol, Water, Hexane, Dichloromethane | Very Good*              | 1.865 µM IC50          | Plasmodium falciparum     | Nd                        |
| Abutilon grandiflorum            | Malvaceae         | Tanzania         | Roots              | Ethyl Acetate      | Moderate                 | 10 µg/ml IC50          | Plasmodium falciparum     | Nd                        |
| Acacia nilotica                  | Fabaceae          | Kenya            | Inner Barks        | Methanol           | Very Good                | 4.48 µg/ml IC50        | Plasmodium falciparum     | No                       |
| Acacia nilotica                  | Fabaceae          | South Africa     | Twigs              | Dichloromethane/Methanol | Moderate              | 13 µg/ml IC50          | Plasmodium falciparum     | Nd                       |
| Acacia polyantha                 | Fabaceae          | Tanzania         | Root Barks         | Ethyl Acetate      | Moderate                 | 13 µg/ml IC50          | Plasmodium falciparum     | Nd                       |
| Acacia tortilis                  | Fabaceae          | Kenya            | Stem Barks         | Methanol           | Moderate                 | 13.4 µg/ml IC50        | Plasmodium falciparum     | Nd                       |
| Acacia xanthoploea               | Fabaceae          | South Africa     | Whole Plant        | Dichloromethane/Methanol | Very Good          | 4.8 µg/ml IC50          | Plasmodium falciparum     | Nd                       |
| Acacia xanthoploea               | Fabaceae          | South Africa     | Stem Barks         | Acetone            | Moderate                 | 10.1 µg/ml IC50        | Plasmodium falciparum     | Nd                       |
| Amorpha fruticosa                | Euphorbiaceae     | Kenya            | Leaves             | Methanol           | Moderate                 | 13.8 µg/ml IC50        | Plasmodium falciparum     | Nd                       |
| Acanthospermum hispidum DC       | Compositae        | Kenya            | Leaves             | Ethyl Acetate      | Moderate                 | 11 µg/ml IC50          | Plasmodium falciparum     | Nd                       |
| Acanthospermum hispidum DC       | Compositae        | Burkina Faso     | Stems, Leaves      | Crude Alkaloid     | Good                     | 4–10 µg/ml IC50        | Plasmodium falciparum     | Nd                       |
| Acanthospermum hispidum DC       | Compositae        | Ivory Coast       | Stems and Leaves   | Ethanol            | Moderate                 | 13.7 µg/ml IC50        | Plasmodium falciparum     | Nd                       |
| Acridocarpus chloropetanus       | Malpighiaceae     | Republic of Congo | Leaves             | Methanolic, Ethanol | Very Good                | 2.8 µg/ml IC50         | Plasmodium falciparum     | No                       |
| Achnanthus aspera                | Amaranthaceae     | South Africa     | Whole plant        | Dichloromethane/Methanol | Good                   | 9.9 µg/ml IC50          | Plasmodium falciparum     | Nd                       |
| Acmella cauliflora               | Compositae        | Kenya            | Whole plant        | Dichloromethane    | Good                     | 5.201–9.939 µg/ml IC50 | Plasmodium falciparum     | Nd                       |
| Adenia cissampeloides            | Passifloraceae    | Ghana            | Whole plant        | Ethanol            | Good                     | 8.521 µg/ml IC50       | Plasmodium falciparum     | Nd                       |
| Adhatoda latibracteata           | Acanthaceae       | Gabon            | Stems              | Dichloromethane    | Very Good                | 0.7–1.6 µg/ml IC50     | Plasmodium falciparum     | No                       |
| Aerva javanica                   | Amaranthaceae     | Sudan            | Whole plant        | Petroleum Ether/Chloroform | Very Good          | <5 µg/ml IC50          | Plasmodium falciparum     | Nd                       |
| Aerva lanata                     | Amaranthaceae     | Tanzania         | Whole plant        | Ethyl Acetate      | Good                     | 8.6 µg/ml IC50         | Plasmodium falciparum     | Nd                       |
| Aframomum giganteum              | Zingiberaceae     | Gabon            | Stems              | Dichloromethane    | Moderate                 | 8.3–13.5 µg/ml IC50    | Plasmodium falciparum     | No                       |

*Very Good* indicates an IC50 value of 1.865 µM or less; *Moderate* indicates an IC50 value of 10 µg/ml or less; *Good* indicates an IC50 value of 4–10 µg/ml; *Very Good* indicates an IC50 value of <5 µg/ml; No indicates no activity detected.
| Plant species       | Plant family | Source            | Country of study | Part of plant used | Extraction solvent          | Antiplasmodial Activity | Strain of Plasmodium Tested | Toxicity (value; assay) |
|---------------------|-------------|-------------------|------------------|--------------------|-----------------------------|------------------------|-----------------------------|---------------------------|
| Agathosma apiculata | Rutaceae    | [22] South Africa | Whole plant      | Dichloromethane/Methanol | Good 5.2 µg/ml IC₅₀         | Plasmodium falciparum D10 | Nd                          |                           |
| Ageratum conyzoides | Compositae  | Kenya             | Whole plant      | Methanol           | Moderate 11.5–12.1 µg/ml IC₅₀ | Plasmodium falciparum D6, W2 | Nd                          |                           |
| Ajuga remota        | Lamiaceae   | Kenya             | Whole plant      | Dichloromethan  | Very Good 2.15–3.444 µg/ml IC₅₀ | Plasmodium falciparum W2, D6 | Nd                          |                           |
| Alafia barteri      | Apocynaceae | [36] Nigeria      | Leaves           | Water              | Very Good 1.5 µg/ml IC₅₀   | Plasmodium falciparum     | Nd                          |                           |
| Albizia coriaria    | Fabaceae    | Kenya             | Stem barks       | Dichloromethane   | Good 6.798–10.679 µg/ml IC₅₀ | Plasmodium falciparum W2, D6 | Nd                          |                           |
| Albizia gummifera   | Fabaceae    | Kenya             | Stem barks       | Methanol           | Moderate 15.2–16.8 µg/ml IC₅₀ | Plasmodium falciparum D6, W2 | Nd                          |                           |
| Alchornea cordifolia| Euphorbiaceae | [39] Ivory Coast | Leaves           | Ethanol            | Very Good 0.2–0.5 µM IC₅₀  | Plasmodium falciparum    | No                          |                           |
| Alstonia boonei     | Apocynaceae | [42] Nigeria      | Stem barks       | Ethanol            | Moderate 15 µg/ml IC₅₀     | Plasmodium falciparum K1 | Nd                          |                           |
| Alstonia congensis  | Apocynaceae | [44] D.R. Congo   | Leaves, Barks    | N-Hexane, Chloroform, Acetone. | 4.84 µg/ml IC₅₀         | Plasmodium falciparum K1 | No                          |                           |
| Aloe marlothii      | Xanthorrhoeaceae | South Africa | Whole plant      | Dichloromethane/Athanol | Moderate 12.5 µg/ml IC₅₀   | Plasmodium falciparum D10 | Nd                          |                           |
| Aloe maculata       | Xanthorrhoeaceae | South Africa | Whole plant      | Dichloromethane/Athanol | Good 3.5 µg/ml IC₅₀       | Plasmodium falciparum D10 | Nd                          |                           |
| Aloe pulcherrima    | Xanthorrhoeaceae | South Africa | Whole plant      | Dichloromethane/Athanol | Moderate 8 µg/ml IC₅₀    | Plasmodium falciparum D10 | Nd                          |                           |
| Aloe ferox          | Xanthorrhoeaceae | South Africa | Whole plant      | Dichloromethane/Athanol | Moderate 12.4 µg/ml IC₅₀  | Plasmodium falciparum D10 | Nd                          |                           |
| Aloe pulcherrima    | Xanthorrhoeaceae | South Africa | Whole plant      | Dichloromethane/Athanol | Moderate 18.6 µg/ml IC₅₀  | Plasmodium falciparum    | No                          |                           |
| Aloe Newspina       | Xanthorrhoeaceae | South Africa | Whole plant      | Methanol           | Moderate 15.4 µg/ml IC₅₀  | Plasmodium falciparum CQ-S | No                          |                           |
| Aloe secundiflora   | Xanthorrhoeaceae | Nigeria      | Leaves           | Ethanol            | Moderate 12.3 µg/ml IC₅₀  | Plasmodium falciparum FCB1 | Nd                          |                           |
| Aloe pulcherrima    | Xanthorrhoeaceae | Egypt        | Leaves, Barks    | Water, Methanol    | Very Good 2—5 µg/ml IC₅₀  | Plasmodium falciparum K1 | Nd                          |                           |
| Plant species               | Plant family | Source            | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | IC50 or ED50 or LD50 | Strain of Plasmodium Tested | Toxicity (value; assay)      |
|-----------------------------|--------------|-------------------|------------------|--------------------|--------------------|-------------------------|----------------------|-----------------------------|------------------------------|
| Ampelocissus africana      | Vitaceae     | [20] Kenya        | Whole plant      | Ethyl Acetate      | Good               | 9.0 µg/ml IC50          |                      | Plasmodium falciparum K1   | Nd                           |
| Andrographis paniculata    | Acanthaceae  | [45] Cambodia     | Whole plant      | Dichloromethane    | Moderate           | 12.7 µg/ml IC50          |                      | Plasmodium falciparum W2   | Nd                           |
| Annona cunerae             | Annonaceae   | [31] Tanzania     | Leaves           | Methanol           | Very Good          | 0.12 µg/ml IC50          |                      | Plasmodium falciparum K1   | No                           |
| Annona chinensis           | Compositae   | [46] D.R. Congo   | Whole plant      | Methanolic and dichloromethane | Good               | 6.3 ± µg/ml IC50         |                      | Plasmodium falciparum (3D7, W2), Plasmodium berghei berghei | No                           |
| Annona reticulata          | Annonaceae   | [47] Cameroon     | Roots            | Ethanol            | Very good          | 1.90 ± µg/ml IC50        |                      | Plasmodium falciparum W2   | Nd                           |
| Annona muriata             | Annonaceae   | [48] Ivory Coast  | Leaves           | Pentane            | Moderate           | 8–18 ± µg/ml IC50        |                      | Plasmodium falciparum (CQ-5, (Nigerian) | Nd                           |
| Anogeissus leiocarpus      | Combretaceae | [50] Nigeria      | Ns               | Methanol, Water, Butanol, Ethyl Acetate | Moderate           | 10.94–13.77 ± µg/ml IC50 |                      | Plasmodium falciparum 3D7, K1 | Nd                           |
| Annonidium munnii          | Annonaceae   | [49] Cameroon     | Leaves           | Methylene Chloride | Very Good          | 3.8 ± µg/ml IC50         |                      | Plasmodium falciparum K1   | No                           |
| Ansellia africana          | Orchidaceae  | [20] Tanzania     | Leaves           | Ethyl Acetate      | Moderate           | 10 ± µg/ml IC50          |                      | Plasmodium falciparum W2   | Nd                           |
| Anthocleista grandiflora  | Gentianaceae | [37] South Africa | Stem barks       | Dichloromethane    | Good               | 8.69 ± µg/ml IC50        |                      | Plasmodium falciparum NF54 | Nd                           |
| Anthocleista nobilis       | Gentianaceae | [52] Burkina Faso | Leaves           | Dichloromethane    | Moderate           | 10 ± µg/ml IC50          |                      | Plasmodium falciparum      | Nd                           |
| Anthocleista vogelli       | Gentianaceae | [53] Nigeria      | Roots            | Petroleum Ether    | Good               | 9.5 ± µg/ml IC50         |                      | Plasmodium falciparum D10  | Nd                           |
| Arenga engleri             | Arecaceae    | [25] South Africa | Stem barks       | Dichloromethane    | Very Good          | 1.7 ± µg/ml IC50         |                      | Plasmodium falciparum UP1 (CQ-R) | Yes (SI = 121; mouse [NBMH]) |
| Artabotrys monteiroae      | Annonaceae   | [22] South Africa | Twigs            | Dichloromethylene/Methanol/Butanol | Good               | 8.7 ± µg/ml IC50         |                      | Plasmodium falciparum D10  | Nd                           |
| Artemisia afra             | Asteraceae   | [54] Zimbabwe     | Leaves           | Petroleum/Ethyl Acetate | Moderate          | 8.9–15.3 ± µg/ml IC50   |                      | Plasmodium falciparum D10  | Nd                           |
| Artemisia annua           | Asteraceae   | [22] South Africa | Leaves           | Dichloromethane    | Good               | 5 ± µg/ml IC50           |                      | Plasmodium falciparum D6, W2 | Nd                           |
| Artocarpus communis        | Moraceae     | [24] Kenya        | Leaves           | Methanol           | Good               | 3.9–9.1 ± µg/ml IC50    |                      | Plasmodium falciparum D6, W2 | Nd                           |
| Asparagus virgatus         | Asparagaceae | [22] South Africa | Whole plant      | Dichloromethane/Methanol | Good               | 8 ± µg/ml IC50           |                      | Plasmodium falciparum D10  | Nd                           |
| Aspilia africana           | Asteraceae   | [56] Uganda       | Shoots           | Ethyl Acetate      | Moderate           | 9.3–11.5 ± µg/ml IC50   |                      | Plasmodium falciparum D10, K1 | Nd                           |
Table 1 (continued)

| Plant species              | Plant family    | Source                | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | IC$_{50}$ or ED$_{50}$ or LD$_{50}$ | Strain of Plasmodium Tested                   | Toxicity (value; assay) |
|---------------------------|-----------------|-----------------------|------------------|--------------------|--------------------|--------------------------|-------------------------------------|-------------------------------------------------|--------------------------|
| Aspilia prulista         | Compositae      | [24] Kenya            | Root barks       | Methanol           | Good               | 6.8–9.7 µg/ml C$_{50}$ | Plasmodium falciparum D6, W2             | No                                                |                         |
| Acanthospermus gregoritica | Acanthaceae     | [22] South Africa     | Twigs            | Dichloromethane/Methanol | Moderate          | 16 µg/ml IC$_{50}$  | Plasmodium falciparum D10              | No                                                |                         |
| Azadirachta indica       | Meliaceae       | [57] India, Pakistan  | Stems, leaves    | Water              | Very Good          | 2.35–6.8 µg/ml IC$_{50}$ | Plasmodium falciparum Fcb1 & F32       | No                                                |                         |
| Azadirachta indica       | Meliaceae       | [45] Cambodia         | Barks            | Dichloromethane    | Very Good          | 4.7 µg/ml IC$_{50}$  | Plasmodium falciparum W2               | No                                                |                         |
| Azadirachta indica       | Meliaceae       | [58] Sudan            | Leaves           | Methanol           | Very Good          | 1.7–5.8 µg/ml IC$_{50}$ | Plasmodium falciparum 3D7, Dd5         | No                                                |                         |
| Azadirachta indica       | Meliaceae       | [59] Togo             | Leaves           | Ethanol            | Very Good          | 2.48–2.5 µg/ml IC$_{50}$ | Plasmodium falciparum W2, D6           | No                                                |                         |
| Balanites aegyptiaca     | Zygophyllaceae  | [24] Kenya            | Root barks       | Methanol           | Good               | 8.9 µg/ml C$_{50}$  | Plasmodium falciparum D6, W2          | No                                                |                         |
| Balanites aegyptiaca     | Zygophyllaceae  | [21] Kenya            | Root barks       | Methanol           | Very Good          | 3.49 µg/ml IC$_{50}$ | Plasmodium falciparum D6              | No                                                |                         |
| Balkanites maughamhi     | Zygophyllaceae  | [25] South Africa     | Stem barks       | Dichloromethane    | Very good          | 1.94 µg/ml IC$_{50}$ | Plasmodium falciparum UP1 (CQ-R)       | No                                                |                         |
| Barringtonia racemosa    | Lecythidaceae   | [22] South Africa     | Twigs            | Dichloromethane/Methanol | Good              | 5.7 µg/ml IC$_{50}$  | Plasmodium falciparum D10             | No                                                |                         |
| Berberis holsti          | Berberidaceae   | [61] Malawi           | Roots            | Dichloromethane/Methanol | Very Good         | 0.17 µg/ml IC$_{50}$ | Plasmodium falciparum 3D7             | No                                                |                         |
| Berberis holsti          | Berberidaceae   | [24] Kenya            | Root barks       | Methanol           | Very Good          | < 5 µg/ml C$_{50}$  | Plasmodium falciparum D6, W2          | No                                                |                         |
| Berberis holsti          | Berberidaceae   | [24] Kenya            | Root barks       | Methanol           | Good               | 19.53 µg/ml IC$_{50}$ | Plasmodium falciparum 3D7, W2         | No                                                |                         |
| Berula erecta            | Apioideae       | [22] South Africa     | Whole plant      | Dichloromethane    | Moderate           | 6.6 µg/ml IC$_{50}$  | Plasmodium falciparum D10             | No                                                |                         |
| Berula erecta            | Apioideae       | [24] Kenya            | Leaves           | Methanol           | Good               | 9.9 µg/ml IC$_{50}$  | Plasmodium falciparum D6, W2          | No                                                |                         |
| Berula erecta            | Apioideae       | [22] South Africa     | Leaves           | Methanol           | Good               | 5 µg/ml IC$_{50}$    | Plasmodium falciparum D10             | No                                                |                         |
| Berula erecta            | Apioideae       | [63] Senegal          | Leaves           | Petroleum ether    | Moderate           | 9–18 µg/ml IC$_{50}$ | Plasmodium falciparum Fcb1, F32       | Yes (IC$_{50}$ = 10 µg/ml; Vero cells)              |                         |
| Bixa orellana            | Bixaceae        | [45] Cambodia         | Leaves           | Water              | Good               | 9.3 µg/ml IC$_{50}$  | Plasmodium falciparum W2              | No                                                |                         |
| Boscia angustifolia      | Capparaceae     | [24] Kenya            | Stem barks       | Water              | Very good          | 1.4–4.7 µg/ml C$_{50}$ | Plasmodium falciparum D6, W2          | No                                                |                         |
| Boscia salicifolia       | Capparaceae     | [26] Kenya            | Stem barks       | Methanol           | good               | 1.1–8.8 µg/ml IC$_{50}$ | Plasmodium falciparum D6, W2          | No                                                |                         |
| Boswellia dalubieli      | Buxaceae        | [50] Nigeria          | Ns                | Methanol, Water, Butanol, Ethyl Acetate | Moderate          | 14.59–15.1 µg/ml IC$_{50}$ | Plasmodium falciparum 3D7, K1         | Yes (SI $\geq$ 101; Mouse [NBMH])                 |                         |
| Boswellia dalubieli      | Buxaceae        | [62] Burkina Faso     | Leaves           | Methanol           | Moderate           | 18.85 µg/ml IC$_{50}$ | Plasmodium falciparum 3D7 & W2        | No                                                |                         |
| Bridelia micranthera     | Phylanthaceae   | [26] Kenya            | Stem barks       | Methanol           | Moderate           | 14.2–19.4 µg/ml IC$_{50}$ | Plasmodium falciparum D6, W2          | No                                                |                         |
| Bridelia mollissutch     | Phylanthaceae   | [37] South Africa     | Roots            | Dichloromethane    | Very good          | 3.06 µg/ml IC$_{50}$  | Plasmodium falciparum NHF4             | No                                                |                         |
| Brucea javanica          | Simaroubaceae   | [45] Cambodia         | Roots            | Dichloromethane    | Very good          | 1.0 µg/ml IC$_{50}$   | Plasmodium falciparum W2              | No                                                |                         |
| Bruguiera gymnorrhiza    | Rhizophoraceae  | [22] South Africa     | Twigs            | Dichloromethane/Methanol | Moderate          | 11.7 µg/ml IC$_{50}$  | Plasmodium falciparum D10             | No                                                |                         |
| Plant species                  | Plant family | Source                          | Country of study | Part of plant used | Extraction solvent          | Antiplasmodial Activity | IC50 or ED50 or LD50 | Strain of Plasmodium Tested | Toxicity (value; assay)                      |
|-------------------------------|--------------|---------------------------------|------------------|-------------------|-----------------------------|-------------------------|------------------------|-----------------------------|-----------------------------------------------|
| Burchellia bubalina          | Rubiaceae    | [22] South Africa                | Twigs            | Dichloromethane/Methanol | Moderate                    | 18 µg/ml IC50            | Plasmodium falciparum D10 | Nd                          |                                |
| Caesalpinia bonducella       | Fabaceae     | [64] Nigeria                     | Aerial Parts     | Ethyl Acetate      | Moderate                    | 16 µg/ml EC50            | Plasmodium falciparum    | Nd                          | Yes (SI = 0.29–0.69; mouse mammary tumour [FM3A]) |
| Canthium setosum             | Rubiaceae    | [65] Benin                       | Aerial Parts     | Dichloromethane    | Very good                   | 2.77–4.80 µg/ml IC50    | Plasmodium falciparum D10 | Nd                          |                                |
| Capparis tomentosa Lam       | Capparaceae  | [37] South Africa                | Whole Plant      | Dichloromethane/Methanol | Moderate                    | 20 µg/ml IC50            | Plasmodium falciparum D10 | Nd                          |                                |
| Carica papaya                | Caricaceae   | [66] Nigeria                     | Leaves           | Ethyl Acetate      | Very good                   | 2.96 µg/ml IC50          | Plasmodium falciparum D10 | No                          |                                |
| Carissa edulis               | Apocynaceae  | [21] Kenya                       | Root barks       | Methanol           | Good                        | 6.41 µg/ml IC50          | Plasmodium falciparum    | No                          |                                |
| Carpolobia alba              | Polygalaceae | [53] Nigeria                     | Roots            | Dichloromethane    | Good                        | 7.10 µg/ml IC50          | Plasmodium falciparum D10 | Nd                          |                                |
| Cassia abbreviata            | Fabaceae     | [60] Malawi                      | Roots            | Dichloromethane    | Very Good                   | 2.88 µg/ml IC50          | Plasmodium falciparum V/5 | Nd                          |                                |
| Cassia alata                 | Fabaceae     | [67] D.R.Congo                   | Leaves           | Ethanol, Methanol, Petroleum Ether, Chloroform | Very Good | <0.1—5.4 µg/ml IC50 | Plasmodium Falciparum | Nd                          |                                |
| Senna occidentalis L         | Fabaceae     | [68] Mozambique And Portugal     | Roots            | N-Hexane           | Moderate                    | 19.3 µg/ml IC50          | Plasmodium falciparum 3D7 | Nd                          |                                |
| Cassia siamea                | Fabaceae     | [26] Kenya                       | Root Barks       | Methanol           | Moderate                    | 18.8 µg/ml IC50          | Plasmodium falciparum D6, W2 | Nd                          |                                |
| Cassia tara                  | Fabaceae     | [23] Sudan                       | Aerial parts     | Methanol           | Good                        | 4–10 µg/ml IC50          | Plasmodium falciparum W2 | Nd                          |                                |
| Catha edulis                 | Celastraceae | [22] South Africa                | Roots            | Dichloromethane    | Very Good                   | 3.3–5.2 µg/ml IC50       | Plasmodium falciparum 3D7, Dd2 | No                          |                                |
| Cedrelopsis greeri           | Rutaceae     | [71] Madagascar                  | Leaves           | Water              | Moderate                    | 0.68 µg/ml IC50          | Plasmodium falciparum D10 | Nd                          |                                |
| Celtis integrifolia          | Cannabaceae  | [52] Burkina Faso                | Leaves           | Dichloromethane    | Very Good                   | 3.7 µg/ml IC50           | Plasmodium falciparum    | Yes (SI ≥ 0.5; HepG2 cells) |                                |
| Centella asiatica            | Apioaceae    | [22] South Africa                | Leaves           | Dichloromethane/Methanol | Good                    | 8.3 µg/ml IC50           | Plasmodium falciparum D10 | Nd                          |                                |
| Cephalanthus natalensis      | Rubiaceae    | [22] South Africa                | Twigs            | Dichloromethane/Methanol | Moderate                    | 14–15 µg/ml IC50         | Plasmodium falciparum K1, NF54 | Nd                          |                                |
| Ceratotheca sesamoides       | Pedaliaceae  | [63] Senegal                     | Leaves           | Petroleum ether    | Moderate                    | 15–23 µg/ml IC50         | Plasmodium falciparum FcM29, FcB1, Plasmodium vinckei petter | Yes (IC50 = 50 µg/ml; Vero cells) |                                |
### Table 1 (continued)

| Plant species             | Plant family   | Source          | Country of study | Part of plant used | Extraction solvent                          | Antiplasmodial Activity | IC50 or ED50 or LD50 | Strain of Plasmodium Tested | Toxicity (value; assay) |
|---------------------------|----------------|-----------------|------------------|-------------------|---------------------------------------------|--------------------------|---------------------|-------------------------------|-------------------------|
| Chrysophyllum perpulchrum | Sapotaceae     | [43]            | Ivory Coast      | Stem Barks        | Ethanol                                     | Moderate                | 12.8 µg/ml IC50        | Plasmodium falciparum Fcb1   | Nd                      |
| Cinchona succirubra       | Rubiaceae      | [73]            | S. Tome' And Prí 'Niçoipe | Barks             | Petroleum Ether, Dichloromethane, Ethyl Acetate, Methanol | Good                    | < 10 µg/ml IC50         | Plasmodium falciparum 3D07 And Dd2 | Nd                      |
| Cinnamomum camphora       | Lauraceae      | [57]            | Ivory Coast      | Cortex            | Water                                       | Moderate                | 9.37–16.6 µg/ml IC50   | Plasmodium falciparum Fcb1 & F32 | Nd                      |
| Cissampelos mucronata     | Menispermaceae | [20]            | Tanzania         | Roots             | Ethyl Acetate                               | Very Good               | 0.38 µg/ml IC50         | Plasmodium falciparum K1    | Nd                      |
| Cissampelos pareira       | Menispermaceae | [26]            | Kenya            | Leaves            | Methanol                                    | Very Good               | 4.4 µg/ml IC50          | Plasmodium falciparum D6, W2 | Nd                      |
| Cissus populnea           | Vitaceae       | [50]            | Nigeria          | Ns                | Methanol, Water, Butanol, Ethyl Acetate     | Moderate                | 15.81–19.91 µg/ml IC50  | Plasmodium falciparum 3D07, K1 | Yes (SI ≥ 84, Mouse [NBMH]) |
| Citropsis articulata      | Rutaceae       | [75]            | Uganda           | Root Barks        | Ethyl Acetate                               | Nd                      | nd                  | Plasmodium falciparum Fcb1 | Nd                      |
| Clausena anisota          | Rutaceae       | [24]            | Kenya            | Stem Barks        | Methanol                                    | Good                    | 8.4–9.2 µg/ml IC50     | Plasmodium falciparum D6, W2 | Nd                      |
| Clematis braschiata Thunb | Ranunculaceae  | [37]            | South Africa     | Twigs             | Dichloromethane/Methanol                    | Moderate                | 18 µg/ml IC50          | Plasmodium falciparum D10 | Nd                      |
| Clerodendrum eriophyllum  | Lamiaceae      | [21]            | Kenya            | Root Barks        | Methanol                                    | Very Good               | 4.15 µg/ml IC50         | Plasmodium falciparum NF54  | Nd                      |
| Clerodendrum gloribum E. Mey | Lamiaceae   | [72]            | Kenya            | Root Barks        | Dichloromethane                             | Very Good               | 2.7–5.3 µg/ml IC50     | Plasmodium falciparum K1, NF54 | Nd                      |
| Clerodendrum gloribum var. gloribum | Lamiaceae | [24]            | South Africa     | Leaves            | Dichloromethane                             | Moderate                | 8.89 µg/ml IC50         | Plasmodium falciparum NF54  | Nd                      |
| Clerodendrum johnstonii   | Lamiaceae      | [24]            | Kenya            | Root Barks        | Methanol                                    | Good                    | 8.5 µg/ml IC50          | Plasmodium falciparum D6, W2 | Nd                      |
| Clusia abyssinica         | Peraceae       | [24]            | Tanzania         | Roots             | Ethyl Acetate                               | Moderate                | 19 µg/ml IC50          | Plasmodium falciparum D10 | Nd                      |
| Clusia rotundifolia       | Lamiaceae      | [76]            | Kenya            | Root Barks        | Methanol                                    | Good                    | 4.7–8.3 µg/ml IC50     | Plasmodium falciparum D6, W2 | Nd                      |
| Clovea myriocaroides      | Lamiaceae      | [20]            | Tanzania         | Root Barks        | Ethyl Acetate                               | Moderate                | 11 µg/ml IC50          | Plasmodium falciparum K1    | Nd                      |
| Clusia rotundifolia       | Lamiaceae      | [72]            | Kenya            | Root Barks        | Dichloromethane                             | Moderate                | 10.9–15.8 µg/ml IC50   | Plasmodium falciparum K1, NF54 | Nd                      |
| Clusia rotundifolia       | Lamiaceae      | [24]            | Kenya            | Leaves            | Dichloromethane                             | Good                    | 3.9–15.7 µg/ml IC50    | Plasmodium falciparum D6, W2 | Nd                      |
| Clusia rotundifolia       | Lamiaceae      | [77]            | Uganda           | Leaves            | Ethyl Acetate                               | Very Good               | 0.03–0.21 µg/ml IC50   | Plasmodium falciparum NF54 & FCR3 | Nd                      |
| Clusia rotundifolia       | Lamiaceae      | [24]            | Kenya            | Leaves            | Methanol                                    | Moderate                | 7.8–11.3 µg/ml IC50    | Plasmodium falciparum D6, W2 | Nd                      |
| Plant species        | Plant family    | Source                  | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | IC_{50} or ED_{50} or LD_{50} | Strain of Plasmodium Tested | Toxicity (value; assay) |
|----------------------|-----------------|-------------------------|------------------|--------------------|--------------------|-------------------------|----------------------------|-----------------------------|-------------------------|
| Clivia hirsuta       | Peraceae        | [22] South Africa       | Whole Plant      | Dichloromethane/Methanol | Moderate           | 15 µg/ml IC_{50}        | Plasmodium falciparum      | D10                         | Nd                      |
| Clivia robusta       | Peraceae        | [24] Kenya              | Leaves           | Methanol           | Good               | 3.4–7.5 µg/ml IC_{50}   | Plasmodium falciparum      | D6, W2                     | Nd                      |
| Cochlospermum        | Bixaceae        | [78] Burkina Faso       | Rhi-zomes        | Methanol, Dichloromethane | Good*              | 2.4–11.5 µg/ml IC_{50}  | Plasmodium falciparum      | 3D7                        | Nd                      |
| Cochlospermum        | Bixaceae        | [51] Ivory Coast        | Roots            | Methylene Chloride | Very Good          | 4.4 µg/ml IC_{50}        | Plasmodium falciparum      | K1                          | No                      |
| Coula edulis         | Olacaceae       | [24] Cameroon           | Stem, Leaves     | Water              | Very Good          | 0.4–1.56 µg/ml IC_{50}  | Plasmodium falciparum      | CFCb1 & F32                | Nd                      |
| Copaifera            | Malvaceae       | [48] Ivory Coast        | Leaves           | Ethyl Acetate      | Good               | 6.5 µg/ml IC_{50}        | Plasmodium falciparum      | K1                          | Nd                      |
| Combretum col-       | Combretaceae    | [52] Burkina Faso       | Leaves           | Dichloromethane    | Very Good          | 0.2 µg/ml IC_{50}        | Plasmodium falciparum      |                            | Nd                      |
| Combretum micran-    | Combretaceae    | [57] Ivory Coast        | Stem, Leaves     | Water              | Very Good          | 0.88–1.7 µg/ml IC_{50}  | Plasmodium falciparum      |                            | Nd                      |
| Combretum psid-      | Combretaceae    | [20] Tanzania           | Root Barks       | Ethyl Acetate      | Good               | 6.63 µg/ml IC_{50}       | Plasmodium falciparum      |                            | Nd                      |
| Combretum zeyheri    | Combretaceae    | [22] South Africa       | Twigs            | Dichloromethane/Methanol | Moderate           | 15 µg/ml IC_{50}        | Plasmodium falciparum      | D10                         | Nd                      |
| Coniphora africana   | Bursenaceae     | [24] Kenya              | Stem Barks       | Methanol           | Good               | 9.6–10.2 µg/ml IC_{50}  | Plasmodium falciparum      | D6, W2                     | Nd                      |
| Coniphora schimperi  | Bursenaceae     | [26] Kenya              | Stem Barks       | Methanol           | Very Good          | 3.9–5.2 µg/ml IC_{50}   | Plasmodium falciparum      |                            | Nd                      |
| Conyza alba          | Asteraceae      | [21] Kenya              | Inner Barks      | Methanol           | Very Good          | 4.63 µg/ml IC_{50}       | Plasmodium falciparum      |                            | Nd                      |
| Conyza podocepha     | Asteraceae      | [22] South Africa       | Whole Plant      | Dichloromethane/Methanol | Very Good          | 2 µg/ml IC_{50}         | Plasmodium falciparum      | D10                         | Nd                      |
| Conyza scabrida      | Asteraceae      | [22] South Africa       | Whole Plant      | Dichloromethane/Methanol | Good              | 6.8 µg/ml IC_{50}       | Plasmodium falciparum      | D10                         | Nd                      |
| Copalifera religiosa | Fabaceae        | [33] Gabon              | Leaves           | Dichloromethane    | Good               | 8.5–13.4 µg/ml IC_{50}  | Plasmodium falciparum      | FCB, 3D7                    | Yes (IC_{50} = 4.87 µg/ml human embryonic lung cells [MRC-5]) |
| Cordia myxa          | Boraginaceae    | [52] Burkina Faso       | Leaves           | Dichloromethane    | Good               | 6.2 µg/ml IC_{50}       | Plasmodium falciparum      |                            | Nd                      |
| Coula edulis         | Olacaceae       | [80] Cameroon           | Stem Barks       | Methanol           | Good               | 5.79–13.8 µg/ml IC_{50} | Plasmodium falciparum      | 3D7, DD2                    | No                      |
| Crossocentrs lembiuga| Rubiaceae       | [27] Burkina Faso       | Leaves           | Crude Alkaloid     | Good               | 4–10 µg/ml IC_{50}      | Plasmodium falciparum      | W2                         | Nd                      |
| Croton bukeana       | Fabaceae        | [22] South Africa       | Roots            | Dichloromethane    | Good               | 9.5 µg/ml IC_{50}       | Plasmodium falciparum      | D10                         | Nd                      |
| Croton gratissimus var. subgratissimus | Euphorbiaceae | [22] South Africa | Leaves | Dichloromethane | Very Good | 3.5 µg/ml IC_{50} | Plasmodium falciparum | D10 | Nd |
| Croton labatus       | Euphorbiaceae   | [65] Benin              | Roots            | Methanol           | Good               | 2.80–6.56 µg/ml IC_{50} | Plasmodium falciparum      | 3D7 & K1                    | Nd                      |
| Croton macrostachyus | Euphorbiaceae   | [30] Kenya              | Leaevs, Stems    | Dichloromethane    | Very Good          | 2.72 µg/ml IC_{50}       | Plasmodium falciparum      | W2, D6                     | Nd                      |
| Plant species                  | Plant family | Source          | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | IC50 or ED50 or LD50 | Strain of Plasmodium Tested | Toxicity (value; assay) |
|-------------------------------|--------------|-----------------|------------------|-------------------|-------------------|------------------------|---------------------|---------------------------|------------------------|
| Croton menghartii            | Euphorbiaceae | [22] South Africa | Leaves          | Dichloromethane/Methanol | Very Good          | 1.7 µg/ml IC50         | Plasmodium falciparum D10 | Nd                        |                       |
| Croton pseudopulchellus      | Euphorbiaceae | [25] South Africa | Stem Barks      | Chloroform        | Very Good          | 3.45 µg/ml IC50        | Plasmodium falciparum UP1 (CQ-R) | Nd                        |                       |
| Croton zambesiiclus          | Euphorbiaceae | [55] Cameroon    | Stem Barks      | Ethanol, Water, Dichloromethane, Methanol, Hexane | Good               | 0.88–9.14 µg/ml IC50   | Plasmodium falciparum W2     | Nd                        |                       |
| [34] Sudan                   | Fruits       | Petroleum Ether/Chloroform | Very Good          |  < 5 µg/ml IC50 | Plasmodium falciparum | Nd                        |                       |                       |
| Cryptolepis sanguinolenta    | Apocynaceae   | [81] Guinea-Bissau | Leaves, Roots   | Chloroform       | Very Good          | 3.45 µg/ml IC50        | Plasmodium falciparum K1, T996 | Nd                        |                       |
| [34] Sudan                   | Fruits       | Petroleum Ether/Chloroform | Very Good          |  < 5 µg/ml IC50 | Plasmodium falciparum | Nd                        |                       |                       |
| Cussonia spicata Thunb       | Araliaceae    | [22] South Africa | Fruits          | Dichloromethane/Methanol | Moderate          | 14 µg/ml IC50         | Plasmodium falciparum D10 | Nd                        |                       |
| Cussonia zimmermannii        | Araliaceae    | [37] South Africa | Root Barks      | Dichloromethane   | Very Good          | 3.25 µg/ml IC50        | Plasmodium falciparum NF54 | Nd                        |                       |
| Cussonia zimmermannii        | Araliaceae    | [20] Tanzania    | Root Barks      | Petroleum Ether   | Very Good          | 3.3 µg/ml IC50         | Plasmodium falciparum K1     | Nd                        |                       |
| Cuviera longiflora Rubiaceae | [80] Cameroon | Leaves          | Dichloromethane/Methanol | Moderate          | 13.91–20.24 µg/ml IC50 | Plasmodium falciparum 3D7, DD2 | No                         |                       |
| Cyathula prostrate            | Amaryanthaceae | [43] Ivory Coast | Whole Plant     | Ethanol           | Moderate           | 12.4 µg/ml IC50        | Plasmodium falciparum FC81 | Nd                        |                       |
| Cyathula schimperiens         | Amaryanthaceae | [24] Kenya      | Root Barks      | Methanol          | Moderate           | 5–17.6 µg/ml C50       | Plasmodium falciparum D6, W2     | Nd                        |                       |
| Cymbopogon validus            | Poaceae       | [22] South Africa | Whole Plant     | Dichloromethane/Methanol | Good              | 5.8 µg/ml IC50         | Plasmodium falciparum D10     | Nd                        |                       |
| Cyperus articulatus           | Cyperaceae    | [24] Kenya      | Tubers          | Methanol          | Good               | 4.8–8.7 µg/ml C50      | Plasmodium falciparum D6, W2     | Nd                        |                       |
| Cyphostemma spp               | Vitaceae      | [86] Namibia    | Whole Plant     | Methanol          | Very Good          | 3.276 µg/ml IC50       | Plasmodium falciparum 3D7      | Nd                        |                       |
| Dacryodes edulis              | Bursaracaeae  | [80] Cameroon   | Leaves          | Dichloromethane/Methanol | Good              | 6.45–8.62 µg/ml IC50   | Plasmodium falciparum 3D7, DD2     | No                        |                       |
| Dacryodes edulis              | Bursaracaeae  | [85] Cameroon   | Root Barks      | Methylene Chloride/Methanol | Very Good         | 0.37 µg/ml IC50        | Plasmodium falciparum |Nd                        |                       |
| Dichapetalum guineense        | Dicapetalaceae | [65] Benin      | Leaves          | Methanol          | Moderate           | 7.35–20 µg/ml IC50     | Plasmodium falciparum 3D7 & K1 | Nd                        |                       |
| Dichrostachys cinerea Wight et Arn | Fabaceae   | [37] South Africa | Roots          | Dichloromethane | Very Good          | 2.1 µg/ml IC50         | Plasmodium falciparum NF54     | Nd                        |                       |
Table 1 (continued)

| Plant species        | Plant family | Source | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | IC_{50} or ED_{50} or LD_{50} | Strain of Plasmodium Tested | Toxicity (value; assay) |
|----------------------|--------------|--------|------------------|--------------------|--------------------|-------------------------|-------------------------------|-------------------------------|---------------------------|
| Dicoma tomentosa     | Asteraceae   | [62]   | Burkina Faso     | Whole plant        | Dichloromethane, Methanol | Good                   | 7.04–7.90 µg/ml IC_{50}       | Plasmodium falciparum 3D7 & W2 | Nd                        |
|                       |              | [87]   | Burkina Faso     | Whole plant        | Dichloromethane      | Very Good               | 1.9–3.4 µg/ml IC_{50}          | Plasmodium Falciparum 3D7, W2, Plasmodium berghei | Nd                        |
| Diospyros abyssinica | Ebenaceae    | [75]   | Uganda           | Leaves             | Ethyl Acetate        | Nd                      | nd                            | Plasmodium falciparum Fcb2    | Nd                        |
| Diospyros mespiliformis | Ebenaceae    | [86]   | Namibia          | Leaves, Roots      | Methanol             | Very Good               | 3.179–3.523 µg/ml IC_{50}      | Plasmodium falciparum 3D7    | Nd                        |
| Diospyros monbutensis | Ebenaceae    | [37]   | South Africa     | Roots              | Dichloromethane      | Very Good               | 4.40 µg/ml IC_{50}             | Plasmodium falciparum NF54    | Nd                        |
| Dombeya shupangae    | Malvaceae    | [20]   | Tanzania          | Roots              | Ethyl Acetate        | Good                   | 7.5 µg/ml IC_{50}              | Plasmodium falciparum K1     | Nd                        |
| Dorstenia convesa    | Moraceae     | [56]   | Cameroon          | Twigs              | Ethanol, Water, Dichloromethane, Methanol, Hexane | Good | 0.28–8.95 µg/ml IC_{50} | Plasmodium falciparum W2 | Nd                        |
| Dorstenia klaineana  | Moraceae     | [33]   | Gabon             | Stems              | Methanol             | Moderate               | 16.7–17.0 µg/ml IC_{50}        | Plasmodium falciparum Fcbm, W2 | Yes (SI = 16.2–28.89; human embryonic lung cells [MRC-SI]) |
| Dracaena cambodiabia | Asparagaceae | [45]   | Cambodia          | Stems              | Dichloromethane      | Good                   | 8.7 µg/ml IC_{50}              | Plasmodium falciparum W2     | Nd                        |
| Drypetes natalensis  | Putranjivaceae | [31] | Tanzania          | Roots              | Ethanol              | Very Good               | 1.06 µg/ml IC_{50}             | Plasmodium falciparum K1     | No                       |
| Ekebergia capensis   | Meliaceae    | [22]   | South Africa      | Fruits             | Dichloromethane/Methanol | Moderate               | 10 µg/ml IC_{50}               | Plasmodium falciparum D10    | Nd                        |
| Ekebergia capensis   | Meliaceae    | [76]   | Kenya             | Stem Barks         | Chloroform           | Good                   | 3.9—13.4 µg/ml IC_{50}         | Plasmodium falciparum K39, ENT30, NF54, V1/S | Nd                        |
| Elaeis guineensis    | Arecaceae    | [21]   | Kenya             | Inner Barks        | Methanol             | Very Good               | 3.97 µg/ml IC_{50}             | Plasmodium falciparum D6     | No                       |
| Elaeodendron buchananii | Celastraceae | [24]   | Ghana             | Leaves             | Ethanol              | Very Good               | 1.195 µg/ml IC_{50}            | Plasmodium falciparum 3D7    | Nd                        |
| Enantia chlorantha   | Annonaceae   | [24]   | Kenya             | Stem Barks         | Methanol             | Moderate               | 17.1 µg/ml IC_{50}             | Plasmodium falciparum D6, W2 | Nd                        |
|                       |              | [55]   | Cameroon          | Stem Barks         | Ethanol, Water, Dichloromethane, Methanol, Hexane | Good | 0.68–14.72 µg/ml IC_{50} | Plasmodium falciparum W2 | Nd                        |
|                       |              | [40]   | DR Congo          | Stem Barks         | Water                | Good                   | 7.77 µg/ml IC_{50}             | Plasmodium falciparum K1     | Yes (CC_{50} = 3.0 µg/ml; human embryonic lung cells [MRC-SI]) |
| Entandrophyagna angolense | Meliaceae    | [89]   | Cameroon          | Stem Barks         | Dichloromethane/Methanol | Moderate               | 18.4 µg/ml IC_{50}             | Plasmodium falciparum W2     | Nd                        |
| Entandrophyagna caudatum | Meliaceae    | [25]   | South Africa      | Stem Barks         | Dichloromethane      | Very Good               | 2.9 µg/ml IC_{50}              | Plasmodium falciparum UP1 (CQ-R) | No                        |
| Plant species               | Plant family | Source        | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | Strain of Plasmodium Tested | Toxicity (value; assay) |
|----------------------------|--------------|---------------|------------------|--------------------|--------------------|--------------------------|-------------------------------|--------------------------|
| Entandrophragma palustre   | Meliaceae    | D.R. Congo    | Stem barks       | Methanol           | Moderate           | 15.84 µg/ml IC50         | Plasmodium falciparum 3D7, W2, Plasmodium berghei berghei | Nd                       |
| Erigeron floribundus       | Asteraceae   | Ivory Coast   | Leaves           | Pentane            | Good               | 4.3-10 µg/ml IC50        | Plasmodium falciparum FCM29, Plasmodium falciparum CQ-5 (Nigerian) | Nd                       |
| Eriooglossum edule         | Sapindaceae  | Cambodia      | Barks            | Dichloromethane    | Very Good          | 1.7 µg/ml IC50           | Plasmodium falciparum      | Nd                       |
| Erythrina abyssinica       | Fabaceae     | Uganda        | Barks            | Ethyl Acetate      | Nd                 | nd                       | Plasmodium falciparum Fcb3 | Nd                       |
| Erythrina lysistemon       | Fabaceae     | South Africa  | Stem Barks       | Acetone            | Very Good          | 4.8 µg/ml IC50           | Plasmodium falciparum (CQ-R) | Nd                       |
| Erythrina sacleuxii        | Fabaceae     | Tanzania      | Root Barks       | Ethyl Acetate      | Very Good          | 3.0 µg/ml IC50           | Plasmodium falciparum K1   | Nd                       |
| Erythrococca anomata       | Euphorbiaceae| Ivory Coast   | Leaves           | Ethanol            | Moderate           | 13.1 µg/dl IC50          | Plasmodium falciparum FCB1 | Nd                       |
| Euclia divinorum           | Ebenaceae    | Kenya         | Root Barks       | Methanol           | Good               | 6.9–12.4 µg/ml IC50      | Plasmodium falciparum D6, W2 | Nd                       |
| Euclia natalensis          | Ebenaceae    | South Africa  | Twigs            | Dichloromethane/Methanol | Very Good | 4.6 µg/ml IC50           | Plasmodium falciparum D10   | Nd                       |
| Eucomis autumnalis         | Asparagaceae | South Africa  | Bulbs            | Dichloromethane/Methanol | Good     | 9.5 µg/ml IC50           | Plasmodium falciparum D10   | Nd                       |
| Euphorbia hirta            | Euphorbiaceae| D.R. Congo    | Aerial Parts     | Methanol, Ethanol  | Gooda              | 1.1—5.4 µg/ml IC50       | Plasmodium falciparum      | No                       |
|                           |              |               | Whole Plant      | Petroleum Ether    | Very Good          | 1.2 µg/ml IC50           | Plasmodium falciparum      | Nd                       |
| Euphorbia triculli         | Euphorbiaceae| South Africa  | Leaves           | Dichloromethane    | Moderate           | 12 µg/ml IC50           | Plasmodium falciparum D10   | Nd                       |
| Fadogia agrestis           | Rubiaceae    | Burkina Faso  | Leaves           | Crude Alkaloid     | Good               | 4–10 µg/ml IC50          | Plasmodium falciparum W2   | Nd                       |
| Fagara macrophylla         | Rutaceae     | Ivory Coast   | Stem Barks       | Ethanol            | Very Good          | 2.3 µg/ml IC50           | Plasmodium falciparum Fcb1/Colombia Strain | No                       |
| Fagapanis angolensis       | Rutaceae     | Kenya         | Stem Barks       | Methanol           | Good               | 4.2–6.9 µg/ml IC50       | Plasmodium falciparum D6, W2 | Nd                       |
| Fagraea fragrans           | Gentianaceae | Cambodia      | Stems            | Dichloromethane    | Moderate           | 12.8 µg/ml IC50          | Plasmodium falciparum W2   | Nd                       |
| Ficus capraefolia          | Moraceae     | Burkina Faso  | Leaves           | Dichloromethane    | Very Good          | 1.8 µg/ml IC50           | Plasmodium falciparum      | Yes (SI ≥ 77; mouse [NBMH]) |
| Ficus platyphylla          | Moraceae     | Nigeria       | Ns               | Methanol, Water, Butanol, Ethyl Acetate | Moderate | 13.77–15.28 µg/ml IC50 | Plasmodium falciparum 3D7, K1 | Yes (SI = 0.4; HepG2 cells) |
| Ficus sur                  | Moraceae     | Kenya         | Stem Barks       | Methanol           | Moderate           | 8.5–15.9 µg/ml IC50      | Plasmodium falciparum D6, W2 | Nd                       |
|                           |              | Kenya         | Stem Barks       | Chloroform, Hexane | Moderate           | 9.0–19.2 µg/ml IC50      | Plasmodium falciparum K39 (CQ-S), ENT30, NF54, V1/S | Nd                       |
| Ficus thornningii          | Moraceae     | Republic Of Congo | Leaves   | Methanol, Ethanol  | Good               | 9.61 µg/ml IC50          | Plasmodium falciparum      | No                       |
|                           |              | Nigeria       | Ns               | Methanol, Water, Butanol, Ethyl Acetate | Moderate | 14.09–25.06 µg/ml IC50 | Plasmodium falciparum 3D7, K1 | Yes (SI ≥ 103; mouse [NBMH]) |
| Plant species        | Plant family       | Source           | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | IC50 or ED50 or LD50 | Strain of Plasmodium Tested | Toxicity (value; assay) |
|----------------------|-------------------|------------------|------------------|-------------------|-------------------|-------------------------|------------------------|---------------------------|---------------------------|
| Ficus sycomorus      | Moraceae          | Burkina Faso     | [27]             | Leaves            | Crude Alkaloid    | Good                    | 4–10 µg/ml IC50         | Plasmodium falciparum W2  | Nd                        |
| Flueggea virosa      | Phyllanthaceae    | Comoros          | [91]             | Leaves            | Water/Methanol    | Very Good               | 2 µg/ml IC50            | Plasmodium falciparum W2  | No                        |
|                      |                   | Kenya            | [26]             | Stem Barks        | Methanol          | Very Good               | 2.2–3.6 µg/ml IC50      | Plasmodium falciparum D6, W2 | Nd                        |
|                      |                   | South Africa     | [22]             | Leaves, Twigs     | Water             | Moderate                | 11.4 µg/ml IC50         | Plasmodium falciparum D10 | Nd                        |
| Fuerstia africana    | Lamiaceae         | Rwanda           | [92]             | Leaves, Stems     | Methanol          | Good                    | 4.1–6.9 µg/ml IC50      | Plasmodium falciparum 3D7, W2 | Yes (SI = 1.9; human normal foetal lung fibroblast [WI-38]) |
|                      |                   | Kenya            | [21]             | Leaves            | Methanol          | Very Good               | 3.75 µg/ml IC50         | Plasmodium falciparum D6  | No                        |
|                      |                   | Kenya            | [24]             | Whole Plant       | Methanol          | Very Good               | 0.9–2.4 µg/ml IC50      | Plasmodium falciparum D6, W2 | Nd                        |
| Funtumia elastica    | Apocynaceae       | Ivory Coast      | [43]             | Stem Barks        | Ethanol           | Very Good               | 3.6 µg/ml IC50          | Plasmodium falciparum FCB1 | Nd                        |
|                      |                   | Ivory Coast      | [28]             | Stem Barks        | Ethanol           | Very Good               | 3.3 µg/ml IC50          | Plasmodium falciparum Fcb4/ Colombia Strain | No                        |
| Funtumia latifolia   | Apocynaceae       | Uganda           | [75]             | Leaves            | Ethyl Acetate     | Nd                      | nd                     | Plasmodium falciparum Fcb4 | Nd                        |
| Garcinia kola        | Clusiaceae        | D.R. Congo       | [67]             | Seeds             | Ethanol, Methanol, Petroleum Ether, Chloroform | Good | 1.02—15.75 µg/ml IC50 | Plasmodium falciparum     | Nd                        |
| Gardenia lutea       | Rubiaceae         | Sudan            | [69]             | Stem Barks        | Petroleum Ether   | Very Good               | 1.6 µg/ml IC50          | Plasmodium falciparum     | Nd                        |
| Gardenia sakotensis  | Rubiaceae         | Burkina Faso     | [23]             | Leaves            | Methanol          | Good                    | 3.3–5.2 µg/ml IC50      | Plasmodium falciparum 3D7, D2 | No                        |
| Glirussus oppositi‑ | Malluginaceae     | Mali             | [62]             | Aerial parts      | Dichloromethane   | Moderate                | 14.01 µg/ml IC50        | Plasmodium falciparum 3D7 & W2 | Nd                        |
| folius               |                   |                  | [93]             |                  | Chloroform        | Moderate                | 15.52–18.70 µg/ml IC50  | Plasmodium falciparum W2 & 3D7 | No                        |
| Gloriosa superba     | Colchicaceae      | South Africa     | [22]             | Whole plant       | Dichloromethane/Methanol | Moderate | 17 µg/ml IC50      | Plasmodium falciparum D10 | Nd                        |
| Gnidia cuneata       | Thymeleaceae      | South Africa     | [22]             | Stems             | Dichloromethane   | Moderate                | 15.9 µg/ml IC50         | Plasmodium falciparum D10 | Nd                        |
| Gnidia kraussiana var. kraussiana | Thymeleaceae | South Africa | [22]             | Leaves, Twigs     | Dichloromethane/Methanol | Moderate | 10.8 µg/ml IC50 | Plasmodium falciparum D10 | Nd                        |
| Gomphrena celosoides | Amaranthaceae     | Benin            | [65]             | Aerial Parts      | Methanol          | Good                    | 4.26–14.97 µg/ml IC50   | Plasmodium falciparum 3D? & K1 | Nd                        |
|                      |                   | Togo             | [70]             | Aerial Parts      | Water             | Moderate                | < 15 µg/ml IC50         | Plasmodium falciparum K1  | Nd                        |
|                      |                   | Tanzania         | [20]             | Whole plant       | Ethyl Acetate     | Moderate                | 15 µg/ml IC50           | Plasmodium falciparum K1  | Nd                        |
| Guiera senegalensis  | Combretaceae      | Ivory Coast      | [57]             | Stem, Leave       | Water             | Good                    | 0.79–7.03 µg/ml IC50    | Plasmodium falciparum Fcb1 & F32 | Nd                        |
|                      |                   | Mali             | [94]             | Roots             | Chloroform        | Very Good               | < 4 µg/ml IC50          | Plasmodium falciparum     | Nd                        |
| Gutenbergia cordifolia | Asteraceae       | Kenya            | [21]             | Leaves            | Methanol          | Very Good               | 4.40 µg/ml IC50         | Plasmodium falciparum D6  | No                        |
| Gynandropsis gynandra | Cleomaceae       | Tanzania         | [20]             | Roots             | Ethyl Acetate     | Moderate                | 14 µg/ml IC50           | Plasmodium falciparum K1  | Nd                        |
| Plant species       | Plant family      | Source          | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | IC50 or ED50 or LD50 | Strain of Plasmodium Tested | Toxicity (value; assay) |
|---------------------|-------------------|-----------------|------------------|--------------------|--------------------|-------------------------|------------------------|-----------------------------|--------------------------|
| H. suaveolens       | Lamiaceae         | Nigeria         | [53]              | Leaves             | Petroleum Ether    | Very Good               | 2.54 µg/ml IC50        | Plasmodium falciparum      | Nd                       |
| Haplophyllum        | Rutaceae          | Sudan           | [23]              | Aerial Parts       | Methanol           | Very Good               | 1.2–1.5 µg/ml IC50     | Plasmodium falciparum      | No                       |
| Harrisonia abys-    | Rutaceae          | Sudan           | [58]              | Stem Barks         | Methanol           | Good                    | 4.7–10 µg/ml IC50       | Plasmodium falciparum      | Nd                       |
| Harrisonia perforata| Rutaceae          | Cambodia        | [45]              | StemS              | Dichloromethane    | Good                    | 6.0 µg/ml IC50          | Plasmodium falciparum W2   | Nd                       |
| Harungana mad-       | Hypericaceae       | D.R.Congo       | [40]              | Stem Barks         | Water              | Good                    | 9.64 µg/ml IC50         | Plasmodium falciparum K1   | No                       |
| Harrisonia          | Hypericaceae       | Tanzania        | [20]              | Roots              | Ethyl Acetate      | Very Good               | 4.0 µg/ml IC50          | Plasmodium falciparum K1   | Nd                       |
| Helichrysum         | Asteraceae         | Madagascar      | [96]              | Leaves             | Essential Oil      | In Active               | 25 mg/l                | Plasmodium falciparum Fcb1 | Nd                       |
| Heli-              | Asteraceae         | South Africa    | [97]              | Leaves             | Water, Essential Oil| Very Good              | 1.25 µg/ml IC50         | Plasmodium falciparum FCR-3| Yes                      |
| Heli-              | Asteraceae         | South Africa    | [22]              | Whole plant        | Dichloromethane/Methanol | Good                | 6.8 µg/ml IC50          | Plasmodium falciparum D10  | Nd                       |
| Hermannia           | Malvaceae          | South Africa    | [22]              | Whole plant        | Dichloromethane/Methanol | Good                | 6.9 µg/ml IC50          | Plasmodium falciparum D10  | Nd                       |
| Hexalobus           | Annonaceae         | Cameroon        | [98]              | Stem Barks         | Water              | Very Good               | 2.0 µg/ml IC50          | Plasmodium falciparum W6   | Nd                       |
| Hippobromus         | Sapindaceae        | South Africa    | [22]              | Twigs              | Dichloromethane/Methanol | Good                | 5.9 µg/ml IC50          | Plasmodium falciparum D10  | Nd                       |
| Holanthera          | Apocynaceae        | Cameroon        | [99]              | Stem Barkss        | Water, Ethanol     | Good                    | 1.02 – 18.53 µg/ml IC50 | Plasmodium falciparum W2, D6, FCR-3, 3D7 | Nd                       |
| Hoslandia           | Lamiaceae          | Tanzania        | [20]              | Root Barks         | Petroleum Ether    | Moderate                | 10 µg/ml IC50           | Plasmodium falciparum K1   | Nd                       |
| Hunteria eburnea    | Apocynaceae        | Uganda          | [75]              | Leaves             | Methanol           | Moderate                | 15.2–25.6 µg/ml IC50    | Plasmodium falciparum D6, W2 | Nd                       |
| Hunteria            | Apocynaceae        | Ivory Coast     | [43]              | Stem Barks         | Ethanol            | Very Good               | 2.2 µg/ml IC50          | Plasmodium falciparum Fcb5 | Nd                       |
| Hybanthus           | Violaceae          | Benin           | [65]              | Aerial Parts       | Methanol           | Moderate                | 2.57–> 20 µg/ml IC50    | Plasmodium falciparum 3D7 & K1 | Nd                       |
| Hybrus              | Phyllanthaceae      | Ivory Coast     | [51]              | Leaves             | Methylene Chloride | Good                    | 6.9 µg/ml IC50          | Plasmodium falciparum K1   | Yes (SI = 6–10; rat skeletal muscle myoblast [L6]) |
| Hypericum           | Hypericaceae       | South Africa    | [22]              | Leaves/ Flowers    | Dichloromethane/Methanol | Very Good  | 1.4 µg/ml IC50         | Plasmodium falciparum D10  | Nd                       |
| Hypericum           | Hypericaceae       | Cameroon        | [80]              | Stem Barks         | Methanol, N-Hexane, Ethyl Acetate, N-Butanol | Very Good | 3.98 µg/ml IC50        | Plasmodium falciparum W2, SHF4 | Nd                       |
| Plant species          | Plant family     | Source            | Country of study | Part of plant used | Extraction solvent                  | Antiplasmodial Activity | IC50 or ED50 or LD50 | Strain of Plasmodium Tested | Toxicity (value; assay) |
|------------------------|------------------|-------------------|------------------|--------------------|-------------------------------------|-------------------------|-----------------------|---------------------------|--------------------------|
| Hypoestes forskoalli   | Acanthaceae      | [24] Kenya        | Root Barks       | Methanol           | Good                                | 4.3–6.7 µg/ml IC50      | Plasmodium falciparum D6, W2 | Nd                        |                         |
| Hyptis pectinata       | Lamiaceae        | [22] South Africa | Leaves, Stem, Flower | Dichloromethane/Methanol | Moderate                           | 17.3 µg/ml IC50         | Plasmodium falciparum D10 | Nd                        |                         |
| Icacinia senegalensis  | Icacinaceae      | [100] Senegal     | Leaves           | Methanol           | Good                               | 4.7–8 µg/ml IC50        | Plasmodium falciparum 3D7, 7G | No                       |                         |
| Isolona hexaloba       | Annonaceae       | [40] D.R. Congo   | Root Barks       | Water              | Moderate                           | 15.28 µg/ml IC50        | Plasmodium falciparum K1     | No                       |                         |
| Khaya grandifoliola    | Meliaceae        | [101] Nigeria     | Ns               | Methanol-Methylene Chloride | Gooda                             | 1.25—9.63 µg/ml IC50    | Plasmodium falciparum W2   | Nd                        |                         |
| Khaya senegalensis     | Meliaceae        | [50] Nigeria      | Ns               | Methanol, Water, Butanol, Ethyl Acetate | Moderate                          | 15.46–28.12 µg/ml IC50   | Plasmodium falciparum 3D7, K1 | Yes (SI ≥ 69; mouse [NBMH]) |                         |
| Kigelia africana       | Bignoniaceae     | [24] Kenya        | Leaves           | Methanol           | Moderate                           | 15.9 µg/ml IC50         | Plasmodium falciparum D6, W2 | Nd                        |                         |
| Kirkia wilmsii         | Kirkiaecae       | [80] Cameroon     | Stem Barks       | Ethyl Acetate      | Moderate                           | 11.15 µg/ml IC50        | Plasmodium falciparum W2     | No                       |                         |
| Kniphofia foliosa      | Xanthorrhoeaceae | [102] Ethiopia    | Roots            | Dichloromethane    | Very Good                          | 3.7 µg/ml IC50          | Plasmodium falciparum D10   | Nd                        |                         |
| Landolphia tanceolata  | Apocynaceae      | [103] Congo Brazzaville | Roots          | Dichloromethane    | Moderate                           | 11 µg/ml IC50           | Plasmodium falciparum Fcm29-Cameroon | Nd                       |                         |
| Lannea edulis          | Anacardiaceae    | [20] Kenya        | Whole Plant      | Ethyl Acetate      | Moderate                           | 17 µg/ml IC50           | Plasmodium falciparum K1      | Nd                       |                         |
| Lantana camara         | Verbenaceae      | [22] South Africa | Leaves, Twigs    | Dichloromethane/Methanol | Moderate                           | 11 µg/ml IC50           | Plasmodium falciparum D10     | Nd                       |                         |
| Leonotis mollisima     | Lamiaceae        | [20] Tanzania     | Leaves           | Ethyl Acetate      | Good                               | 9 µg/ml IC50            | Plasmodium falciparum K1      | Nd                       |                         |
| Leonotis africana      | Lamiaceae        | [33] Gabon        | Stems            | Dichloromethane    | Moderate                           | 15.2–27.1 µg/ml IC50    | Plasmodium falciparum Fcbm W2 | Yes (SI = 6.07–6.82; human embryonic lung cells [MRC-5]) |                         |
| Leonotis leonurus      | Lamiaceae        | [22] South Africa | Leaves, Twigs    | Dichloromethane/Methanol | Good                              | 5.4 µg/ml IC50         | Plasmodium falciparum D10     | Nd                       |                         |
| Leonotis nepetifolia   | Lamiaceae        | [22] South Africa | Whole Plant      | Dichloromethane/Methanol | Moderate                           | 15 µg/ml IC50           | Plasmodium falciparum D10     | Nd                       |                         |
| Leonotis acymifolia    | Lamiaceae        | [22] South Africa | Leaves           | Dichloromethane/Methanol | Good                               | 6.1 µg/ml IC50         | Plasmodium falciparum D10     | Nd                       |                         |
| Leptadenia madagas-   | Apocynaceae      | [91] Comoros      | Ns               | Dichloromethane    | Good                               | 9 µg/ml IC50            | Plasmodium falciparum W2      | No                       |                         |
| cascanensis            |                 |                   |                  |                    |                  |                     |                                      |                         |                         |
| Leucas calostachys     | Lamiaceae        | [95] Kenya        | Whole Plant      | Water              | Very Good                          | 0.79 µg/ml IC50         | Plasmodium Knowlesi          | Nd                       |                         |
| Leucas martiniensis    | Lamiaceae        | [22] South Africa | Whole Plant      | Dichloromethane/Methanol | Moderate                           | 13.3 µg/ml IC50        | Plasmodium falciparum D10     | Nd                       |                         |
| Plant species       | Plant family       | Source      | Country of study | Part of plant used | Extraction solvent                  | Antiplasmodial Activity | IC$_{50}$ or ED$_{50}$ or LD$_{50}$ | Strain of Plasmodium Tested | Toxicity (value; assay) |
|---------------------|-------------------|-------------|------------------|-------------------|-------------------------------------|-------------------------|--------------------------------------|-------------------------------|--------------------------|
| *Lippia javanica*   | Verbenaceae       | [24] Kenya  | Root barks       | Methanol          | Good                                | 5.9 µg/ml IC$_{50}$     | Plasmodium falciparum D6, W2        | Nd                           |                         |
|                     |                   | [104] Kenya | Roots            | Dichloromethanol/ Ethyl Acetate | Moderate                  | 16.7—19.2 µg/ml IC$_{50}$ | Plasmodium falciparum K39, V1/S     | Nd                           |                         |
|                     |                   | [22] South Africa | Roots             | Dichloromethane | Very Good                              | 3.8 µg/ml IC$_{50}$     | Plasmodium falciparum D10           | Nd                           |                         |
|                     |                   | [25] South Africa | Leaves           | Acetone           | Very Good                              | 4.26 µg/ml IC$_{50}$   | Plasmodium falciparum UP1 (CQ-R)     | Nd                           |                         |
| *Lippia multiflora* | Verbenaceae       | [57] Ivory Coast | Leaves           | Water             | Very Good                              | 1.18—2.34 µg/ml IC$_{50}$ | Plasmodium falciparum Fcb1 & F32   | Nd                           |                         |
| *Lophira lanceolata*| Ochnaceae         | [52] Burkina Faso | Leaves           | Dichloromethanol | Very Good                              | 4.7 µg/ml IC$_{50}$     | Plasmodium falciparum               | Nd                           |                         |
| *Ludwigia erecta*   | Onagraceae        | [24] Kenya  | Whole plant      | Methanol          | Very Good                              | 0.9—1.6 µg/ml IC$_{50}$ | Plasmodium falciparum D6, W2        | Nd                           |                         |
| *Macroystis squarrosa* | Rutaceae        | [22] South Africa | Stems            | Dichloromethanol/Methanol | Moderate                  | 16 µg/ml IC$_{50}$     | Plasmodium falciparum D6, W2        | Nd                           |                         |
| *Maesa lanceolata*  | Primulaceae       | [22] South Africa | Twigs            | Dichloromethanol/Methanol | Good                      | 5.9 µg/ml IC$_{50}$   | Plasmodium falciparum D10           | Nd                           |                         |
| *Markhamia lutea*   | Bignoniaceae      | [76] Uganda  | Leaves           | Ethyl Acetate     | Nd                                    | Nd                     | Plasmodium falciparum Fcb6          | Nd                           |                         |
| *Maytenus heterophylla* | Celastraceae    | [24] Kenya  | Root barks       | Methanol          | Very Good                              | 1.8—3.9 µg/ml IC$_{50}$ | Plasmodium falciparum D6, W2        | Nd                           |                         |
| *Maytenus obtusifolia* | Celastraceae    | [24] Kenya  | Root barks       | Methanol          | Good                                  | <1.9—5.8 µg/ml IC$_{50}$ | Plasmodium falciparum D6, W2        | Nd                           |                         |
| *Maytenus pitterlioides* | Celastraceae    | [26] Kenya  | Root barks       | Methanol          | Good                                  | 4.4—10.2 µg/ml IC$_{50}$ | Plasmodium falciparum D6, W2        | Nd                           |                         |
| *Maytenus senegalensis* | Celastraceae    | [58] Sudan  | Stem barks       | Methanol          | Nd                                    | 3.9—10 µg/ml IC$_{50}$ | Plasmodium falciparum D37, Dd9      | Nd                           |                         |
|                     |                   | [26] Kenya  | Root barks       | Methanol          | Good                                  | 4.7—9.8 µg/ml IC$_{50}$ | Plasmodium falciparum D6, W2        | Nd                           |                         |
|                     |                   | [22] South Africa | Roots            | Dichloromethanol | Moderate                              | 15.5 µg/ml IC$_{50}$   | Plasmodium falciparum D10           | Nd                           |                         |
|                     |                   | [20] Tanzania | Stem barks       | Ethyl Acetate     | Very Good                              | 0.16 µg/ml IC$_{50}$   | Plasmodium falciparum K1            | Nd                           |                         |
|                     |                   | [31] Tanzania | Roots            | Ethanol           | Very Good                              | 2.05 µg/ml IC$_{50}$   | Plasmodium falciparum K1            | No                           |                         |
| *Maytenus undata*   | Celastraceae      | [26] Kenya  | Leaves           | Water             | Very Good                              | 0.95—1.9 µg/ml IC$_{50}$ | Plasmodium falciparum D6, W2        | Nd                           |                         |
| *Melia azedarach*   | Meliaceae         | [46] D.R. Congo | Leaves           | Dichloromethanol  | Moderate                              | 19.14 µg/ml IC$_{50}$  | Plasmodium falciparum 3D7, W2, Plasmodium berghei berghei | Nd                           |                         |
| *Microdesmis keeyana* | Pandaceae         | [51] Ivory Coast | Leaves           | Methylene Chloride | Moderate                              | 12.2 µg/ml IC$_{50}$   | Plasmodium falciparum K1            | No                           |                         |
| *Microglossa pynfolia* | Asteraceae       | [24] Kenya  | Leaves           | Methanol          | Moderate                              | 10.4 µg/ml IC$_{50}$   | Plasmodium falciparum D6, W2        | Nd                           |                         |
|                     |                   | [77] Uganda  | Leaves           | Ethyl Acetate     | Very Good                              | 0.03—0.05 µg/ml IC$_{50}$ | Plasmodium falciparum NF54 & FCR3  | Nd                           |                         |
|                     |                   | [92] Rwanda  | Leaves           | Dichloromethane   | Very Good                              | 1.5—2.4 µg/ml IC$_{50}$ | Plasmodium falciparum 3D7, W2, Yes (SI = 3.2; human normal foetal lungfibroblast [WI-38]) | Nd                           |                         |
| *Mikania cordata*   | Compositae        | [20] Tanzania | Leaves           | Ethyl Acetate     | Moderate                              | 14 µg/ml IC$_{50}$     | Plasmodium falciparum K1            | Nd                           |                         |
Table 1 (continued)

| Plant species       | Plant family | Source of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | IC50 or ED50 or LD50 | Strain of Plasmodium Tested | Toxicity (value; assay) |
|---------------------|--------------|-----------------|--------------------|--------------------|-------------------------|----------------------|-----------------------------|--------------------------|
| Millettia zechiana  | Fabaceae     | [28] Ivory Coast | Stem Barks         | Ethanol            | Moderate                | 16.1 µg/ml IC50       | Plasmodium falciparum Fcb1/Colombia Strain | Nd                       |
|                     |              | [43] Ivory Coast | Stem Barks         | Ethanol            | Moderate                | 14.1 µg/ml IC50       | Plasmodium falciparum Fcb1 | Nd                       |
| Momordica balsamina| Cucurbitaceae| [22] South Africa| Stems              | Dichloromethane/Methanol | Good                   | 5.3 µg/ml IC50        | Plasmodium falciparum D10 | Nd                       |
|                     |              | [68] Mozambique  | Aerial Parts       | ns                 | Very Good*              | 1 µM                 | Plasmodium berghei, Plasmodium falciparum | Nd                       |
| Momordica charantia | Cucurbitaceae| [88] Nigeria     | Leaves             | Methanol           | Very Good               | 12.5 nM              | Plasmodium falciparum   | Nd                       |
| Momordica foetida   | Cucurbitaceae| [77] Uganda      | Leaves             | Water              | Good                    | 0.35–6.16 µg/ml IC50  | Plasmodium falciparum NF54 & FCR3 | Nd                       |
| Monodora myristica  | Annonaceae   | [33] Gabon       | Stem               | Methanol           | Good                    | 5.5–6.1 µg/ml IC50    | Plasmodium falciparum Fcbm W2 | No                      |
|                     |              | [49] Cameroon    | Leaves             | Methanol           | Good                    | 9.03 µg/ml IC50       | Plasmodium falciparum W2 | Nd                       |
| Morinda lucida      | Rubiaceae    | [74] S. Tome’ & Pr Inc | Barks         | Ethanol            | Good < 10 µg/ml IC50    | Plasmodium falciparum D37 and Dd2 | Nd                       |
|                     |              | [88] Nigeria     | Leaves             | Methanol           | Very Good               | 25 nM                | Plasmodium falciparum   | Nd                       |
|                     |              | [53] Nigeria     | Roots              | Dichloromethane    | Moderate                | 13.37 µg/ml IC50      | Plasmodium falciparum D10 | Nd                       |
| Morinda marindoides | Rubiaceae    | [43] Ivory Coast | Leaves             | Ethanol            | Good                    | 9.8 µg/ml IC50        | Plasmodium falciparum Fcb1 | Nd                       |
|                     |              | [28] Ivory Coast | Leaves             | Ethanol            | Moderate                | 11.6 µg/ml IC50       | Plasmodium falciparum Fcb1/Colombia Strain | Nd                       |
| Moringa oleifera    | Moringaceae  | [26] Kenya       | Leaves             | Methanol           | Moderate                | 9.8 µg/ml IC50        | Plasmodium falciparum D6, W2 | Nd                       |
| Motandra guineensis | Apocynaceae  | [43] Ivory Coast | Leaves             | Ethanol            | Moderate                | 16.3 µg/ml IC50       | Plasmodium falciparum Fcb1 | Nd                       |
| Mundulea seneca     | Fabaceae     | [86] Namibia     | Leaves, Shoots     | Methanol           | Very Good               | 3.279–3.352 µg/ml IC50 | Plasmodium falciparum D37 | Nd                       |
| Mitragyna inermis   | Rubiaceae    | [93] Mali        | Leaves             | Chloroform         | Very Good               | 4.36–4.82 µg/ml IC50  | Plasmodium falciparum W2 & 3D7 | No                      |
| Nauclea latifolia   | Rubiaceae    | [93] Mali        | Barks              | Chloroform         | Good                    | 5.36–6.2 µg/ml IC50   | Plasmodium falciparum W2 & 3D7 | Yes (IC50 = 50 µg/ml; BALB/C mouse) |
|                     |              | [28] Ivory Coast | Barks              | Ethanol            | Good                    | 8.9 µg/ml IC50        | Plasmodium falciparum D37 | No                      |
|                     |              | [106] Ivory Coast| Roots, Stem        | Water              | Good                    | 0.6–7.5 µg/ml IC50    | Plasmodium falciparum Fcb1-Colombian And Nigerian Strains | Nd                       |
|                     |              | [43] Ivory Coast | Roots, Barks       | Ethanol            | Good                    | 7.3 µg/ml IC50        | Plasmodium falciparum Fcb1 | Nd                       |
| Nauclea pobe- gounii | Rubiaceae    | [107] D.R.Congo  | Stem Barks         | Ethanol            | In Active               | 32 µg/ml IC50         | Plasmodium falciparum, Plasmodium yeoli, Plasmodium berghei | No                      |
| Plant species                  | Plant family    | Source            | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | IC50 or ED50 or LD50 | Strain of Plasmodium Tested | Toxicity (value; assay) |
|-------------------------------|----------------|-------------------|------------------|-------------------|-------------------|-------------------------|------------------------|----------------------------|--------------------------|
| Neoboutonia glabrescens       | Euphorbiaceae  | Cameroon          | [55]              | Leaves            | Ethanol, Water, Dichloromethylene, Methanol, Hexane | Good                   | 7.56 µg/ml IC50          | Plasmodium falciparum W2 | Nd                       |
| Neorautanenia mits            | Fabaceae       | Tanzania          | [31]              | Tubers            | Ethanol           | Very Good               | 1.58 µg/ml IC50          | Plasmodium falciparum K1 | No                       |
| Neopokaba laevis              | Bignognaceae   | Togo              | [108]             | Leaves            | Ethanol           | Moderate                | 12.6 µg/ml IC50          | Plasmodium falciparum     | Nd                       |
| Newbouldia laevis             | Fabaceae       | Nigeria           | [109]             | Leaves            | Water             | Moderate                | 19.5 µg/ml IC50          | Plasmodium falciparum     | Nd                       |
|                           |                | Nigeria           | [53]              | Roots             | Dichloromethylene  | Good                   | 5.00 µg/ml IC50          | Plasmodium falciparum D10 | Nd                       |
| Ocimum americana              | Lamiaceae      | Kenya             | [24]              | Whole Plant       | Methanol          | Moderate                | 8.9–12.1 µg/ml IC50      | Plasmodium falciparum D6, W2 | Nd                       |
| Ocimum basilicum              | Lamiaceae      | D.R. Congo        | [159]             | Leaves            | Ethanol, Methanol, Petroleum Ether, Chloroform | Good                   | < 0.35–18 µg/ml IC50     | Plasmodium falciparum     | Nd                       |
| Ocimum gratissimun            | Lamiaceae      | Kenya             | [26]              | Leaves            | Methanol          | Moderate                | 16.4 µg/ml IC50          | Plasmodium falciparum D6, W2 | Nd                       |
| Ocimum kilimandschwaricum     | Lamiaceae      | Kenya             | [30]              | Leaves, Twigs     | Dichloromethane   | Good                   | 8.616 µg/ml IC50         | Plasmodium falciparum D6, W2 | Nd                       |
| Olax gambeckola               | Olacaceae      | Ivory Coast       | [43]              | Whole Plant       | Ethanol           | Good                   | 5.2 µg/ml IC50           | Plasmodium falciparum FCB1 | Nd                       |
| Olea europaea                 | Oleaceae       | Kenya             | [24]              | Stem Barks        | Methanol          | Moderate                | 17.3 µg/ml IC50          | Plasmodium falciparum D6, W2 | Nd                       |
|                              |                | Kenya             | [21]              | Inner Barks       | Methanol          | Good                   | 9.48 µg/ml IC50          | Plasmodium falciparum D6  | No                       |
|                              |                | South Africa      | [22]              | Leaves            | Dichloromethane/Methanol | Moderate             | 12.0 µg/ml IC50          | Plasmodium falciparum D10 | Nd                       |
| Opilia celidifolia            | Opiliaceae     | Burkina Faso      | [52]              | Leaves            | Dichloromethane   | Very Good               | 2.8 µg/ml IC50           | Plasmodium falciparum     | Yes (SI = 0.4; HepG2 cells) |
|Ormocarpum trachycarpum        | Fabaceae       | Kenya             | [77]              | Stem Barks        | Dichloromethane/Ethyl Acetate | Moderate             | 17.5—19.6 µg/ml IC50     | Plasmodium falciparum K39, V1/S | Nd                       |
|Osteospermum imbricatum        | Asteraceae     | South Africa      | [22]              | Stems             | Dichloromethane/Methanol | Good                   | 7.3 µg/ml IC50           | Plasmodium falciparum D10 | Nd                       |
|Phyllanthus amarus             | Phyllanthaceae | Nigeria           | [53]              | Leaves            | Petroleum Ether   | Very Good               | 4.99 µg/ml IC50          | Plasmodium falciparum D10 | Nd                       |
|Pachypodanthium confine       | Annonaceae     | Cameroon          | [98]              | Stem Barks        | Water             | Moderate               | 16.6 µg/ml IC50          | Plasmodium falciparum W3  | Nd                       |
|Pappea capensis                | Sapindaceae    | South Africa      | [37]              | Twigs             | Dichloromethane   | Good                   | 5.47 µg/ml IC50          | Plasmodium falciparum NF54 | Nd                       |
| Plant species         | Plant family      | Source       | Country of study | Part of plant used | Extraction solvent              | Antiplasmodial Activity | IC50 or ED50 or LD50 | Strain of Plasmodium Tested | Toxicity (value; assay) |
|-----------------------|-------------------|--------------|------------------|-------------------|--------------------------------|-------------------------|-----------------------|-----------------------------|--------------------------|
| Parinari curatellifolia | Chrysobalanaceae  | [22] South Africa | Roots           | Dichloromethane   | Good                           | 5.3 µg/ml IC50           | Plasmodium falciparum D10 | Nd                          |                         |
|                       |                   | [24] Kenya    | Root Barks      | Methanol          | Good                           | 3.9–7.9 µg/ml IC50       | Plasmodium falciparum D6, W2 | Nd                          |                         |
|                       |                   | [37] South Africa | Stem Barks    | Dichloromethane   | Good                           | 6.99 µg/ml IC50           | Plasmodium falciparum NF54 | Nd                          |                         |
| Parinari excelsa      | Chrysobalanaceae  | [20] Tanzania | Stem Barks      | Ethyl Acetate     | Moderate                        | 10 µg/ml IC50             | Plasmodium falciparum K1  | Nd                          |                         |
|                       |                   | [75] Uganda   | Barks           | Ethyl Acetate     | Nd                             | Nd                       |                       |                             |                         |
| Parkinsonia aculeata  | Fabaceae          | [22] South Africa | Twigs           | Dichloromethane/Methanol | Good                           | 9 µg/ml IC50             | Plasmodium falciparum D10 | Nd                          |                         |
| Pavetta corymbosa     | Rubiaceae         | [65] Benin    | Aerial parts    | Methanol          | Moderate                        | 5.54–20 µg/ml IC50       | Plasmodium falciparum 3D7 & K1 | Nd                          |                         |
|                       |                   | [110] Togo    | Aerial parts    | Methanol          | Very Good                       | 2.042 µg/ml IC50         | Plasmodium falciparum    | Nd                          |                         |
| Pavetta crassipes     | Rubiaceae         | [27] Burkina Faso | Leaves         | Crude Alkaloid    | Very Good                       | <4 µg/ml IC50             | Plasmodium falciparum W2  | Nd                          |                         |
|                       |                   | [71] Togo     | Aerial parts    | Water             | Good                            | <7 µg/ml IC50             | Plasmodium falciparum    | Nd                          |                         |
| Pelargonium alchemilloides | Geraniaceae    | [22] South Africa | Whole plant     | Dichloromethane/Methanol | Moderate                       | 15 µg/ml IC50            | Plasmodium falciparum D10 | Nd                          |                         |
| Pentas lanceolata     | Rubiaceae         | [21] Kenya    | Root Barks      | Methanol          | Good                            | 5.15 µg/ml IC50           | Plasmodium falciparum D6  | No                          |                         |
| Pentas longiflora     | Rubiaceae         | [26] Kenya    | Root Barks      | Methanol          | Moderate                        | 13.3 µg/ml IC50           | Plasmodium falciparum D6, W2 | Nd                          |                         |
| Pentzia globosa       | Asteraceae        | [22] South Africa | Roots           | Dichloromethane   | Good                            | 8 µg/ml IC50             | Plasmodium falciparum D10 | Nd                          |                         |
| Phyllanthus amarus     | Phyllanthaceae    | [111] Ghana   | Whole Plant     | Ethanol           | Moderate                        | 11.7 µg/ml IC50           | Plasmodium falciparum Dd2 | No                          |                         |
| Phyllanthus fraternus  | Phyllanthaceae    | [112] Ghana   | Whole Plant     | Methanol          | Very Good                       | 0.44 µg/ml IC50           | Plasmodium falciparum 3D7, W2 | No                          |                         |
| Phyllanthus muellinenus | Phyllanthaceae   | [28] Ivory Coast | Leaves         | Ethanol           | Good                            | 9.4 µg/ml IC50            | Plasmodium falciparum Fcb1/ Colombia Strain | No                          |                         |
|                       |                   | [43] Ivory Coast | Leaves         | Ethanol           | Moderate                        | 10.3 µg/ml IC50           | Plasmodium falciparum Fcb1 | Nd                          |                         |
| Phyllanthus niruri     | Phyllanthaceae    | [69] D.R.Congo | Whole Plant     | Petroleum Ether   | Very Good                       | 1.3 µg/ml IC50            | Plasmodium falciparum     | Nd                          |                         |
| Phyllanthus uniflora   | Phyllanthaceae    | [45] Cambodia | Whole Plant     | Water             | Very Good                       | 2.4 µg/ml IC50            | Plasmodium falciparum W2  | Nd                          |                         |
| Physalis angulata      | Solanaceae        | [28] Ivory Coast | Whole Plant     | Ethanol           | Good                            | 7.9 µg/ml IC50            | Plasmodium falciparum Fcb1/ Colombia Strain | Nd                          |                         |
|                       |                   | [43] Ivory Coast | Whole Plant     | Ethanol           | Good                            | 7.9 µg/ml IC50            | Plasmodium falciparum FC1 | Nd                          |                         |
|                       |                   | [44] D.R. Congo | Leaves         | Methanol and dichloromethane | Very good                      | 1.27 µg/ml IC50           | Plasmodium falciparum 3D7, W2, Plasmodium berghei | No                          |                         |
| Plant species                  | Plant family  | Source         | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | IC50 or ED50 or LD50 | Strain of Plasmodium Tested | Toxicity (value; assay) |
|-------------------------------|---------------|----------------|------------------|--------------------|--------------------|------------------------|----------------------|-----------------------------|-------------------------|
| *Picralima nitida*            | Apocynaceae   | Nigeria        | Roots            | Ethanol            | Good               | 6.29 µg/ml IC50        | Plasmodium falciparum D10 | Nd                         |                         |
|                               |               | [53]           |                  |                    |                    |                        |                      |                             |                         |
|                               |               | Nigeria        | Stems            | Methanol           | Good               | 6.0–6.3 µg/ml IC50     | Plasmodium falciparum W2 | No                         |                         |
|                               |               | Cameroon       | Seeds            | Methanol           | Moderate           | 10.9 µg/ml IC50        | Plasmodium falciparum W2 | Nd                         |                         |
|                               |               | [89]           |                  |                    |                    |                        |                      |                             |                         |
|                               |               | Ivory Coast    | Root, Stem, Barks | Ns                 | Very Good          | 0.188–1.581 µg/ml IC50 | Plasmodium falciparum   | Nd                         |                         |
|                               |               | [114]          |                  |                    |                    |                        |                      |                             |                         |
| *Piper capense*               | Piperaceae    | Comoros        | Ns               | Dichloromethane    | Good               | 7 µg/ml IC50           | Plasmodium falciparum W2 | No                         |                         |
|                               |               | [91]           |                  |                    |                    |                        |                      |                             |                         |
| *Piptadeniastrum afric anus*  | Leguminosae   | D.R. Congo     | Stem, Barks      | Water had           | Good               | 6.11 µg/ml IC50        | Plasmodium falciparum K1 | Yes (SI = 1.4–1.5, human embryonic lung cells [MRC-5]) |                         |
|                               |               | [40]           |                  |                    |                    |                        |                      |                             |                         |
|                               |               | D.R. Congo     | Stem, Barks      | Water had           | Good               | 6.11 µg/ml IC50        | Plasmodium falciparum K1 | No                         |                         |
|                               |               | Cameroon       | Leaves           | Methanol           | Good               | 6.72 µg/ml IC50        | Plasmodium falciparum W2 | No                         |                         |
|                               |               | [49]           |                  |                    |                    |                        |                      |                             |                         |
|                               |               | Kenya          | Leaves           | Methanol           | Moderate            | 17.6–18.9 µg/ml IC50   | Plasmodium falciparum D6, W2 | No                         |                         |
|                               |               | [24]           |                  |                    |                    |                        |                      |                             |                         |
|                               |               | South Africa   | Whole Plant      | Dichloromethane    | Very Good          | 3 µg/ml IC50           | Plasmodium falciparum D10 | No                         |                         |
|                               |               | [22]           |                  |                    |                    |                        |                      |                             |                         |
|                               |               | South Africa   | Leaves           | Dichloromethane    | Very Good          | 3 µg/ml IC50           | Plasmodium falciparum D10 | No                         |                         |
|                               |               | [22]           |                  |                    |                    |                        |                      |                             |                         |
|                               |               | Kenya          | Root, Barks      | Methanol           | Good               | 6.43 µg/ml IC50        | Plasmodium falciparum D6 | No                         |                         |
|                               |               | [21]           |                  |                    |                    |                        |                      |                             |                         |
|                               |               | South Africa   | Twigs            | Dichloromethane-Methanol | Good              | 6.8 µg/ml IC50         | Plasmodium falciparum D10 | No                         |                         |
|                               |               | [22]           |                  |                    |                    |                        |                      |                             |                         |
|                               |               | Ghana          | Stem, Barks      | Ethanol, N-Hexane, Dichloromethane, Methanol-Ethyl Acetate | Good             | 3–6 µg/ml IC50         | Plasmodium falciparum K1  | No                         |                         |
|                               |               | [115]          |                  |                    |                    |                        |                      |                             |                         |
|                               |               | Ghana          | Stem, Barks      | Methanol, Chloroform, Cyclohexane, Ethyl Acetate | Good             | 4.53–10.17 µM IC50     | Plasmodium falciparum D10 | No                         |                         |
|                               |               | [116]          |                  |                    |                    |                        |                      |                             |                         |
|                               |               | Cameroon       | Stem, Barks      | Ethanol, Water, Dichloromethane, Methanol, Hexane | Very Good      | 4.30 µg/ml IC50        | Plasmodium falciparum W2  | No                         |                         |
|                               |               | [55]           |                  |                    |                    |                        |                      |                             |                         |
|                               |               | Cameroon       | Stem, Barks      | Methanol           | Very Good          | 3.43 µg/ml IC50        | Plasmodium falciparum W2  | No                         |                         |
|                               |               | [49]           |                  |                    |                    |                        |                      |                             |                         |
|                               |               | Cameroon       | Twigs            | Methanol           | Very Good          | 3.23 µg/ml IC50        | Plasmodium falciparum W2  | No                         |                         |
|                               |               | [49]           |                  |                    |                    |                        |                      |                             |                         |
|                               |               | Kenya          | Rhizome          | N-Hexane, Chloroform | Very Good     | 2.33—4.62 µg/ml IC50   | Plasmodium falciparum    | No                         |                         |
|                               |               | [117]          |                  |                    |                    |                        |                      |                             |                         |
|                               |               | Kenya          | Leaves           | Methanol           | Moderate           | 11.1 µg/ml IC50        | Plasmodium falciparum D6, W2 | No                         |                         |
|                               |               | [26]           |                  |                    |                    |                        |                      |                             |                         |
|                               |               | Nigeria        | Ns               | Methanol, Water, Butanol, Ethyl Acetate | Moderate | 14.97–15.28 µg/ml IC50 | Plasmodium falciparum 3D7, K1 | Yes (SI ≥ 99; mouse heart-derived cells [NBH]) |                         |
| Plant species          | Plant family | Source | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | Strain of Plasmodium Tested | Toxicity (value; assay) |
|------------------------|--------------|--------|------------------|--------------------|--------------------|-------------------------|----------------------------|--------------------------|
| Prunus africana        | Rosaceae     | [24]   | Kenya            | Stem Barks         | Methanol           | Moderate                | Plasmodium falciparum D6, W2 | Nd                       |
| Pseudospondias         | Anacardiaceae| [31]   | Tanzania         | Roots              | Ethanol            | Very Good               | Plasmodium falciparum K1    | No                       |
| Psidium guajava        | Myrtaceae    | [40]   | DR Congo         | Leaves             | Water              | Good                    | Plasmodium falciparum K1    | No                       |
| Psiadia punctata       | Asteraceae   | [22]   | South Africa     | Twigs              | Dichloromethane    | Good                    | Plasmodium falciparum D10   | Nd                       |
| Pterocarpus angolensis | Fabaceae     | [22]   | South Africa     | Roots              | Dichloromethane    | Moderate                | Plasmodium falciparum K1    | Nd                       |
| Pterocarpus erinaceus  | Fabaceae     | [118]  | Burkin Faso      | Leaves             | Ethanol, Chloroform| Good                    | Plasmodium falciparum D10   | Nd                       |
| Psorospermum senegalense| Hypericaceae | [63]   | Burkina Faso     | Leaves             | Dichloromethane    | Moderate                | Plasmodium falciparum 3D, W2 | No                       |
| Psidium guajava        | Myrtaceae    | [20]   | Tanzania         | Leaves             | Ethyl Acetate      | Moderate                | Plasmodium falciparum K1    | Nd                       |
| Pycnanthus angolensis  | Mynsticacae  | [28]   | Ivory Coast      | Stem Barks         | Ethanol            | Moderate                | Plasmodium falciparum Fcm29-Colombia Strain | Nd                       |
| Quassia africana       | Simaroubaceae| [103]  | Congo Brazzaville | Leaves            | Water, Ethanol, Dichloromethane | Very Good | Plasmodium falciparum Fcm29-Colombia Strain | Yes (IC_{50} = 6.7 µg/ml KB cells) |
| Ranunculus multifidus  | Ranunculaceae| [22]   | D.R. Congo       | Root Barks         | Water              | Very Good               | Plasmodium falciparum K1    | No                       |
| Rauvolfia caffra Sand  | Apocynaceae  | [37]   | South Africa     | Roots              | Dichloromethane    | Very Good               | Plasmodium falciparum NF54  | Nd                       |
| Rauvolfia oblongifolia| Apocynaceae  | [26]   | Kenya            | Root Barks         | Methanol           | Good                    | Plasmodium falciparum D6, W2 | Nd                       |
| Rauvolfia vomitoria    | Apocynaceae  | [53]   | Nigeria          | Roots              | Dichloromethane    | Very Good               | Plasmodium falciparum D10   | Nd                       |
| Quassia africana       | Simaroubaceae| [21]   | Kenya            | Root Barks         | Methanol           | Very Good               | Plasmodium falciparum D6    | Nd                       |
| Rheum officinale       | Rhamnaceae   | [77]   | Kenya            | Root Barks         | Methanol           | Moderate                | Plasmodium falciparum K39 (CQ-S), ENT30, NF54, V1/S | Nd                       |
| Rheum officinale       | Rhamnaceae   | [22]   | South Africa     | Twigs              | Dichloromethane/Methanol | Good | Plasmodium falciparum D10 | Nd                       |
| Plant species         | Plant family     | Source          | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | IC₅₀ or ED₅₀ or LD₃₀ | Strain of Plasmodium Tested | Toxicity (value; assay) |
|----------------------|------------------|-----------------|------------------|--------------------|--------------------|--------------------------|-----------------------|-----------------------------|--------------------------|
| Rumex abyssinicus    | Polygonaceae     | [92]            | Rwanda           | Roots              | Water              | Good                     | 8.0 µg/ml IC₅₀         | Plasmodium falciparum D10   | Nd                       |
| Rubia cordifolia     | Rubiaceae        | [95]            | Kenya            | Leaves/Seeds/Stems| Methanol           | Very Good                | 1.20 µg/ml IC₅₀         | Plasmodium Knowlesi         | Nd                       |
| Ricinus communis     | Euphorbiaceae    | [22]            | South Africa     | Stems              | Water              | Good                     | 3.1–4.3 µg/ml IC₅₀     | Plasmodium falciparum D6, W2 | Nd                       |
| Salvia radula        | Lamiaceae        | [22]            | South Africa     | Aerial Parts       | Methanol           | Good                     | 8.713 µg/ml IC₅₀       | Plasmodium falciparum FCR-3 | Nd                       |
| Salvia australis      | Lamiaceae        | [120]           | South Africa     | Aerial Parts       | Methanol/Chloroform| Moderate                | 15.863 µg/ml IC₅₀      | Plasmodium falciparum FCR-3 | Nd                       |
| Salvia bioculata      | Lamiaceae        | [120]           | South Africa     | Aerial Parts       | Methanol/Chloroform| Moderate                | 15.833 µg/ml IC₅₀      | Plasmodium falciparum FCR-3 | Nd                       |
| Salvia carnea         | Lamiaceae        | [20]            | Tanzania         | Roots              | Petroleum Ether    | Very Good                | 0.8 µg/ml IC₅₀         | Plasmodium falciparum K1    | Nd                       |
| Salvia corymbosa      | Lamiaceae        | [22]            | South Africa     | Aerial Parts       | Methanol           | Good                     | 6.235 µg/ml IC₅₀       | Plasmodium falciparum FCR-3 | Nd                       |
| Salvia dolomitica    | Lamiaceae        | [120]           | South Africa     | Aerial Parts       | Methanol/Chloroform| Moderate                | 13.953 µg/ml IC₅₀      | Plasmodium falciparum FCR-3 | Nd                       |
| Salvia divinorum      | Lamiaceae        | [22]            | South Africa     | Whole Plant        | Methanol/Chloroform| Moderate                | 11.873 µg/ml IC₅₀      | Plasmodium falciparum FCR-3 | Nd                       |
| Salvia radula         | Lamiaceae        | [120]           | South Africa     | Aerial Parts       | Methanol/Chloroform| Very Good               | 3.913 µg/ml IC₅₀       | Plasmodium falciparum FCR-3 | Yes (IC₅₀ = 20.12 µg/ml Kidney cells) |
| Salvia repens         | Lamiaceae        | [120]           | South Africa     | Aerial Parts       | Methanol/Chloroform| Good                   | 8.253 µg/ml IC₅₀       | Plasmodium falciparum FCR-3 | Nd                       |
| Salvia runcinata      | Lamiaceae        | [22]            | South Africa     | Whole Plant        | Methanol/Chloroform| Moderate                | 10.8 µg/ml IC₅₀        | Plasmodium falciparum D10   | Nd                       |
| Salvia schultenii     | Lamiaceae        | [120]           | South Africa     | Aerial Parts       | Methanol/Chloroform| Moderate                | 16.613 µg/ml IC₅₀      | Plasmodium falciparum FCR-3 | Nd                       |
| Salvia stenotaphyllum | Lamiaceae        | [120]           | South Africa     | Aerial Parts       | Methanol/Chloroform| Moderate                | 17.513 µg/ml IC₅₀      | Plasmodium falciparum FCR-3 | Nd                       |
| Sonchus schwantesii   | Compositae       | [95]            | Kenya            | Barks/ Roots       | Methanol           | Very Good               | 2.10 µg/ml IC₅₀        | Plasmodium Knowlesi         | Nd                       |
| Scaevola plumieri     | Goodeniaceae     | [22]            | South Africa     | Twigs              | Dichloromethane    | Moderate                | 11 µg/ml IC₅₀          | Plasmodium falciparum D10   | Nd                       |
| Schefflera umbellifera| Araliaceae       | [22]            | South Africa     | Leaves             | Dichloromethane    | Very Good               | 3.7 µg/ml IC₅₀         | Plasmodium falciparum D10   | Nd                       |
| Schizogygia cofaeoides| Apocynaceae     | [26]            | Kenya            | Leaves             | Methanol           | Moderate                | 10.5 µg/ml IC₅₀        | Plasmodium falciparum D6, W2| Nd                       |
| Schkhunia pinnata     | Compositae       | [24]            | Kenya            | Whole Plant        | Methanol           | Good                    | 1.3–6.8 µg/ml IC₅₀     | Plasmodium falciparum D6, W2| Nd                       |
| Schrankia leptocarpa  | Fabaceae         | [65]            | Benin            | Aerial Parts       | Methanol           | Moderate                | 3.38–20 µg/ml IC₅₀     | Plasmodium falciparum 3D7 & K1| Nd                       |
| Plant species       | Plant family       | Source           | Country of study | Part of plant used | Extraction solvent   | Antiplasmodial Activity | IC50 or ED50 or LD50 | Strain of Plasmodium Tested | Toxicity (value; assay) |
|---------------------|-------------------|------------------|------------------|--------------------|----------------------|-------------------------|------------------------|---------------------------|--------------------------|
| Scolocarya birrea   | Anacardiaceae     | [24]              | Kenya            | Stem Barks         | Methanol             | Moderate                | 5.9–24.9 µg/ml IC50   | Plasmodium falciparum D6, W2 | Nd                       |
| Secamone azelii     | Apocynaceae       | [65]              | Benin            | Aerial Parts       | Methanol             | Moderate                | 6.48–20 µg/ml IC50     | Plasmodium falciparum 3D7 & K1 | Nd                       |
| Securidaca longipedunculata | Polygalaceae | [121]             | Mali             | Leaves             | Dichloromethane      | Good                    | 6.9 µg/ml IC50         | Plasmodium falciparum 3D7 | Nd                       |
| Securinea virosa    | Phyllanthaceae    | [52]              | Burkina Faso     | Leaves             | Dichloromethane      | Good                    | 7.1 µg/ml IC50         | Plasmodium falciparum     | Nd                       |
| Senecio oxyriifolius| Asteraceae        | [22]              | South Africa     | Whole plant        | Dichloromethane/Methanol | Moderate           | 13 µg/ml IC50          | Plasmodium falciparum D10 | Nd                       |
| Senecio stuhlmannii | Asteraceae        | [56]              | Uganda           | Shoots             | Ethyl Acetate        | Moderate                | 14.0–15.2 µg/ml IC50   | Plasmodium falciparum D10, K1 | Nd                       |
| Senega didymobotrya | Fabaceae          | [22]              | South Africa     | Twigs              | Dichloromethane/Methanol | Good                | 9.5 µg/ml IC50         | Plasmodium falciparum D10 | Nd                       |
| Senna petersiana    | Fabaceae          | [22]              | South Africa     | Twigs              | Dichloromethane/Methanol | Moderate           | 13 µg/ml IC50          | Plasmodium falciparum D10 | Nd                       |
| Sida acuta          | Malvaceae         | [118]             | Burkina Faso     | Whole Plant Ns     | Ethanol, Chloroform, Water | Very Good          | 0.87–0.92 µg/ml IC50  | Plasmodium falciparum 3D7 And Dd2 | Nd                       |
| Solanum panduriforme| Solanaceae        | [25]              | South Africa     | Leaves             | Acetone              | Very Good              | 3.62 µg/ml IC50        | Plasmodium falciparum UP1 (CQ-R) | Nd                       |
| Solanecia mannii    | Asteraceae        | [92]              | Rwanda           | Leaves             | Dichloromethane      | Moderate                | 12.7–18.2 µg/ml IC50   | Plasmodium falciparum 3D7, W2 | Nd                       |
| Spilanthes mauritiana | Asteraceae       | [22]              | South Africa     | Stems              | Dichloromethane/Methanol | Good                 | 5.3 µg/ml IC50        | Plasmodium falciparum D10 | Nd                       |
| Staudia gabonensis | Myristicaceae     | [33]              | Gabon            | Stems              | Methanol             | Very Good              | 0.8 µg/ml IC50         | Plasmodium falciparum Fcbm W2 | Nd                       |
| Stephania abyssinica| Menispermaceae    | [24]              | Kenya            | Root Barks         | Methanol             | Good                    | 4.7–6.1 µg/ml IC50    | Plasmodium falciparum D6, W2 | Nd                       |
| Stephania rotundata | Menispermaceae    | [45]              | Cambodia         | Tubers             | Dichloromethane      | Very Good              | 1.0 µg/ml IC50         | Plasmodium falciparum W2 | Nd                       |
| Struchagia sparganophorum | Asteraceae  | [73]              | S. Torn, And Pri 'Ncipe | Leaves          | Petroleum Ether      | Good                    | < 10 µg/ml IC50       | Plasmodium falciparum 3D7 And Dd2 | Nd                       |
| Stynchonopsis thouarsii | Menispermaceae  | [122]             | Madagascar       | Stem Barks         | Methanol             | Very Good              | 3.1—4.2 µM           | Plasmodium falciparum NF54, Plasmodium yoelli 265 BY | No                       |
| Stynchos henningi   | Loganiaceae       | [72]              | Kenya            | Twigs              | Methanol             | Moderate                | 14.6–17.9 µg/ml IC50   | Plasmodium falciparum K1, NF54 | Nd                       |
| Stynchos pungens    | Loganiaceae       | [22]              | South Africa     | Leaves             | Dichloromethane      | Moderate                | 12.6 µg/ml IC50        | Plasmodium falciparum D10 | Nd                       |
| Stynchos spinosa    | Loganiaceae       | [123]             | Senegal          | Leaves, Stem       | Methanol, Water       | Moderate                | 15 µg/ml IC50         | Plasmodium falciparum     | Nd                       |
| Stynchos icaja      | Loganiaceae       | [46]              | D.R. congo       | Root barks         | Methanolic and dichloromethane | Very good           | 0.69 µg/ml IC50       | Plasmodium falciparum 3D7, W2, Plasmodium berghei berghei | Nd                       |
| Plant species                  | Plant family         | Source          | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | \( IC_{50} \) or \( ED_{50} \) or \( LD_{50} \) | Strain of Plasmodium Tested | Toxicity (value; assay) |
|-------------------------------|----------------------|-----------------|------------------|-------------------|--------------------|--------------------------|---------------------------------|-----------------------------|--------------------------|
| Suregada zanzibaricensis      | Euphorbiaceae        | [26] Kenya      | Leaves           | Methanol          | Good               | 5.8–6.7 µg/ml IC\(_{50}\) | Plasmodium falciparum D6, W2   | Nd                          |
| |                      |                     | [124] Kenya     | Leaves           | Methanol          | Very Good          | 1.82–4.66 µg/ml IC\(_{50}\) | Plasmodium falciparum D6, W2   | Nd                          |
| Syzygium cordatum subsp. cordatum | Myrtaceae           | [22] South Africa | Twigs            | Dichloromethane/Methanol | Moderate           | 14.7 µg/ml IC\(_{50}\) | Plasmodium falciparum D10       | Nd                          |
| |                      |                     | [37] South Africa | Leaves           | Dichloromethane   | Good               | 6.15 µg/ml IC\(_{50}\) | Plasmodium falciparum NF54      | Nd                          |
| Tabernaemon tana elegans      | Apocynaceae          | [37] South Africa | Roots            | Dichloromethane   | Very Good          | 0.33 µg/ml IC\(_{50}\) | Plasmodium falciparum NF54      | Nd                          |
| Tabernaemon tana pachysiphon  | Apocynaceae          | [26] Kenya      | Flower           | Methanol          | Very Good          | 4.4–4.8 µg/ml IC\(_{50}\) | Plasmodium falciparum D6, W2   | Nd                          |
| Tagetes minuta                | Asteraceae           | [75] Uganda     | Leaves           | Ethyl Acetate     | Nd                 | Nd                       | Plasmodium falciparum Fcb8      | Nd                          |
| Tamarindus indica             | Fabaceae             | [23] Sudan      | Stem, Barks      | Methanol          | Moderate           | 10 µg/ml IC\(_{50}\) | Plasmodium falciparum 3D7, Dd2 | No                          |
| |                      |                     | [110] Togo      | Fruits           | Water             | Very Good          | 4.786 µg/ml IC\(_{50}\) | Plasmodium falciparum          | Nd                          |
| Tapinanthus dodoneliformus    | Loranthaceae         | [52] Burkina Faso | Leaves           | Methanol          | Good               | 5.2 µg/ml IC\(_{50}\) | Plasmodium falciparum          | Nd                          |
| Taraxanthus camphoratus       | Asteraceae           | [22] South Africa | Whole Plant      | Dichloromethane/Methanol | Good               | 6 µg/ml IC\(_{50}\) | Plasmodium falciparum D10       | Nd                          |
| Teclea nobilis                | Rutaceae             | [24] Kenya      | Stem, Barks      | Methanol          | Moderate           | 3.9–20.4 µg/ml IC\(_{50}\) | Plasmodium falciparum D6, W2   | Nd                          |
| |                      |                     | [75] Uganda     | Barks            | Ethyl Acetate     | Nd                 | Nd                       | Plasmodium falciparum Fcb9      | Nd                          |
| Tecoma capensis               | Bignoniaceae         | [22] South Africa | Twigs            | Dichloromethane/Methanol | Moderate           | 12.28–14.09 µg/ml IC\(_{50}\) | Plasmodium falciparum 3D7, K1   | Yes (SI \(\geq\) 114; mouse heart-derived cells [NBMH]) |
| |                      |                     | [52] Burkina Faso | Leaves           | Methanol          | Very Good          | 1.9 µg/ml IC\(_{50}\) | Plasmodium falciparum          | Nd                          |
| Terminalia avicennioides      | Combretaceae         | [50] Nigeria    | Ns               | Methanol, Water, Butanol, Ethyl Acetate | Moderate | 12.28–14.09 µg/ml IC\(_{50}\) | Plasmodium falciparum 3D7, K1   | Yes (SI \(\geq\) 114; mouse heart-derived cells [NBMH]) |
| |                      |                     | [92] Ghana      | Leaves           | Methanol          | Moderate           | 11.7–26.3 µg/ml IC\(_{50}\) | Plasmodium falciparum 3D7, W2   | No                         |
| Terminalia macroptera         | Combretaceae         | [27] Burkina Faso | Roots            | Water             | Very Good          | 1 µg/ml IC\(_{50}\) | Plasmodium falciparum W2        | No                         |
| Terminalia mollis             | Combretaceae         | [26] Kenya      | Stem, Barks      | Methanol          | Moderate           | 7.9 µg/ml IC\(_{50}\) | Plasmodium falciparum 3D7, W2   | No                         |
| Terminalia spinosa             | Combretaceae         | [69] DR Congo   | Leaves           | Petroleum Ether   | Very Good          | 1.7 µg/ml IC\(_{50}\) | Plasmodium falciparum           | No                         |
| Tetrapleura tetraptera        | Fabaceae             | [33] Gabon      | Leaves           | Dichloromethane   | Moderate           | 10.1–13.0 µg/ml IC\(_{50}\) | Plasmodium falciparum FCb, 3D7  | No                         |
| Plant species       | Plant family       | Source          | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | IC₅₀ or ED₅₀ or LD₅₀ | Strain of Plasmodium Tested | Toxicity (value; assay) |
|---------------------|-------------------|-----------------|------------------|--------------------|--------------------|-------------------------|-----------------------|-----------------------------|--------------------------|
| Thalia geniculata   | Marantaceae       | [65] Benin       | Roots            | Methanol           | Moderate           | 2.83 - > 20 µg/ml IC₅₀ | Plasmodium falciparum    | Nd                          |
| Tinospora bakis     | Menispermaceae    | [34] Sudan       | Whole Plant      | Petroleum Ether/ Chloroform | Very Good          | < 5 µg/ml IC₅₀         | Plasmodium falciparum    | Nd                          |
| Tithonia diversifolia | Asteraceae       | [73] S. Tomé’ And Pri ‘Ncipe | Aerial Parts | Petroleum Ether, Dichloromethane | Good            | < 10 µg/ml IC₅₀        | Plasmodium falciparum    | Nd                          |
| Todalia asiatica    | Rutaceae          | [26] Kenya       | Root Barks       | Methanol           | Good              | < 0.5 µg/ml IC₅₀       | Plasmodium falciparum    | Nd                          |
| Trichilia emetica   | Meliaceae         | [121] Mali       | Leaves           | Dichloromethane    | Moderate          | 11.9 µg/ml IC₅₀        | Plasmodium falciparum    | Nd                          |
| Triclisia dictyo-   | Menispermaceae    | [40] D.R. Congo | Leaves           | Water              | Good              | 5.13 µg/ml IC₅₀        | Plasmodium falciparum    | No                         |
| Tridax procumbens   | Asteraceae        | [22] South Africa | Whole Plant      | Dichloromethane/Methanol | Moderate       | 17 µg/ml IC₅₀          | Plasmodium falciparum    | Nd                          |
| Trimumfetta welwitschii var. hirsuta | Malvaceae | [22] South Africa | Leaves           | Dichloromethane/Methanol | Very Good       | 3.6 µg/ml IC₅₀          | Plasmodium falciparum    | Nd                          |
| Turraea floribunda  | Meliaceae         | [22] South Africa | Leaves           | Dichloromethane/Methanol | Good            | 8.8 µg/ml IC₅₀         | Plasmodium falciparum    | Nd                          |
| Turraea robusta     | Meliaceae         | [26] Kenya       | Stem Barks       | Methanol           | Good              | 5.5 µg/ml IC₅₀         | Plasmodium falciparum    | Nd                          |
| Tylosolea fassoglenis | Fabaceae         | [30] Kenya       | Tubers           | Dichloromethane    | Very Good         | 0.77–0.896 µg/ml IC₅₀ | Plasmodium falciparum    | Nd                          |
| Uapaca paludosa     | Phyllanthaceae    | [103] Congo Brazzaville | Barks           | Dichloromethane    | Good              | 8 µg/ml IC₅₀           | Plasmodium falciparum    | Nd                          |
| Uvaria acuminata    | Annonaceae        | [26] Kenya       | Root Barks       | Methanol           | Good              | 6.9–8.9 µg/ml IC₅₀     | Plasmodium falciparum    | Nd                          |
| Uvaria scheffleri   | Annonaceae        | [26] Kenya       | Leaves           | Methanol           | Good              | 6.8 µg/ml IC₅₀         | Plasmodium falciparum    | Nd                          |
| Uvaria afzelii      | Annonaceae        | [48] Ivory Coast | Roots            | Pentane            | Moderate          | 9–22 µg/ml IC₅₀        | Plasmodium falciparum    | No                         |
| Uvariastrum zenkeri | Annonaceae        | [49] Cameroon     | Twigs            | Ethanol            | Very Good         | 1.89 µg/ml IC₅₀        | Plasmodium falciparum    | Nd                          |
| Uvariodendron molundense | Annonaceae | [49] Cameroon     | Twigs            | Methanol           | Very Good         | 4.79 µg/ml IC₅₀        | Plasmodium falciparum    | Nd                          |
| Plant species               | Plant family      | Source            | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | IC₅₀ or ED₅₀ or LD₅₀ | Strain of Plasmodium Tested | Toxicity (value; assay) |
|----------------------------|-------------------|-------------------|------------------|-------------------|-------------------|-------------------------|----------------------|---------------------------|--------------------------|
| Uvariopsis congolana       | Annonaceae        | [55]              | Cameroon         | Stems             | Ethanol, Water, Dichloromethane, Methanol, Hexane | Very Good              | 4.47 µg/ml IC₅₀         | Plasmodium falciparum W2   | Nd                       |
| Vangueria infausta Burch. subsp. Infausta | Rubiaceae | [37]              | South Africa     | Roots             | Dichloromethane   | Very Good              | 1.84 µg/ml IC₅₀         | Plasmodium falciparum K1   | Nd                       |
| Vepris lanceolata          | Rutaceae          | [20]              | Kenya            | Roots             | Ethyl Acetate     | Good                   | 7.0 µg/ml IC₅₀          | Plasmodium falciparum 3D7 And Dd2 | Nd                       |
| Vernonia amygdalina        | Asteraceae        | [74]              | S. Tome’ And Príñancipe | Leaves         | Ethyl Acetate     | Moderate               | 10 µg/ml IC₅₀          | Plasmodium falciparum 3D7 And Dd2 | Nd                       |
| Vernonia brachycalyx       | Asteraceae        | [104]             | Kenya            | Leaves            | Dichloromethane   | Moderate               | 8.72–11.27 µg/ml IC₅₀  | Plasmodium falciparum 3D7, DD2 | No                       |
| Vernonia cinerea           | Asteraceae        | [45]              | Cambodia         | Whole Plant       | Dichloromethane   | Good                   | 18.3 µg/ml IC₅₀         | Plasmodium falciparum W2   | Nd                       |
| Vernonia coloata           | Asteraceae        | [57]              | Ivory Coast      | Stems, Leaves    | Water             | Good                   | 2.35–9.38 µg/ml IC₅₀   | Plasmodium falciparum Pow, Dd2 | Nd                       |
| Vernonia fastigiata        | Asteraceae        | [22]              | South Africa     | Leaves            | Dichloromethane/Methanol | Very Good              | 4.7 µg/ml IC₅₀          | Plasmodium falciparum D10  | Nd                       |
| Vernonia guineensis        | Asteraceae        | [128]             | Cameroon         | Leaves            | Dichloromethane   | Very Good              | 1.635—2.253 µg/ml IC₅₀ | Plasmodium falciparum No    | No                       |
| Vernonia lasiopus Compositae | Compositae      | [12]              | Kenya            | Leaves            | Chloroform, Ethylacetate, Methanol | Very Good              | 1.0–3.2 µg/ml IC₅₀      | Plasmodium falciparum K39, (CQ-S), EN730, NF54, V1/S | Nd                       |
| Vernonia myrianthra        | Asteraceae        | [22]              | South Africa     | Leaves            | Dichloromethane   | Very Good              | 4.7–4.9 µg/ml IC₅₀      | Plasmodium falciparum K1, NF54 | Nd                       |
| Vernonia oligocephala      | Asteraceae        | [22]              | South Africa     | Leaves            | Dichloromethane/Methanol | Very Good              | 3.5 µg/ml IC₅₀          | Plasmodium falciparum D10  | Nd                       |
| Vismia guineensis          | Hypericaceae      | [48]              | Ivory Coast      | Leaves            | Pentane           | Moderate               | 15–20 µg/ml IC₅₀        | Plasmodium falciparum FC929, CQ-S (Nigerian) | Nd                       |
| Warburgia ugandensis       | Canellaceae       | [72]              | Kenya            | Stem Barks       | Dichloromethane   | Very Good              | 1.4–2.2 µg/ml IC₅₀      | Plasmodium falciparum K1, NF54 | Nd                       |
|                           |                   | [24]              | Kenya            | Root Barks       | Methanol          | Good                   | 4.1–6.1 µg/ml IC₅₀      | Plasmodium falciparum D6, W2 | Nd                       |
| Plant species            | Plant family       | Source        | Country of study | Part of plant used | Extraction solvent | Antiplasmodial Activity | Strain of Plasmodium Tested | Toxicity (value; assay) |
|-------------------------|-------------------|---------------|------------------|--------------------|--------------------|-------------------------|----------------------------|--------------------------|
| Warburgia stuhlmannii   | Canellaceae       | [26] Kenya    | Stem Barks       | Methanol           | Very Good          | 1.8–2.3 µg/ml IC$_{50}$ | Plasmodium falciparum D6, W2 | Nd                       |
| Ximenia americana       | Olacaceae         | [57] Ivory Coast | Stem, Leave     | Water              | Very Good          | 0.6–2.6 µg/ml IC$_{50}$ | Plasmodium falciparum Fcb1 & F32 | Nd                       |
| Xylopia aethiopica      | Annonaceae        | [98] Cameroon | Stem Barks       | Methanol           | Very Good          | 3.75 µg/ml IC$_{50}$    | Plasmodium falciparum W5    | Nd                       |
| Xylopia africana        | Annonaceae        | [49] Cameroon | Stem Barks       | Methanol           | Very Good          | 1.07 µg/ml IC$_{50}$    | Plasmodium falciparum W2    | Nd                       |
| Xylopia parviflora      | Annonaceae        | [37] South Africa | Roots           | Dichloromethane    | Very Good          | 2.19 µg/ml IC$_{50}$    | Plasmodium falciparum NF54  | Nd                       |
| Xylopia phloiodora      | Annonaceae        | [98] Cameroon | Stem Barks       | Water              | Moderatea          | 17.9 µg/ml IC$_{50}$    | Plasmodium falciparum W2    | Nd                       |
| Xysmalobium undulatum   | Apocynaceae       | [22] South Africa | Whole Plant     | Dichloromethane/Methanol | Good     | 6 µg/ml IC$_{50}$    | Plasmodium falciparum D10  | Nd                       |
| Zanthoxylum chalybeum   | Rutaceae          | [137] Kenya   | Root Barks       | Water              | Good               | 2.32–5.52 µg/ml IC$_{50}$ | Plasmodium falciparum NF54, ENT30 | Nd                       |
| Zanthoxylum gilletii    | Rutaceae          | [43] Ivory Coast | Stem Barks      | Ethanol            | Very Good          | 2.8 µg/ml IC$_{50}$    | Plasmodium falciparum FCB1  | Nd                       |
| Zanthoxylum heitzii     | Rutaceae          | [129] Republic Of Congo | Barkss          | Hexane             | Very Gooda         | 0.0089 µg/ml IC$_{50}$ | Plasmodium falciparum, Plasmodium berghei | Nd                       |
| Zanthoxylum tsihanimposa| Rutaceae          | [130] Madagascar | Stem Barks      | Dichloromethane+Methanol | Very Gooda     | 98.4 µM IC$_{50}$   | Plasmodium falciparum FCM29 | Nd                       |
| Zanthoxylum usambarensis| Rutaceae         | [24] Kenya    | Root Barks       | Methanol           | Good               | 3.2–5.5 µg/ml IC$_{50}$ | Plasmodium falciparum D6, W2 | Nd                       |
| Zea mays                | Poaceae           | [131] Nigeria | Leaves           | Ethanol, ethyl acetate | Good       | 3.69–9.31 µg/ml IC$_{50}$ | Plasmodium falciparum 3D7, INDO, Plasmodium berghei | Nd                       |
| Zeheria scabra          | Cucurbitaceae     | [22] South Africa | Whole Plant     | Dichloromethane/Methanol | Good     | 5.6 µg/ml IC$_{50}$  | Plasmodium falciparum D10  | Nd                       |
| Ziziphus abbyssica      | Rhamnaceae        | [24] Kenya    | Leaves           | Methanol           | Moderate           | 17.5 µg/ml IC$_{50}$   | Plasmodium falciparum D6, W2 | Nd                       |
| Ziziphus mucronata      | Rhamnaceae        | [22] South Africa | Leaves          | Dichloromethane    | Moderate           | 12 µg/ml IC$_{50}$    | Plasmodium falciparum D10  | Nd                       |
| Ziziphus cambodiana     | Rhamnaceae        | [45] Cambodia | Stems            | Dichloromethane    | Very Good          | 4.13 µg/ml IC$_{50}$  | Plasmodium falciparum UP1 (CQ-R) | Nd                       |

Nd Not done, Ns Not specified, SI Selectivity index

*a Activity determined using pure compounds isolated from plant
Table 2 In vivo antimalarial activity of African medicinal plants

| Plant species             | Plant family          | Source | Country of study | Part of plant used | Extraction solvent | Antimarial activity | Parasite suppression rate | Strain of Plasmodium tested | Toxicity (value; assay) |
|---------------------------|-----------------------|--------|------------------|-------------------|-------------------|---------------------|--------------------------|---------------------------|------------------------|
| Acacia nilotica          | Fabaceae              | [132]  | Nigeria          | Roots             | Water             | Moderate            | 79.5% at 400 mg/kg/day  | Plasmodium berghei NK65   | No                     |
|                           |                       |        |                  |                   |                   |                     |                          |                           |                        |
|                           |                       | [133]  | Nigeria          | Roots             | Methanol          | Very good          | 62.59% at 150 mg/kg/day| Plasmodium berghei NK65   | No                     |
| Adansonia digitata       | Malvaceae             | [134]  | Nigeria          | Stem barks        | Methanol          | Moderate           | 90.18% at 400 mg/kg/day| Plasmodium berghei        | Nd                     |
|                           |                       |        |                  |                   |                   |                     |                          |                           |                        |
|                           |                       | [135]  | Kenya            | Stem barks        | Ethanol           | Very good          | >60% at 100 mg/kg/day  | Plasmodium berghei        | No                     |
|                           |                       |        |                  |                   |                   |                     |                          |                           |                        |
|                           |                       | [135]  | Kenya            | Stem barks        | Water             | Very good          | 60.47% at 100 mg/kg/day| Plasmodium berghei        | No                     |
| Ageratum conyzoides      | Asteraceae            | [136]  | Nigeria          | Leaves            | Water             | Moderate            | 89.87% at 400 mg/kg/day| Plasmodium berghei NK65   | Nd                     |
| Alvizia gummifera        | Fabaceae              | [137]  | Kenya            | Root barks        | Methanol          | Very good          | 72.9% at 20 mg/kg/day  | Plasmodium falciparum NF54 and ENT36 | Nd                     |
|                           |                       |        |                  |                   |                   |                     |                          |                           |                        |
| Allophylus africanus     | Sapindaceae           | [138]  | Nigeria          | Stems, roots      | Ns                 | Very good          | 92.82–97.81 at 50 mg/kg/day | Plasmodium berghei NK65 | Nd                     |
|                           |                       |        |                  |                   |                   |                     |                          |                           |                        |
| Aloe pulcherrima         | Xanthorrhoeaceae      | [139]  | Ethiopia         | Leaves            | Methanol          | Good               | 56.2 at 200 mg/kg/day  | Plasmodium berghei        | No                     |
| Anthocleista djallonensis| Gentianaceae          | [140]  | Nigeria          | Roots             | Chloroform, ethyl acetate, methanol | Moderate | 64.81–78.66% at 500 mg/kg/day | Plasmodium berghei ANKA | No                     |
|                           |                       |        |                  |                   |                   |                     |                          |                           |                        |
| Artemisia macivarae      | Asteraceae            | [141]  | Nigeria          | Whole plant       | Chloroform        | Very good          | 80% at 100 mg/kg      | Plasmodium berghei        | Nd                     |
| Aspilia africana         | Asteraceae            | [142]  | Nigeria          | Leaves            | Ethanol           | Moderate           | 92.23% at 400 mg/kg/day| Plasmodium berghei NK65  | No                     |
| Azadirachta indica       | Meliaceae             | [143]  | Kenya            | Leaves            | Methanol          | Good               | 83.48% at 250 mg/kg/day| Plasmodium falciparum D6 and W2 | No                     |
|                           |                       |        |                  |                   |                   |                     |                          |                           |                        |
| Balanites rotundifolia   | Zygophyllaceae        | [146]  | Ethiopia         | Leaves            | Methanol          | Moderate           | 69.28% at 300 mg/kg/day| Plasmodium berghei NK65  | No                     |
| Blighia sapida           | Sapindaceae           | [147]  | Nigeria          | Leaves            | Ethanol           | Good               | 57% at 200 mg/kg/day   | Plasmodium berghei ANKA   | No                     |
Table 2 (continued)

| Plant species            | Plant family      | Source       | Country of study | Part of plant used | Extraction solvent | Antimalarial activity | Parasite suppression rate | Strain of Plasmodium tested | Toxicity (value; assay) |
|--------------------------|-------------------|--------------|------------------|--------------------|--------------------|------------------------|--------------------------|---------------------------|--------------------------|
| Bombax buonopozense      | Malvaceae         | Nigeria      | Root barks       | Water              | Good               | 93% at 200 mg/kg/day   | Plasmodium berghei       | Nd                        |                          |
| Brassica nigra           | Brassicaceae      | Ethiopia     | Seeds            | Methanol           | Moderate           | 53.13% at 400 mg/kg/day| Plasmodium berghei       | Nd                        |                          |
| Calpurnia aurea          | Fabaceae          | Ethiopia     | Leaves           | Hydroalcohol       | Very good          | 51.15% at 60 mg/kg     | Plasmodium berghei       | No                       |                          |
| Carica papaya            | Caricaceae        | Nigeria      | Leaves           | Ethanol            | Good               | 59.29% at 200 mg/kg    | Plasmodium berghei       | Nd                        |                          |
| Senna occidentalis       | Fabaceae          | D.R. Congo   | Root barks       | Ethanol            | Good               | 68% at 200 mg/kg       | Plasmodium berghei       | No                       |                          |
| Cassia sieberiana        | Fabaceae          | Nigeria      | Stems            | Ethanol            | Good               | 63.9% at 300 g/kg/day  | Plasmodium berghei       | No                       |                          |
| Cassia sanguinea         | Fabaceae          | Nigeria      | Root barks       | Methanol           | Good               | 79.06% at 200 mg/kg/day| Plasmodium berghei       | Yes (LD<sub>50</sub> = 847 mg/kg; mice) |                          |
| Chrozophora senegalensis | Euphorbiaceous    | Nigeria      | Whole plant      | Methanol           | Very good          | 51.8% at 75 mg/kg/day  | Plasmodium berghei       | Nd                       |                          |
| Chrysophyllum albiflorum | Sapotaceae        | Nigeria      | Seeds, pulp      | Ethanol            | Moderate           | 72.97% at 500 mg/kg    | Plasmodium berghei       | No                       |                          |
| Clausena anisota         | Rutaceae          | Nigeria      | Leaves           | Ethanol            | Very good          | 82.02% at 78 mg/kg/day | Plasmodium berghei       | Yes (LD<sub>50</sub> = 393.7 mg/kg; albino mice) |                          |
| Combretum molle          | Combretaceae      | Ethiopia     | Seeds            | Methanol           | Good               | 63.5% at 250 mg/kg/day | Plasmodium berghei       | Nd                       |                          |
| Commiphora africana      | Burseraceae       | Tanzania     | Stem barks       | Dichloromethane    | Moderate           | 64.24% at 400 mg/kg/day| Plasmodium falciparum    | No                       |                          |
| Crossopteryx febrifuga   | Rubiaceae         | Nigeria      | Stem barks       | Ethanol            | Good               | 63.65% at 200 mg/kg/day| Plasmodium berghei var.  | Nd                       |                          |
| Croton macrostachyus     | Euphorbiaceous    | Kenya        | Stem barks       | Ethyl acetate      | Moderate           | 82% at 500 mg/kg/day   | Plasmodium berghei       | Nd                       |                          |
| Cryptolepis sanguinolenta| Apocynaceae       | Congo        | Root barks       | Ethanol            | Moderate           | 75.07% at 400 mg/kg/day| Plasmodium falciparum, Plasmodium berghei | Nd                       |                          |
| Cucumis metuliferus      | Cucurbitaceae     | Tanzania     | Leaves           | Chloroform         | Moderate           | 70.69% at 600 mg/kg/day| Plasmodium berghei       | Nd                       |                          |
| Plant species      | Plant family   | Source   | Country of study | Part of plant used | Extraction solvent | Antimalarial activity | Parasite suppression rate | Strain of Plasmodium tested | Toxicity (value; assay) |
|--------------------|----------------|----------|------------------|--------------------|-------------------|-----------------------|--------------------------|-----------------------------|-----------------------|
| Dichrostachys cinerea | Fabaceae       | [159]    | Tanzania         | Stem barks         | Methanol          | Moderate              | 53.12% at 400 mg/kg/day   | Plasmodium falciparum (D6, Dd2), Plasmodium berghei | No                    |
| Dodonaea angustifolia | Sapindaceae    | [164]    | Ethiopia         | Roots              | N-butanol         | Moderate              | 55.8% at 400 mg/kg/day   | Plasmodium berghei         | Nd                    |
| Enantia chlorantha Oliv | Annonaceae    | [165]    | Nigeria          | Stem barks         | Ethanol           | Moderate              | 75.23% at 500 mg/kg      | Plasmodium berghei NK-65 | Nd                    |
| Erigeron floribundus | Asteraceae     | [144]    | Cameroon         | Whole plant        | Ethanol           | Good                  | 62.4% at 240 mg/kg/day   | Plasmodium berghei NK65  | No                    |
| Euphorbia cordifolia | Euphorbiaceae  | [166]    | Cameroon         | Whole plant        | Aqueous           | Very good             | 94.70% at 200 mg/kg/day  | Plasmodium berghei        | No                    |
| Euphorbia hirta L   | Euphorbiaceae  | [162]    | Congo            | Whole plant        | Ethanol           | Moderate              | 69.44% at 400 mg/kg/day  | Plasmodium falciparum, Plasmodium berghei NK65 | Nd                    |
| Faidherbia albida   | Fabaceae       | [167]    | Nigeria          | Stem barks         | Ethanol           | Moderate              | 89.5 at 400 mg/kg/day    | Plasmodium berghei NK65  | Nd                    |
| Grewia plagiocephyla | Malvaceae      | [143]    | Kenya            | Leaves             | Methanol          | Moderate              | 77.9 at 250 mg/kg/day    | Plasmodium falciparum D6 and W2 | Nd                    |
| Grewia trichocarpa  | Malvaceae      | [168]    | Kenya            | Root               | Water             | Good                  | 35.8% at 10 mg/kg/day    | Plasmodium berghei        | Yes (LD<sub>50</sub> = 2449 mg/kg; mice) |
| Garcinia kola       | Clusiaceae     | [169]    | Nigeria          | Seeds              | Petroleum ether   | Very good*            | 93% at 200 mg/kg/day     | Plasmodium berghei        | Nd                    |
| Hippocratea africana | Celastraceae   | [170]    | Nigeria          | Nd                 | Ethanol           | Moderate              | 90.9% at 600 mg/kg/day   | Plasmodium berghei        | Yes (LD<sub>50</sub> = 2449 mg/kg; mice) |
| Hostuldia opposita | Lamiaeceae     | [143]    | Kenya            | Leaves             | Methanol          | Moderate              | 79.67% at 250 mg/kg/day  | Plasmodium falciparum D6 and W2 | Yes (IC<sub>50</sub> = 37 µg/ml; Vero E6 cells) |
| Icacina senegalensis | Icacinaceae    | [171]    | Nigeria          | Leaves             | Methanol          | Very good             | 80% at 100 mg/kg/day     | Plasmodium berghei        | Yes (LD<sub>50</sub> > 2000 mg/kg; mice) |
| Indigofera spicata  | Fabaceae       | [172]    | Ethiopia         | Roots              | Methanol          | Moderate              | 53.42% at 600 mg/kg/day  | Plasmodium berghei ANKA   | Nd                    |
| Lannea schweinfurthii | Anacardiaceae  | [143]    | Kenya            | Leaves             | Methanol          | Moderate              | 83.48% at 250 mg/kg/day  | Plasmodium falciparum D6 and W2 | Yes (IC<sub>50</sub> = 76 µg/ml; Vero E6 cells) |
| Lippia kitulensis   | Verbenaceae    | [163]    | Tanzania         | Leaves             | Ethyl acetate     | Moderate              | 70.14% at 600 mg/kg/day  | Plasmodium berghei ANKA   | Nd                    |
| Lophira lanceolata  | Ochnaceae      | [173]    | Nigeria          | Leaves             | Methanol          | Moderate              | 80% at 400 mg/kg/day     | Plasmodium berghei        | No                    |
| Maerua crassifolia  | Capparaceae    | [174]    | Nigeria          | Leaves             | Methanol          | Moderate              | 86% at 400 mg/kg/day     | Plasmodium berghei NK65   | No                    |
| Plant species                  | Plant family    | Source               | Country of study | Part of plant used | Extraction solvent | Antimalarial activity | Parasite suppression rate | Strain of Plasmodium tested         | Toxicity (value; assay) |
|-------------------------------|-----------------|----------------------|------------------|--------------------|--------------------|------------------------|-------------------------------|------------------------------------|------------------------|
| Maytenus senegalensis         | Celastraceae    | [175]                | Tanzania         | Root barks         | Ethanol            | Very good              | 98.1% at 100 mg/kg/day      | Plasmodium berghei             | No                     |
| Morinda morindoides           | Rubiaceae       | [152]                | D.R. Congo       | Leaves             | Dichloromethane    | Good                  | 74% at 200 mg/kg/day        | Plasmodium berghei             | No                     |
| Mucuna pruriens               | Fabaceae        | [176]                | Nigeria          | Leaves             | Water              | Good                  | 71.75% at 270 mg/kg/day     | Plasmodium berghei             | No                     |
| Nauclea latifolia             | Rubiaceae       | [177]                | Nigeria          | Leaves             | Ethanol            | Moderate              | 60.63% at 500 mg/kg/day     | Plasmodium berghei             | No                     |
|                              |                 | [165]                | Nigeria          | Roots              | Ethanol            | Moderate              | 71.15% at 500 mg/kg/day     | Plasmodium berghei             | Nd                     |
| Oldenlandia affinis           | Rubiaceae       | [178]                | Nigeria          | Aerial parts       | Methanol, water, dichloromethane | Moderate | 75% at 400 mg/kg/day | Plasmodium berghei | No |
| Peschiera fuchsiaeufolia      | Apocynaceae     | [179]                | Madagascar       | Stem barks         | Ns                 | Good*                 | 43.4% at 10 mg/kg/day       | Plasmodium yoelii N67, Plasmodium falciparum FMC29 | Nd |
| Phyllanthus amarus            | Phyllanthaceae  | [180]                | Nigeria          | Whole plant        | Water and ethanol  | Good                  | 79% at 1600 mg/kg/day       | Plasmodium yoelii             | Nd                     |
| Phyllanthus niruri            | Phyllanthaceae  | [152]                | D.R. Congo       | Whole plant        | Ethanol            | Good                  | 73% at 200 mg/kg/day        | Plasmodium berghei             | No                     |
|                              |                 | [181]                | Nigeria          | Aerial parts       | Methanol/chloroform | Very good | 90.48% at 100 mg/kg/day | Plasmodium berghei             | Nd                     |
| Phytolacca dodonandra         | Phytolaccaceae  | [182]                | Ethiopia         | Leaves             | Methanol           | Moderate              | 55.24% at 400 mg/kg/day     | Plasmodium berghei             | Nd                     |
| Picralima nitida              | Apocynaceae     | [183]                | Nigeria          | Seeds              | Ethanol            | Good                  | 73% at 115 mg/kg/day        | Plasmodium berghei             | No                     |
| Pilostigma thonningii         | Fabaceae        | [184]                | Nigeria          | Leaves             | Ethanol            | Moderate              | 91% at 400 mg/kg/day        | Plasmodium berghei             | Nd                     |
| Premna chrysantha             | Lamiaceae       | [143]                | Kenya            | Leaves             | Methanol           | Good                  | 65.08% at 250 mg/kg/day     | Plasmodium falciparum D6 and W2 | Nd |
| Pseudocedrela kotschyi        | Meliaceae       | [185]                | Nigeria          | Leaves             | Ethanol            | Moderate              | 90% at 400 mg/kg/day        | Plasmodium berghei             | No,                   |
| Rhus natalensis               | Anacardiaceae   | [143]                | Kenya            | Leaves             | Methanol           | Moderate              | 82.7% at 250 mg/kg/day      | Plasmodium falciparum D6 and W2 | Nd |
| Salacia nitida                | Celastraceae    | [165]                | Nigeria          | Roots              | Ethanol            | Moderate              | 71.15% at 250 mg/kg/day     | Plasmodium berghei             | Nd                     |
| Stachytarpheta cayennensis    | Verbenaceae     | [186]                | Nigeria          | Leaves             | Ethanol            | Good                  | 78.2% at 270 mg/kg/day      | Plasmodium berghei             | Yes (LD$_{50}$ = 938.08 mg/kg, albino mice) |
| Plant species       | Plant family  | Source | Country of study | Part of plant used | Extraction solvent | Antimarial activity | Parasite suppression rate | Strain of Plasmodium tested | Toxicity (value; assay) |
|---------------------|---------------|--------|------------------|--------------------|-------------------|---------------------|--------------------------|-----------------------------|--------------------------|
| Telfairia occidentalis | Cucurbitaceae | [187] Nigeria | Leaves | Water | Good | 72.17% at 200 mg/kg/day | Plasmodium berghei ANKA | No |
| Tithonia diversifolia | Asteraceae | [160] Nigeria | Aerial parts | Ethanol | Good | 74.97% at 200 mg/kg/day | Plasmodium berghei var. ANKA | Nd |
| Todalia asiatica | Rutaceae | [188] Kenya | Root barks | Methanol | Moderate | 59.3% at 500 mg/kg/day | Plasmodium berghei NK66 | Nd |
| Trema orientalis | Cannabaceae | [189] Nigeria | Stem barks | Methanol | Good | 70% at 200 mg/kg/day | Plasmodium berghei | Nd |
| Trichilia megalantha | Meliaceae | [190] Nigeria | Stem barks | Methanol, chloroform | Good | 89.1–100% at 200 mg/kg/day | Plasmodium berghei ANKA | Nd |
| Triphophyllium peltatum | Diancophyllaceae | [191] Ivory Coast | Roots, stem barks | Dichloromethane | Very good* | 99% at 50 mg/kg/day | Plasmodium berghei ANKA | Nd |
| Uvaria acuminate | Annonaceae | [143] Kenya | Roots | Methanol | Good | 27.0% at 250 mg/kg/day | Plasmodium falciparum D6 and W2 | Nd |
| Uvaria chamae P. Beauv | Annonaceae | [170] Nigeria | Nd | Ethanol | Moderate | 72.2% at 600 mg/kg/day | Plasmodium berghei | Yes (LD_{50} = 3464 mg/kg; mice) |
| Verbena hastata | Verbenaceae | [192] Nigeria | Leaves | Ethanol | Moderate | 70% at 400 mg/kg/day | Plasmodium berghei | No |
| Vernonia amygdalina | Asteraceae | [193] Uganda | Leaves | Water | Good | 73% at 200 mg/kg/day | Plasmodium berghei | No |
| | | [194] Nigeria | Leaves | Water | Good | 50.78—62.66% at 125 mg/kg/day | Plasmodium berghei ANKA | Nd |
| | | [195] Botswana | Leaves and root barks | Ethanol | Moderate | 67% at 500 mg/kg/day | Plasmodium berghei | Nd |
| Vernonia lasiopus | Asteraceae | [188] Kenya | Root barks | Methanol | Moderate | 59.3% at 500 mg/kg/day | Plasmodium berghei NK67 | Nd |
| Withania somnifera | Solanaceae | [196] Ethiopia | Leaves | Methanol | Moderate | 57% at 300 mg/kg/day | Plasmodium berghei ANKA | Nd |
| Xylopia aethiopica | Annonaceae | [141] Nigeria | Fruits | Chloroform | Very good | 60% at 100 mg/kg/day | Plasmodium berghei | Nd |
| Artemisia abyssinica | Asteraceae | [197] Ethiopia | Aerial parts | Hydroalcohol | Good | 64.7% at 200 mg/kg/day | Plasmodium berghei | Nd |
| Rotheca myricoides | Lamiaceae | [198] Ethiopia | Leaves | Methanol | Good | 54.14% at 200 mg/kg/day | Plasmodium berghei | No |
| Dodonaea angustifolia | Sapindaceae | [198] Ethiopia | Roots | Methanol | Good | 57.74% at 200 mg/kg/day | Plasmodium berghei | No |
Africa is slothful. Despite a considerable number of plant species that have demonstrated significant antiplasmodial activity in vitro, fewer plants have been evaluated in vivo and only one clinical trial with *Cochlospermum planchonii* (Bixaceae) has been conducted so far. This reinforces the need for basic and clinical research in the region. Van Wyk [213] had also arrived at the same conclusion.

This review revealed research articles from 31 African countries. Most of the articles were from Nigeria. This is suggestive that Nigeria is leading the podium in research on anti-malarial drug discovery and development, deservedly so, because she is probably the most affected country in the world. It is noteworthy that South Africa which is generally more technologically advanced than Nigeria had very few (8) articles. The African region is the most affected in the world recording the greatest number of cases and malaria attributed deaths. However, the distribution of malaria in Africa is not even, with sub-Saharan Africa harboring disproportionately the greatest number of cases. This is suggestive that research to identify new anti-malarial drugs may be related to the burden of the disease, thus the government policy to control the disease. There is, therefore, the need for policy-driven research into new anti-malarial all across the African region. In this review, IC50 values of < 20 µg/ml were considered as the cutoff of significant anti-malarial activity. This cutoff is considered the minimum to qualify as a first-pass “hit” in anti-malarial drugs screening [214]. Five hundred and two (502) plant species from 169 families were observed to have moderate to very good anti-malarial activity. The most investigated plant families were *Euphorbiaceae, Fabaceae, Rubiaceae*, and *Annonaceae*. However, the plant families containing the most active plants were *Apocynaceae, Celestraceae*, and *Rutaceae*. This finding suggests that more emphasis should be given to plants in these families for anti-malarial drug discovery. Besides, the most investigated plant species were *Azadirachta indica, Nauclea latifolia, Picrodina nitida*, and *Zanthoxylum chalybeum*. *Alchornea cordifolia*, *Flueggea virosa*, *Cryptolepis sanguinolenta*, and *Zanthoxylum chalybeum* were the only plant species with consistently very good antiplasmodial and anti-malarial activities between studies. This is very surprising that no clinical trial using any of these plants has been conducted. Further studies on these plant species should be performed.

This study revealed that overall, a majority of the plants investigated had very good antiplasmodial activity in vitro. That activity decreases as you move to in vivo in most studies, with a majority of plants demonstrating only moderate activity. For example, Gathirwa et al. [146] showed that the activity of *Uvaria acuminate* decreased from good activity in vitro to inactive in vivo. However, a few studies show that plant activity could also increase from in vitro to in vivo analysis. Other examples include studies by Muthaura et al. [20] using *Boscia angustifolia*, Kweyamba et al. [162] using *Commiphora Africana*, and Ajaiyeoba et al. [204] using *Annona senegalensis*. This suggests that plants could still have significant anti-malarial activity in vivo although they failed to in vitro. Most investigators usually progress to in vivo studies only when they observe significant antiplasmodial activity in vitro. This may explain the findings of a smaller number of in vivo studies in the current study. The investigation of the anti-malarial activities of plants should continue in vivo despite the dismal performance of the plants in vitro.

| Plant species | Plant family | Source | Country of study | Part of plant used | Extraction solvent | Antimalarial activity | Parasite suppression rate | Strain of Plasmodium tested | Toxicity (value; assay) |
|---------------|--------------|--------|------------------|--------------------|--------------------|----------------------|--------------------------|---------------------------|--------------------------|
| *Clutia abysinica* | Peraceae | [199] | Kenya | Leaves | Methanol | Moderate | 40.45% at 100 mg/kg/day | *Plasmodium falciparum, Plasmodium berghei ANKA* | No |
| *Pittosporum viridiflorum* | Pittosporaceae | [199] | Kenya | Leaves | Methanol | Moderate | 54.77% at 100 mg/kg/day | *Plasmodium falciparum D6 & W2, Plasmodium berghei ANKA* | Yes (SI = 2.5; Vero E6 cells) |

Nd Not done, Ns Not specified, SI Selectivity index

* Activity determined using pure compounds isolated from plant
| Plant species                | Plant family | Source         | Country of study | Part of plant used | Extraction solvent       | Overall activity | In vitro IC50 or ED50 or LD50 | In vivo IC50 or LD50 | Strain of Plasmodium tested | parasite suppression rate | Toxicity (value; assay) |
|-----------------------------|--------------|----------------|------------------|--------------------|--------------------------|-----------------|-------------------------------|------------------------|--------------------------|--------------------------|--------------------------|
| *Sphaeranthus suaveolens*   | Compositae   | Kenya          | Whole plant      | Methanol           | Moderate                 | Moderate In active | 7.93–56.73 µg/ml IC50 | 46.74% at 100 mg/kg/day | *Plasmodium falciparum D6 and W2, Plasmodium berghei ANKA* | 46.74% at 100 mg/kg/day | No                       |
| *Abutilon grandiflorum*     | Malvaceae    | Tanzania       | Roots            | Ethyl acetate      | Good                     | Moderate Very good | 9–14 µg/mL IC50          | 83–87% at 20 µg/ml/day | *Plasmodium falciparum HB3 and FCB, Plasmodium vinckeigen* | Yes (IC50 = 36 µg/mL; human colon carcinoma cell line [HT29]) | No                       |
| *Alchornea laxiflora*       | Euphorbiaceae| Nigeria        | Roots            | Ethyl acetate, dichlo-romethane | Good                     | Inactive Very good | 38.44—40.17 µg/mL IC50 | 65.73% at 150 mg/kg/day | *Plasmodium falciparum 3D2, INDO, Plasmodium berghei* | >57% at 100 mg/kg/day | No                       |
| *Annona senegalensis*       | Annonaceae   | Nigeria        | Leaves           | Methanol           | Moderate                 | In active Very good | 28.8 µg/mL IC50         | <57% at 100 mg/kg/day | *Plasmodium berghei* | >57% at 100 mg/kg/day | No                       |
| *Boscia angustifolia*       | Capparaceae  | Kenya          | Stem barks       | Methanol           | Moderate                 | Moderate Very good | 7.43–35.93 µg/mL IC50 | 60.12% at 100 mg/kg/day | *Plasmodium falciparum D6 & W2, Plasmodium berghei ANKA* | No                       |
| *Chrozophora senegalensis*  | Euphorbiaceae| Senegal        | Leaves           | Water              | Very good                | Very good Very good | 1.6–1.9 µg/mL IC50      | 65% at 10 mg/kg/day   | *Plasmodium falciparum FcM29, Fcb1, Plasmodium vinckeigen petteri* | No                       |
| *Clerodendrum etophyllum*   | Lamiaceae    | Kenya          | Root barks       | Methanol           | Moderate                 | Good             | 9.51–10.56 µg/mL IC50   | 90.13% at 100 mg/kg/day | *Plasmodium falciparum D6 & W2, Plasmodium berghei ANKA* | No                       |

Table 3: In vitro and in vivo studies on African medicinal plants.
| Plant species          | Plant family | Source          | Country of study | Part of plant used | Extraction solvent | Overall activity | In vitro IC50 or ED<sub>50</sub> or LD<sub>50</sub> | Strain of Plasmodium tested                                                                 | parasite suppression rate |
|-----------------------|--------------|-----------------|------------------|--------------------|-------------------|------------------|-------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|--------------------------|
| Cocos nucifera        | Arecaceae    | [202] Nigeria   | Husk              | Ethyl acetate      | Moderate          | Moderate         | 10.94 µg/ml IC<sub>50</sub>                      | Plasmodium falciparum W2, Plasmodium berghei NK65                                                                 | 98.6% at 125 mg/kg/day    |
| Commiphora africana   | Burseraceae  | [159] Tanzania  | Stem bark         | Dichloromethane    | Moderate          | Very good        | 4.54 µg/ml IC<sub>50</sub>                      | Plasmodium falciparum D6, Dd2, Plasmodium berghei                                                                 | 64.24% at 400 mg/kg/day   |
| Ficus thomningii      | Moraceae     | [203] Nigeria   | Whole plant       | Hexane             | Moderate          | Good             | 2.7–10.4 µg/ml IC<sub>50</sub>                  | Plasmodium falciparum NF54, K1, Plasmodium berghei NK65                                                                 | 84.5% at 500 mg/kg/day    |
| Flueggea virosa       | Phyllanthaceae | [199] Kenya     | Leaves            | Methanol           | Very good         | Very good        | 2.28–3.64 µg/ml IC<sub>50</sub>                  | Plasmodium falciparum D6 and W2, Plasmodium berghei ANKA                                                                 | 70.91% at 100 mg/kg/day   |
| Fuerstia africana     | Lamiaceae    | [199] Kenya     | Whole plant       | Methanol           | Very good         | Very good        | 0.98–2.40 µg/ml IC<sub>50</sub>                  | Plasmodium falciparum D6 and W2, Plasmodium berghei ANKA                                                                 | 61.85% at 100 mg/kg/day   |
| Harungana madagascariensis | Hypericaceae | [199] Kenya     | Leaves            | Water              | Moderate          | Inactive         | 39.07–43.7 µg/ml IC<sub>50</sub>                  | Plasmodium falciparum D6 and W2, Plasmodium berghei ANKA                                                                 | 88.04% at 100 mg/kg/day   |
|                       |              | [204] Nigeria   | Stem bark         | Ethanol            | Very good         | Inactive         | 0.052–0.517 µg/ml IC<sub>50</sub>                | Plasmodium yoelii nigeriensis N67, Plasmodium falciparum                                                                 | 28.6–44.8% Nd             |
| Plant species           | Plant family     | Source | Country of study | Part of plant used | Extraction solvent | Overall activity | In vitro IC₅₀ or ED₅₀ or LD₅₀ | Strain of Plasmodium tested | Parasite suppression rate | Toxicity (value; assay) |
|------------------------|------------------|--------|------------------|--------------------|--------------------|------------------|----------------------------|-----------------------------|---------------------------|--------------------------|
| Lannea schweinfurthii  | Anacardiaceae    | [205]  | Kenya            | Stem barks         | Methanol           | Moderate         | Moderate                 | Very good                   | Plasmodium falciparum D₆, W₂, Plasmodium berghei | 91.37% at 100 mg/kg/day | Yes (SI = 6.21–19.79; Vero cells) |
| Lophira alata          | Ochnaceae        | [203]  | Nigeria          | Whole plant        | Hexane             | Good             | Moderate                 | Very good                   | Plasmodium falciparum NF₅₄, K₁, Plasmodium berghei NK₆₅ | 74.45% at 500 mg/kg/day | No                       |
| Ludwigia erecta        | Onagraceae       | [199]  | Kenya            | Whole plant        | Water              | Very good        | Very good                | In active                   | Plasmodium falciparum D₆ & W₂, Plasmodium berghei ANKA | 49.64% at 100 mg/kg/day | No                       |
| Maytenus putterlickioides | Celastraceae   | [199]  | Kenya            | Root barks         | Methanol           | Good             | Good                     | Very good                   | Plasmodium falciparum D₆ and W₂, Plasmodium berghei ANKA | 78.66% at 100 mg/kg/day | No                       |
| Maytenus undata        | Celastraceae     | [199]  | Kenya            | Leaves             | Methanol           | Good             | Good                     | Very good                   | Plasmodium falciparum D₆ and W₂, Plasmodium berghei ANKA | 76.29% at 100 mg/kg/day | No                       |
| Mimusops caffra        | Sapotaceae       | [206]  | South Africa     | Leaves             | Dichloromethane    | Good             | Good                     | Very good                   | Plasmodium falciparum D₁₀, Plasmodium berghei ANKA | 94.01% at 400 mg/kg/day | Nd                       |
| Schkuhria pinnata      | Compositae       | [199]  | Kenya            | Whole plant        | Methanol           | Good             | In active                | 1.3–6.83 µg/ml  IC₅₀ | Plasmodium falciparum D₆ & W₂, Plasmodium berghei ANKA | 49.9% at 100 mg/kg/day | No                       |
| Plant species                  | Plant family     | Source          | Country of study | Part of plant used | Extraction solvent | Overall activity | In vitro     | Strain of Plasmodium tested | IC50 or ED50 or LD50 | parasite suppression rate | Toxicity (value; assay) |
|-------------------------------|------------------|-----------------|------------------|--------------------|-------------------|------------------|--------------|----------------------------|------------------------|--------------------------|------------------------|
| Sclerocarya birrea            | Anacardiaceae    | [205] Kenya     | Stem barks       | Methanol           | Moderate          | Moderate         | Very good    | Plasmodium falciparum D6, W2, Plasmodium berghei | 5.91–24.96 µg/ml IC50 | 63.49% at 100 mg/kg/day | No                     |
| Toddalia asiatica            | Rutaceae         | [117] Kenya     | Fruits           | Ethyl acetate      | Very good         | Moderate         | Very good    | Plasmodium falciparum W2 & D6, Plasmodium berghei | 1.87 µg/ml IC50         | 81.34% at 500 mg/kg/day | No                     |
| Turraea robusta              | Meliaceae        | [205] Kenya     | Root barks       | Methanol           | Good              | Good            | Very good    | Plasmodium falciparum D6, W2, Plasmodium berghei | 2.09–10.32 µg/ml IC50 | 78.2% at 100 mg/kg/day | Yes (SI = 2.36–11.67; Vero cells) |
| Uapaca nitida                | Phyllanthaceae   | [207] Tanzania  | Root barks       | Ethanol            | Moderate*         | Inactive        | Inactive     | Plasmodium falciparum K1, T9-96 & Plasmodium berghei | 19.6–25.9 µg/mL IC50 | poor                     | No                     |
| Vernonia ambigua             | Asteraceae       | [208] Nigeria   | Ns               | Water              | Very good         | Inactive        | Very good    | Plasmodium berghei, Plasmodium falciparum | 31.26–50 µg/ml IC50 | 60% at 100 mg/kg/day | No                     |
| [209] Republic of Congo      | Leaves           | Methanol        | Moderate          | Very good          | Plasmodium falciparum, Plasmodium yoelii | 3.58 µg/ml IC50 | No                     |
| Warburgia stuhlmannii        | Camellaceae      | [199] Kenya     | Stem barks       | Water              | Very good         | Moderate         | Very good    | Plasmodium falciparum D6 and W2, Plasmodium berghei, ANKA | 1.81–2.33 µg/ml IC50 | 84.95% at 100 mg/kg/day | No                     |
| Azadirachta indica           | Meliaceae        | [143] Kenya     | Leaves           | Methanol           | Good              | Good            | Good         | Plasmodium falciparum D6 and W2 | 6.24–7.53 µg/ml IC50 | 83.48% at 250 mg/kg/day | No                     |
Table 3 (continued)

| Plant species           | Plant family   | Source     | Country of study | Part of plant used | Extraction solvent | Overall activity | In vitro IC50 or ED50 or LD50 | Strain of Plasmodium tested | parasite suppression rate | Toxicity (value; assay) |
|-------------------------|----------------|------------|------------------|--------------------|-------------------|------------------|-------------------------------|----------------------------|--------------------------|-------------------------|
| Dichrostachys cinerea   | Fabaceae       | Tanzania   | Stem barks       | Methanol           | Moderate          | Good             | Moderate                       | Plasmodium falciparum D6, Dd2, Plasmodium berghei | 53.12% at 400 mg/kg/day | No                      |
| Grewia plagiophylla     | Malvaceae      | Kenya      | Leaves           | Methanol           | Moderate          | Moderate         | Good                           | Plasmodium falciparum D6 and W2 | 77.9% at 250 mg/kg/day | Nd                      |
| Hoslundia opposita     | Lamiaceae      | Kenya      | Leaves           | Methanol           | Moderate          | Good             | Good                          | Plasmodium falciparum D6 and W2 | 79.67% at 250 mg/kg/day | Yes (SI = 0.58; Vero E6 cells) |
| Lannea schweinfurthii  | Anacardiaceae  | Kenya      | Leaves           | Methanol           | Moderate          | Inactive         | Good                          | Plasmodium falciparum D6 and W2 | 83.48% at 250 mg/kg/day | Yes (SI = 1.4; Vero E6 cells) |
| Premna chrysocodia     | Lamiaceae      | Kenya      | Leaves           | Methanol           | Good              | Good             | Good                          | Plasmodium falciparum D6 and W2 | 65.08% at 250 mg/kg/day | Nd                      |
| Rhus natalensis        | Anacardiaceae  | Kenya      | Leaves           | Methanol           | Moderate          | Inactive         | Good                          | Plasmodium falciparum D6 and W2 | 82.7% at 250 mg/kg/day | Nd                      |
| Triphyophyllium peltatum| Dioncophylaceae| Ivory coast | Roots, stem barks| Dichloromethane    | Very good*        | Very good        | Very good                     | Plasmodium falciparum ANKA CRS | 99% at 50 mg/kg/day | Nd                      |
| Uvaria acuminatea      | Anonaceae      | Kenya      | Roots            | Methanol           | Good              | Inactive         | Good                          | Plasmodium falciparum D6 and W2 | 27.0% at 250 mg/kg/day | Nd                      |

Nd Not done, Ns Not specified, SI Selectivity index

* Activity determined using pure compounds isolated from plant
Table 4  Clinical trial on African medicinal plants

| Plant species                  | Plant family | Source      | Country of study | Part of plant used | Extraction solvent | Crude extract? | Antimalarial activity | Parasite suppression rate | Strain of Plasmodium tested | Toxicity |
|-------------------------------|-------------|-------------|------------------|--------------------|--------------------|-----------------|-----------------------|-----------------------------|--------------------------------|---------|
| Cochlospermum planchonii      | Bixaceae    | [210] Burkina Faso | Roots           | Ns                 | Yes                | Moderate        | 52 at 600 ml/day      | Plasmodium falciparum          | No                                   |         |

Nd Not done, Ns Not specified
The current study revealed substantial inter-study variation in the antiplasmodial activity of several plant species. For example, considerable variation in the antiplasmodial activity was observed for *Senna occidentalis*, *Adansonia digitata*, *Acanthospermum hispidum*, *Rotheca myricoides*, *Anogeissus leocarpus*, *Annona muricata*, *Ageratum conyzoides*, *Albizia coriaria*, *Ekebergia capensis*, *Flueggea virosa*, *Lippia javanica*, *Maytenus senegalensis*, *Morinda lucida*, *Picralima nitida*, *Trichilia emetica*, *Vernonia amygdalina*, and *Vernonia colorata*. The factors that could have accounted for these differences may include differences in the extraction solvent thus the extraction yield and extracted metabolite. With dichloromethane, mainly the apolar metabolites are extracted. In contrast, with methanol, from polar to moderate apolar metabolites are extracted.

Most (95.7%) of the studies used crude extract for their investigation and rarely the pure compounds (Additional file 1: Table S2 presents a summary of active compounds that have been identified from some of the plants). The finding of a majority of studies in Africa using only the crude extract of plants may be attributed to the absence of the necessary infrastructure to process the plant materials to get the pure compounds. Furthermore, there may be geographical differences in the areas where the plants were collected and this may also affect the activity of the same plant species. For example, despite using the same extraction solvent, the antiplasmodial activity of *Acacia nilotica* was moderate in South Africa and very good in Sudan. There was also variation between the different assay types. For example, the activities of *Vernonia ambigua* [211] and *Annona senegalensis* [204] have been reported to increase from inactive in vitro to very good in vivo. However, a few plant species including *Alchornea cordifolia*, and *Zanthoxylum chalybeum*, were observed to be consistently very good between studies. These plant species should be exploited further for their antiplasmodial activity. The activities of the plants were equally observed to increase with the isolation of the active compounds thus reinforcing the need for research into identifying the active compounds of African medicinal plants. The marked difference in the antiplasmodial activity of
the crude extract of *Artemisia annua* and the pure compounds points out the issue that even the compounds which show only low potency and may be discarded from the initial screen for further development may still have active components with therapeutic potential [215]. The strain of the *Plasmodium* used may also be another factor accounting for the inter-study variation observed; studies using chloroquine-sensitive strains of the parasite like *P. falciparum* 3D7, D6, NF54 tend to report higher antiplasmodial activity compared to studies using chloroquine-resistant strains like *P. falciparum* W2, Dd5, K1 or D10.

This study revealed that only a few (26.3%) of the plants demonstrated some degree of toxicity. The families hosting the most toxic plant species were Lamiacaeae, Anacardiaceae, Moraceae, and Meliaceae. The most toxic plants were *Azadirachta indica* and *Vernonia amygdalina*. The former [168] is one of the few plant species that demonstrated very good antimalarial activity in some studies. Other plants with high toxicity but very good antimalarial/anti-malarial activities include *Arenge engleri* [25], *Celtis integrifolia* [52], *Ficus platyhylla* [50], *Gutenbergia cordifolia* [21], *Helchrysum cymosum* [97], *Microglossa pyrifolia* [92], *Opilia celtidiformia* [52], *Quassia Africana* [103], *Rumex abyssinicus* [92], *Clausena anisota* [157], *Icacina senegalensis* [171], *Abutilon grandiflorum* [200], and *Lannea schweinfurthii* [205]. The isolation of the active compounds, which has to be done, could eliminate the toxicity, if not all, to a certain degree. For example, *Salvia radula* crude extract (of aerial parts) has been shown to demonstrate some degree of toxicity, but betulafolientriol oxide isolated from the plant was very active with little or no toxicity against human kidney epithelial cells [120]. There was also considerable variation in the toxicity between the assay types (in vitro or in vivo). As many as 32.8% of the plants demonstrated some level of toxicity in vitro meanwhile 26.7% were toxic in vivo. Since it is customary to evaluate toxicity at the in vitro level and toxic plants are discarded before in vivo evaluation, that may explain why fewer plants were toxic in vivo. Toxicity varied within the same plant species from study to study and could be attributed to differences in the study design as well as differences in the parts of the plants used for testing. From this study, the most toxicity was observed with the leaves. Also, a relationship could be established between toxicity and antimalarial activity; as the activity of the plant increases, the toxicity, on the other hand, was observed to decrease. Furthermore, albino mice and Vero E6 cells were the most commonly used assays in the evaluation of toxicity. Unfortunately, the authors could not make a meaningful relationship between the type of assay and toxicity because of the fewer studies assessing the toxicity of the medicinal plants.

This study, however, is limited in that the analyses may have been compounded by the substantial inter-study variation in the methodologies used by different independent studies for the extraction of plant material, the overall extraction yield, the diversity of extracted metabolites as well as the geographical variations in the different sites used in the plant collection. However, the study has provided important baseline data that may be exploited by researchers in the field for the discovery and development of new anti-malarial drugs.

**Conclusion**

This study has revealed the slothful progress in the discovery and development of new anti-malarial drugs from African medicinal plants. Despite the encouraging activities demonstrated by the plants in vitro, fewer plants have been evaluated in vivo and just one clinical trial has been conducted so far with *Cochlospermum planchonii* (Bixaceae). The study also revealed considerable inter-study variation in the antimalarial activities of the plants, however, the activity of some plants including *Alchornea cordifolia*, *Azadirachta indica*, and *Zanthoxylum chalybeum* was consistently very good. The study demonstrates a relationship between antimalarial activity and toxicity whereby the toxicity of the plants decreases as the antimalarial activity increases. Besides, the active compounds were identified in just a handful of the plants. Therefore, there is a need for a policy-driven approach in the discovery and development of new anti-malarial drugs to subvert the rising resistance to the frontline anti-malarial drugs in the world.

**Abbreviations**

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analysis; SI: Selectivity Index; LD50: Median lethal dose; IC50: Half-maximal inhibitory concentration; CC50: 50% Cytotoxic concentration; LC50: Lethal concentration.

**Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s12936-021-03966-0.

**Additional file 1: Table S1.** In vitro and in vivo studies reporting inactive antimalarial or antimalarial activity. Table S2. List of active compounds identified from plants.

**Acknowledgements**

I would like to express my special appreciation and thanks to Professor Dr. Wanderley de Souza for his helpful comments.

**Authors’ contributions**

All authors contributed equally to the study. All authors read and approved the manuscript.
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