Review

Medicinal plants as a fight against murine blood-stage malaria

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A B S T R A C T

Objective: Malaria is an infectious parasitic disease affecting most of countries worldwide. Due to anti-malarial drug resistance, researchers are seeking to find another safe efficient source for treatment of malaria. Since many years ago, medicinal plants were widely used for the treatment of several diseases. In general, most application is done first on experimental animals then human. In this article, medicinal plants as antimalarial agents in experimental animals were reviewed from January 2000 until November 2020.

Materials and methods: In this systematic review published articles were reviewed using the electronic databases NCBI, ISI Web of knowledge, ScienceDirect and Saudi digital library to check articles and theses for M.Sc/Ph.D. The name of the medicinal plant with its taxon ID and family, the used Plasmodium species, plant part used and its extract type and the country of harvest were described.

Results and conclusion: The reviewed plants belonged to 83 families. Medicinal plants of families Asteraceae, Meliaceae, Fabaceae and Lamiaceae are the most abundant for use in laboratory animal antimalarial studies. According to region, published articles from 33 different countries were reviewed. Most of malaria published articles are from Africa especially Nigeria and Ethiopia. Leaves were the most common plant part used for the experimental malaria research. In many regions, research using medicinal plants to eliminate parasites and as a defensive tool is popular.

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Contents

1. Introduction ..................................................................................................... 1724
   1.1. Documented drugs from plant source .............................................................. 1724
   1.2. Models of blood-stage malaria ...................................................................... 1724
   1.3. Activity of plant extracts .............................................................................. 1724
2. Methodology .................................................................................................... 1734
3. Results and discussion .................................................................................... 1734
4. Conclusion ........................................................................................................ 1734
   Acknowledgments ............................................................................................. 1735
   References ......................................................................................................... 1735

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1. Introduction

Malaria, the most important human parasitic disease, is still a major cause of illness and death worldwide. The infection is transmitted by Plasmodium parasites, of which five species have been reported that infect humans (White 2008). Malarial pathogenesis studies, however, are mainly performed with rodent malaria parasites due to their similarity in genome sequence and pathology to the human parasite (Carlton et al. 2002).

In 90 countries, malaria is endemic; most of these are in Africa. The elimination of malaria is increasing in a growing number of countries (Fig. 1). Globally, the number of malaria-endemic countries in 2000 that recorded less than 10,000 cases of malaria rose from 40 in 2010 to 49 in 2018 (WHO, 2019). Between 2010 and 2018, the incidence rate of malaria decreased globally, from 71 to 57 cases per 1000 population at risk (WHO, 2019). Estimated deaths due to malaria decreased globally from 585,000 to 57 cases per 1000 population at risk (WHO, 2019). For instance, the anti-malarial drugs quinine and artemisinin (Fig. 3), which are actually of major interest (Phillipson and O’Neill, 1987), are part of the traditional Chinese treatment of malaria. Also, Cinchona species are still well known for their antimalarial properties, and the alkaloid quinine (Fig. 3) constituent is still recognized as an effective medication (White, 1985). Moreover, Dichroea febrifuga belonging to family Saxifragaceae is another plant which is used for the production of the antimalarial drug, febrifugine (Fig. 3) (Anonymous, 1975).

In order to protect users of malaria drugs, scientific evaluation of the safety, efficacy and efficiency of medicinal plant preparations is critical. Today, many reports showed that medicinal plants are a possible source of new antimalarial drugs or medicinal products (Moyo et al., 2020).

1.1. Documented drugs from plant source

There is a general agreement in the science community that there is a powerful role of natural products in the exploration of new leads for drug therapy production for human diseases. There is always an urgent and continuing call to look for new antimalarial agents where drug resistance has contributed to the inefficiency of most malaria drugs on the market. Most of those agents used in the treatment of malaria are either extracted from plants or are natural products (Moyo et al., 2020).

In the production of chemotherapeutic antimalarial drugs, medicinal plants play a key role. The use of Artemisia annua (Compositae) and its active compound, artemisinin (Fig. 3), which are actually of major interest (Phillipson and O’Neill, 1987), is part of the traditional Chinese treatment of malaria. Also, Cinchona species are still well known for their antimalarial properties, and the alkaloid quinine (Fig. 3) constituent is still recognized as an effective medication (White, 1985). Moreover, Dichroea febrifuga belonging to family Saxifragaceae is another plant which is used for the production of the antimalarial drug, febrifugine (Fig. 3) (Anonymous, 1975).

In order to protect users of malaria drugs, scientific evaluation of the safety, efficacy and efficiency of medicinal plant preparations is critical. Today, many reports showed that medicinal plants are a possible source of new antimalarial drugs or medicinal products (Moyo et al., 2020).

In order to speed up the production of effective alternative treatments from medicinal plants, sufficient pre-clinical trials supporting their safety and efficacy are needed to provide reliable experimental data that provide a basis for research.

1.2. Models of blood-stage malaria

While there are over 100 Plasmodium species that can infect several vertebrates, it is understood that only five species of plasmodium, P. falciparum, P. vivax, P. ovale, P. malariae, and P. knowlesi can affect humans. While P. berghei, P. chabaudi, P. yoelii, and P. vinckei are four Plasmodium species infecting African rodents that have been widely used in vivo rodent malaria research. This is due to the similarity with the human pathogenic P. falcibarum.

Mouse models of rodent malaria infection are particularly useful for examining the pathological consequences of host-parasite interactions and can assess clinical outcomes of infections such as parasitemia, splenomegaly, immune response and change in histopathological, biochemical and hematological parameters (Good et al., 2015).

1.3. Activity of plant extracts

With the objective of targeting parasite-specific metabolic aspects that are not conveyed by the host, extracts from antimalarial medicinal plants are studied. It is probable that the ingredients of the extract will target the parasite in this direction, while causing minimal host damage.

For instance, the anti-malarial drugs quinine and artemisinin are both of plant origin and are known to be a rich reservoir of bioactive secondary metabolites that contain bioactive antimalarial compounds like alkaloids and terpenoids that are used in tradition medicine against fever, inflammation and malaria (Moyo et al., 2020).

However, there has been a steady decrease in the rate of malaria infection reduction in recent years the World Health Organization (WHO) has revealed that the fight against malaria with the resources and funding available is now at a crossroads, leaving many children and pregnant women at risk of infection (WHO, 2015; Benelli and Mehlhorn, 2016).
Table 1
Selected medicinal antimalarial plants from January 2000 to November 2020.

| Parasite name | Plant (Family) | Plant Taxon ID* | Studied plant part | Extract type | Country of harvest | Mouse strain | References |
|---------------|----------------|-----------------|--------------------|--------------|--------------------|--------------|------------|
| *Plasmodium berghei* | Leontis ocmymofila (Lamiaceae) | NCBI:txid483802 | Leaves | Methanol | Ethiopia | Swiss albino | Teklu et al. (2020) |
| *Plasmodium berghei* | Acacia karroo (Fabaceae) | NCBI:txid138024 | Leaves | Methanol | India | BALB/c | Sachdeva et al. (2020) |
| *Plasmodium berghei* | Balanites roxburghii (Zygophyllaceae) | NCBI:txid2603908 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium berghei* | Bassia scoparia (Amaranthaceae) | NCBI:txid83154 | Leaves | Methanol | Ethiopia | Swiss albino | Teka et al. (2020) |
| *Plasmodium berghei* | Berberis aristata (Berberidaceae) | NCBI:txid659592 | Leaves | Methanol | Ethiopia | Swiss albino | Habte et al. (2020b) |
| *Plasmodium berghei* | Brassica juncea (Cruciferae) | NCBI:txid3705 | Leaves | Methanol | Ethiopia | Swiss albino | Ezenyi et al. (2020) |
| *Plasmodium berghei* | Chenopodium album (Amaranthaceae) | NCBI:txid3559 | Leaves | Methanol | Cameroon | Swiss albino | Tchatal Tali et al. (2020) |
| *Plasmodium berghei* | Chrysanthemum indicum (Asteraceae) | NCBI:txid146995 | Leaves | Methanol | Ethiopia | Swiss albino | Habte et al. (2020b) |
| *Plasmodium berghei* | Citrus colosynthis (Cucurbitaceae) | NCBI:txid25529 | Leaves; Seeds | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium berghei* | Citrus maxima (Rutaceae) | NCBI:txid37334 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium berghei* | Coriandrum sativum (Apoiaceae) | NCBI:txid4047 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium berghei* | Rubus ellipticus (Rosaceae) | NCBI:txid59492 | Leaves; Fruits | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium berghei* | Rumex obtusifolius (Polygonaceae) | NCBI:txid3619 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium berghei* | Salvadoras oleoides (Salvadoraceae) | NCBI:txid1173311 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium berghei* | Saraca asoca (Caesalpiniaceae) | NCBI:txid1073321 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium berghei* | Syngonium podophyllum (Arauaceae) | NCBI:txid267621 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium berghei* | Zanthoxylum acontophyllum (Rutaceae) | NCBI:txid1056460 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium berghei* | Capsicum frutescens (Solanaeaceae) | NCBI:txid4073 | Fruits | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium berghei* | Aloe weholensis (Aloaceae) | NCBI:txid1593116 | Leaves | Leaves | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium berghei* | Terminalia neotalia (Combretaceae) | NCBI:txid1799636 | Leaves; Stem | Aqueous, Ethanol; Dichloromethane; Hexane | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium berghei* | Bersama abysinica (Francoaceae) | NCBI:txid113247 | Leaves | Methanol | Ethiopia | Swiss albino | Alehegn et al. (2020) |
| *Plasmodium berghei* | Olea europaea (Oleaceae) | NCBI:txid4146 | Stem | Methanol | Ethiopia | Swiss albino | Kifle et al. (2020) |
| *Plasmodium berghei* | Myrica salicifolia (Myricaceae) | NCBI:txid1509 | Roots | Methanol | Ethiopia | Swiss albino | Dibessa et al. (2020) |
| *Plasmodium berghei* | Aloe pirotae (Aloaceae) | NCBI:txid25641 | Latex | Aqueous | Ethiopia | Swiss albino | Habte et al. (2020b) |
| *Plasmodium berghei* | Schinus molle (Anacardiaceae) | NCBI:txid43851 | Seeds | Aqueous | Ethiopia | Swiss albino | Habte et al. (2020b) |
| *Plasmodium berghei* | Daniellia agea (Caesalpinioideae) | NCBI:txid162734 | Leaves | Methanol | Nigeria | Swiss albino | Ezenyi et al. (2020) |
| *Plasmodium berghei* | Andropogon schirensis (Gramineae) | NCBI:txid205634 | Roots | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium bergeri* | Icacinica trichanta (Icacinaceae) | NCBI:txid341015 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium berghei* | Chasmanthera dependens (Menispermaceae) | NCBI:txid2790913 | Roots | Ethanol | Nigeria | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium bergeri* | Celtis durandii (Ulmaceae) | NCBI:txid1340809 | Roots | Aqueous | Ethiopia | Swiss albino | Ezenyi et al. (2020) |
| *Plasmodium bergeri* | Terminalia briefn (Combretaceae) | NCBI:txid134851 | Seeds | Aqueous | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium bergeri* | Helianthus annuus (Asteraceae) | NCBI:txid4232 | Roots; Flowers; Seeds; Stems | Ethanol | Indonesia | Swiss albino | Biruk et al. (2020) |
| *Plasmodium bergeri* | Terminalia alibida (Combretaceae) | NCBI:txid39992 | Stem | Methanol | Guinea | C57BL/6 | Camara et al. (2019) |
| *Plasmodium bergeri* | Combretum molle (Combretaceae) | NCBI:txid507414 | Stem | Methanol | Ethiopia | Swiss albino | Mulaw et al. (2019) |
| *Plasmodium bergeri* | Cordia africana (Boraginaceae) | NCBI:txid222081 | Leaves | Methanol | Ethiopia | Swiss albino | Wondaf细致 and et al. (2019) |
| *Plasmodium bergeri* | Fagara zanthoxylodes (Rutaceae) | wfo-0000685053 | Leaves | Methanol | Nigeria | Swiss albino | Encri et al. (2019) |
| *Plasmodium bergeri* | Paspalum scrobiculatum (Poaceae) | NCBI:txid173849 | Spikelets | Ethanol | Ghana | BALB/c | Laryea and Borquaye (2019) |
| *Plasmodium bergeri* | Bidens pilosa (Asteraceae) | NCBI:txid42337 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium bergeri* | Acidocarpus alternifolius (Malpighiaeae) | NCBI:txid217121 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium bergeri* | Clappertonia foetida (Triticeae) | NCBI:txid2708755 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium bergeri* | Mitragyna ciliate (Rubiaeaceae) | NCBI:txid170021 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium bergeri* | Parinarium congensis (Chrysobalanaceae) | NCBI:txid1868823 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium bergeri* | Monanthonaxis cafr (Annonaceae) | NCBI:txid992735 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |
| *Plasmodium bergeri* | Datura stramonium (Solanaeaceae) | NCBI:txid4076 | Leaves | Methanol | Ethiopia | Swiss albino | Habte and Assefa (2020a) |

(continued on next page)
| Parasite name | Plant (Family) | Plant Taxon ID* | Studied plant part | Extract type | Country of harvest | Mouse strain | References |
|---------------|----------------|----------------|-------------------|--------------|-------------------|-------------|------------|
| *Plasmodium* berghei | Faurea speciose (Proteaceae) | NCBI:txid206258 | Leaves | Leaves | | | |
| | Syzygium guineense (Myrtaceae) | NCBI:txid134482 | Leaves | Leaves | | | |
| | Croton penduliflorus (Euphorbiaceae) | NCBI:txid2708777 | Leaves | | | | |
| | Euphorbia abyssinica (Euphorbiaceae) | NCBI:txid316813 | Root | Methanol | Ethiopia | Swiss Albino | Muluye et al. (2019) |
| | Salvadoras persica (Salvadoraceae) | NCBI:txid4326 | Roots | Leaves | Aqueous | Ethiopia | Swiss Albino | Gebrehiwot et al. (2019) |
| | Balanites rotundifolia (Zygophyllaceae) | NCBI:txid1670835 | Leaves | | | | |
| | Plasmodium berghei | NCBI:txid181237 | Stem | Methanol; Dichloromethane | Tanzania | BALB/c | Kweyamba et al. (2019); Dikhil et al. (2019); Al-Shaebi et al. (2018); Al-Shaebi et al. (2017); Dikhil et al. (2015); Habluetzel et al. (2019) |
| | Euphorbia abyssinica (Euphorbiaceae) | NCBI:txid316813 | Leaves | | | | |
| | Euphorbia abyssinica (Euphorbiaceae) | NCBI:txid2708777 | Leaves | | | | |
| Plasmodium berghei | NCBI:txid196665 | Leaves | Methanol | | | | |
| | Plasmodium berghei | NCBI:txid198899 | Leaves | Ethanol | | | |
| | Azadirachta indica (Meliaceae) | NCBI:txid124943 | Seeds | Methanol | Burkina Faso | C57BL/6; BALB/c | Haidara et al. (2018) |
| | Ziziphus mauritiana (Rhamnaceae) | NCBI:txid157914 | Leaves | Ethanol | Abidjan | Swiss Albino | Attemene et al. (2018) |
| | Anthocleista djalonensis (Loganiaceae) | NCBI:txid26470 | Leaves | Ethanol | Mali | Swiss Albino | Haidara et al. (2018) |
| | Trema orientalis (Cannabaceae) | NCBI:txid6112 | Fruits | Methanol | Iran | Swiss Albino | Ogunsola et al. (2017) |
| | Solanum nigrum (Solanaceae) | NCBI:txid3057 | Seeds | Methanol | Nigeria | Swiss Albino | Olanlokun et al. (2017) |
| | Teucrium polium (Lamiaceae) | NCBI:txid3992 | Leaves | Ethanol | Mali | Swiss Albino | Haidara et al. (2018) |
| | Lophira alata (Ochnaceae) | NCBI:txid549775 | Leaves | Ethanol | Abidjan | Swiss Albino | Attemene et al. (2018) |
| | Lawsonia inermis (Lythraceae) | NCBI:txid141191 | Leaves; Seeds; Flowers; Stems | Fraxetin; Ethyl acetate | India | BALB/c | Singh et al. (2017a) |
| | Terminalia macroplera (Combretaceae) | NCBI:txid3992 | Leaves | Ethanol | Mali | Swiss Albino | Haidara et al. (2018) |
| | Pterocarpus santalinus (Bignoniaceae) | NCBI:txid13107 | Leaves | Ethanol | Malagasy | Swiss Albino | Haidara et al. (2018) |
| | Plasmodium berghei | NCBI:txid13120 | Leaves | Ethanol | Abidjan | Swiss Albino | Attemene et al. (2018) |
| | Citrus x sinensis (Rutaceae) | NCBI:txid252529 | Leaves | Ethanol | Mali | Swiss Albino | Haidara et al. (2018) |
| | Salis alba (Salicaceae) | NCBI:txid75704 | Leaves | Ethanol | Abidjan | Swiss Albino | Attemene et al. (2018) |
| | Achillea millefolium (Compositae) | NCBI:txid1117157 | Aerial parts | Ethanol | Abidjan | Swiss Albino | Attemene et al. (2018) |
| | Physalis alkekengi (Solanaceae) | NCBI:txid13107 | Leaves | Ethanol | Abidjan | Swiss Albino | Attemene et al. (2018) |
| | Citrus x sinensis (Rutaceae) | NCBI:txid252529 | Leaves | Ethanol | Abidjan | Swiss Albino | Attemene et al. (2018) |
| | Salis alba (Salicaceae) | NCBI:txid75704 | Leaves | Ethanol | Abidjan | Swiss Albino | Attemene et al. (2018) |
| | Verbena officinalis (Lamiaceae) | NCBI:txid13329 | Flowers | Ethanol | Abidjan | Swiss Albino | Attemene et al. (2018) |
| | Portulaca oleracea (Portulacaceae) | NCBI:txid3633 | Leaves | Ethanol | Abidjan | Swiss Albino | Attemene et al. (2018) |
| | Lavandula angustifolia (Lamiaceae) | NCBI:txid19329 | Flowers | Ethanol | Abidjan | Swiss Albino | Attemene et al. (2018) |
| | Plasmodium berghei | Holarrhena floribunda (Apocynaceae) | NCBI:txid2708850 | Leaves | Ethanol | Lomé, Togo | NMRI | Hœnkou et al. (2017); Ololoko et al. (2017) |
| | Ziziphus Mauritiana (Rhamnaceae) | NCBI:txid4577 | Peels | Ethanol | Nigeria | Swiss Albino | Swaller et al. (2017) |
| | Plasmodium berghei | Phygelius virgatus (Phygeliiaceae) | NCBI:txid283121 | Leaves | Ethanol | South Africa, India | Swiss Albino | Singh et al. (2017b) |
| Parasite name | Plant (Family) | Plant Taxon ID* | Studied plant part | Extract type | Country of harvest | Mouse strain | References |
|---------------|---------------|----------------|-------------------|--------------|-------------------|--------------|------------|
| *Plasmodium* berghei | Copaifera reticulata (Fabaceae) | NCBI:txid162716 | Whole plant | Oleoresin | Brazil | BALB/c | de Souza et al. (2017) |
| *Plasmodium* berghei | Strychnos mitis (Loganiaceae) | NCBI:txid1040902 | Leaves | Methanol; Aqueous Ethanol; | Ethiopia | Swiss albino; Swiss albino | Fentahun et al. (2017); Tshiekeledi Tshibangwu et al. (2017); Chukwuocha et al. (2016) |
| *Plasmodium* berghei | Heinsia crinita (Rubiaceae) | NCBI:txid61937 | Stem; Leaves; Fruits | Dichloromethane; Methanol Aqueous | Equateur | Swiss mice | |
| *Plasmodium* chabaudi; *P. berghei* | Cymbopogon citratus (Poaceae) | NCBI:txid66014 | Whole plant | | México | CBA/Ca | |
| *Plasmodium* berghei | Punica granatum (Lythraceae) | NCBI:txid62663 | Peels | Methanol | Saudi Arabia | Swiss albino | Mubaraki et al. (2016) |
| *Plasmodium* berghei | Heinsia crinita (Rubiaceae) | NCBI:txid61937 | Leaves | | Equateur | Swiss mice | |
| *Plasmodium* berghei | Cymbopogon citratus (Poaceae) | NCBI:txid66014 | Whole plant | | México | CBA/Ca | |
| *Plasmodium* berghei | Holarrhena pubescens (Apocynaceae) | NCBI:txid258132 | Roots | Ethyl acetate; Aqueous | Tanzania | Swiss albino | Nondo et al. (2016) |
| *Plasmodium* berghei | Erythrina schliebenii (Fabaceae) | NCBI:txid2590720 | Stem | | | | |
| *Plasmodium* berghei | Hirtella pubescens (Apocynaceae) | NCBI:txid9381 | Roots | | | | |
| *Plasmodium* berghei | Phyllanthus ussuriensis (Euphorbiaceae) | NCBI:txid13917 | Leaves | | | | |
| *Plasmodium* berghei | Caesalpinia bonduc (Caesalpiniaceae) | NCBI:txid13917 | Seeds | | | | |
| *Plasmodium* berghei | Rhoeas antidyserterica (Simaroubaceae) | NCBI:txid145911 | Leaves | | | | |
| *Plasmodium* berghei | Ocimum lamifolium (Nepetoideae) | NCBI:txid13917 | Seeds | | | | |
| *Plasmodium* berghei | Alnus nepalensis (Betulaceae) | NCBI:txid109066 | Leaves | | | | |
| *Plasmodium* berghei | Gongronema latifolium (Apocynaceae) | NCBI:txid103755 | Leaves | | | | |
| *Plasmodium* berghei | Alstonia boonei (Apocynaceae) | NCBI:txid103755 | Leaves | | | | |
| *Plasmodium* berghei | Picralima nitida (Apocynaceae) | NCBI:txid13917 | Seeds | | | | |
| *Plasmodium* berghei | Landolphia owariensis (Apocynaceae) | NCBI:txid141576 | Leaves | | | | |
| *Plasmodium* berghei | Cassia alata (Fabaceae) | NCBI:txid53923 | Leaves | | | | |
| *Plasmodium* berghei | Ocimum suave (Lamiaceae) | NCBI:txid13917 | Leaves | | | | |
| *Plasmodium* berghei | Plectranthus barbatus (Lamiaceae) | NCBI:txid13917 | Leaves | | | | |
| *Plasmodium* berghei | Zanthoxylum chalybeum (Rutaceae) | NCBI:txid1671342 | Aerial part | | | | |
| *Plasmodium* berghei | Ajuga integrifolia (Lamiaceae) | NCBI:txid18959 | Aerial part | | | | |
| *Plasmodium* berghei | Clerodendrum myricoides (Lamiaceae) | NCBI:txid54240 | Leaves | | | | |
| *Plasmodium* berghei | Melia azedarach (Meliaceae) | NCBI:txid15864 | Twigs | | | | |
| *Plasmodium* berghei | Peponium vogelii (Cucurbitaceae) | NCBI:txid1387135 | Leaves | | | | |
| *Plasmodium* berghei | Preussia schimperi (Verbenaceae) | NCBI:txid14139 | Leaves | | | | |
| *Plasmodium* berghei | Andropogon leucostachyus (Poaceae) | NCBI:txid15314 | Aerial part | | | | |
| *Plasmodium* berghei | Croton cajucara (Euphorbiaceae) | NCBI:txid323033 | Leaves | Chloroform | | | |
| *Plasmodium* berghei | Xylopia amazonica (Annonaceae) | NCBI:txid225838 | Aqueous | | | | |
| *Plasmodium* berghei | Scindapsus hederaceus (Araeaceae) | NCBI:txid258317 | Ethyl acetate | | | | |
| *Plasmodium* berghei | Shorea ovalis (Dipterocarpaceae) | NCBI:txid188518 | Stem | | | | |
| *Plasmodium* berghei | Zingiber spectabile (Zingiberaceae) | NCBI:txid188518 | Ethyl acetate | Malaysia | ICR | Baba et al. (2015) |
| Parasite name | Plant (Family) | Plant Taxon ID* | Studied plant part | Extract type | Country of harvest | Mouse strain | References |
|---------------|----------------|----------------|-------------------|--------------|-------------------|--------------|------------|
| *Plasmodium berghei* | *Markhamia tomentosa* (Bignoniaceae) | NCBI:txid2708893 | Leaves | Aqueous | Nigeria | Swiss albino | Bankole et al. (2016) |
| | *Polyalthia longifolia* (Annonaceae) | NCBI:txid235806 | Stem | | | | |
| | *Trichilia heudeloti* (Meliaceae) | NCBI:txid43894 | Stem | | | | |
| | *Vernonia amygdalina* (Asteraceae) | NCBI:txid82755 | Leaves | Aqueous; Ethanol | Ethiopia | BALB/c | Abay et al. (2015) |
| | *Alhagi camelorum* (Fabaceae) | NCBI:txid47037 | Whole plant | Methanol | Iran | Swiss albino | Esmaeili et al. (2015) |
| | *Alhagi camelorum* (Fabaceae) | NCBI:txid47037 | Whole plant | Flowers | | | |
| | *Bambusa arundinacea* (Poaceae) | NCBI:txid4581 | Gum | | | | |
| | *Cassia angustifolia* (Fabaceae) | NCBI:txid53851 | Leaves | | | | |
| | *Carthamus tinctorius* (Asteraceae) | NCBI:txid4222 | Aerial part | | | | |
| | *Cichorium intybus* (Asteraceae) | NCBI:txid13427 | Roots | | | | |
| | *Cichorium intybus* (Asteraceae) | NCBI:txid13427 | Aerial part | | | | |
| | *Convolvulus scammonia* (Convolvulaceae) | NCBI:txid1428931 | Gum resin | | | | |
| | *Cotoneaster nummularia* (Rosaceae) | NCBI:txid1804980 | Fruit | | | | |
| | *Cordia myxa* (Boraginaceae) | NCBI:txid181185 | Fruits | | | | |
| | *Cordia myxa* (Boraginaceae) | NCBI:txid181185 | Flowering branches | | | | |
| | *Fumaria parviflora* (Fumariaceae) | NCBI:txid1464625 | Leaves | | | | |
| | *Hedera helix* (Araliaceae) | NCBI:txid4052 | Aerial part | | | | |
| | *Plantago psyllium* (Plantaginaceae) | NCBI:txid26867 | Seeds | | | | |
| | *Portulaca oleracea* (Portulacaceae) | NCBI:txid46147 | Seeds | | | | |
| | *Rosa damascena* (Rosaceae) | NCBI:txid3765 | Flowers | | | | |
| | *Viola odorata* (Violaceae) | NCBI:txid97441 | Flowers | | | | |
| | *Viola odorata* (Violaceae) | NCBI:txid97441 | Whole plant | | | | |
| | *Ziziphus jujuba* (Rhamnaceae) | NCBI:txid326968 | Fruits | | | | |
| *Plasmodium chabaudi* | *Indigofera oblongifolia* (Fabaceae) | NCBI:txid198899 | Leaves | Methanol | Saudi Arabia | C57Bl/6 | Lubbad et al. (2015) |
| | *Osyris quadripartite* (Santalaceae) | NCBI:txid169279 | Leaves | Aqueous, Chloroform, Methanol | Ethiopia | Swiss albino | Girma et al. (2015) |
| *Plasmodium berghei*; | *Ocimum gratissimum* (Lamiaceae ) | NCBI:txid204144 | Leaves | Ethanol and water | Cameroon | Swiss albino | Tarkang et al. (2014) |
| | *Citrus sinensis* (Rutaceae) | NCBI:txid2711 | Leaves | | | | |
| | *Cymbopogon citratus* (Poaceae) | NCBI:txid66014 | Leaves | | | | |
| | *Carica papaya* (Caricaceae) | NCBI:txid3649 | Leaves | | | | |
| | *Psidium guajava* (Myrtaceae) | NCBI:txid120290 | Leaves | | | | |
| | *Mangifera indica* (Anacardiaceae) | NCBI:txid29780 | Roots; Leaves | | | | |
| | *Echinops kebericho* (Asteraceae) | wfo-0000133310 | Roots | Ethanol | Ethiopia | Swiss albino | Swiss albino | Toma et al. (2015) |
| | *Maytenus senegalensis* (Celastraceae) | NCBI:txid256095 | Root | Ethanol | Tanzania | Swiss albino | Swiss albino | Malebo et al. (2015) |
| Parasite name | Plant (Family) | Plant Taxon ID* | Studied plant part | Extract type | Country of harvest | Mouse strain | References |
|---------------|---------------|---------------|-------------------|--------------|-------------------|-------------|------------|
| *Plasmodium* berghei | Citrus limetta (Rutaceae) | NCBI:txid414735 | Fruits; Peels | Ethanol | India | Swiss albino | Mohanty et al. (2015) |
| *Plasmodium* berghei | Psidium acutangulum (Myrtaceae) | NCBI:txid2478822 | Stems; Leaves; Fruits | Aqueous | France | Swiss albino | Houël et al. (2015) |
| *Plasmodium* berghei | Grewia trichocarpa (Tiliaceae) | NCBI:txid2601743 | Roots | Aqueous | Kenya | Swiss albino | Mwangi et al. (2015) |
| *Plasmodium* berghei | Dicrostachys cinerea (Mimosaceae) | NCBI:txid196665 | Stem | Ethanol; Ethyl acetate; Ether | Nigeria | Swiss albino | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Azadirachta indica (Meliaceae) | NCBI:txid58860 | Roots | Aqueous | India | Swiss albino | Anagu et al. (2013) |
| *Plasmodium* berghei | Telfaria occidentalis (Cucurbitaceae) | NCBI:txid124943 | Roots | Methanol; Ethanol | Rwandan | SPF | Kabiru et al. (2014) |
| *Plasmodium* berghei | Aspidosperma brasiliense (Apocynaceae) | NCBI:txid138044 | Roots | Aqueous | Switzerland | NMRI | Julianti et al. (2014) |
| *Plasmodium* berghei | Carica papaya (Caricaeaceae) | NCBI:txid370897 | Leaves | Methanol; Ethanol | Nigeria | Swiss albino | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Telfaria occidentalis (Cucurbitaceae) | NCBI:txid204226 | Roots | Methanol | Rwanda | SPF | Muganga et al. (2014) |
| *Plasmodium* berghei | Fuertesia africana (Lamiaceae) | NCBI:txid507438 | Methanol | Ethanol; Ethyl acetate | Nigeria | Swiss albino | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Terminalia mollis (Combretaceae) | NCBI:txid1671342 | Leaves | Methanol; Aqueous | Nigeria | Swiss albino | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Zanthoxylum chalybeum (Rutaceae) | NCBI:txid58860 | Roots | Aqueous | Nigeria | Swiss albino | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Telfaria occidentalis (Cucurbitaceae) | NCBI:txid124943 | Roots | Aqueous | Nigeria | Swiss albino | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Conyza sumatrensis (Asteraceae) | NCBI:txid212787 | Leaves | Ethanol | Cameroon | Swiss albino | Boniface et al. (2015) |
| *Plasmodium* berghei | Carica papaya (Caricaeaceae) | NCBI:txid370897 | Leaves | Methanol; Ethanol | Switzerland | NMRI | Julianti et al. (2014) |
| *Plasmodium* berghei | Telfaria occidentalis (Cucurbitaceae) | NCBI:txid397732 | ND | Chloroform; Ethanol | Turkey | BALB/c | Ozbilgin et al. (2014) |
| *Plasmodium* berghei | Leptigallea angolensis (Asteraceae) | NCBI:txid997725 | ND | Chloroform; Ethanol | Brazil | Swiss albino | Simelane et al. (2015) |
| *Plasmodium* berghei | Phylanthus amarus (Phyllanthaceae) | NCBI:txid997703 | ND | Chloroform; Ethanol | Nigeria | Swiss albino | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Centaurea hierapolitana (Asteraceae) | NCBI:txid1436092 | ND | Chloroform; Ethanol | Nigeria | Swiss albino | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Centaurea Lydia (Asteraceae) | NCBI:txid145506 | ND | Chloroform; Ethanol | Nigeria | Swiss albino | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Centaurea polyclada (Asteraceae) | NCBI:txid1530336 | ND | Chloroform; Ethanol | Nigeria | Swiss albino | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Scrophularia floribunda (Scrophulariaceae) | NCBI:txid1357615 | ND | Chloroform; Ethanol | Turkey | BALB/c | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Scrophularia depauperata (Scrophulariaceae) | NCBI:txid1970690 | ND | Chloroform; Ethanol | Turkey | BALB/c | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Scrophularia cryptophila (Scrophulariaceae) | NCBI:txid1970660 | ND | Chloroform; Ethanol | Turkey | BALB/c | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Lavandula stoechas (Labiatae) | NCBI:txid39333 | ND | Chloroform; Ethanol | Turkey | BALB/c | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Rubia davisciana (Rubiaceae) | NCBI:txid25473 | ND | Chloroform; Ethanol | Turkey | BALB/c | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Alkanna tinctoria (Rubiaceae) | NCBI:txid543564 | ND | Chloroform; Ethanol | Turkey | BALB/c | Adegbolagun et al. (2014) |
| *Plasmodium* berghei | Markhamia obtusifolia (Sapotaceae) | NCBI:txid1237616 | Stem | Ethanol | South Africa | Swiss albino | Simelane et al. (2013) |
| *Plasmodium* berghei | Hypoxis colchicifolia (Hypoxidaceae) | NCBI:txid16123 | Bulb | Ethanol | South Africa | Swiss albino | Mwangi et al. (2015) |
| *Plasmodium* berghei | Pluchea lanceolata (Asteraceae) | NCBI:txid1950228 | Aerial part | Ethanol | South Africa | Swiss albino | Mwangi et al. (2015) |
| *Plasmodium* berghei | Melissa officinalis (Labiatae) | NCBI:txid139333 | Aerial part | Ethanol | South Africa | Swiss albino | Mwangi et al. (2015) |
| *Plasmodium* berghei | Althea officinalis (Malvaceae) | NCBI:txid145745 | Flowers | Ethanol | South Africa | Swiss albino | Mwangi et al. (2015) |
| *Plasmodium* berghei | Borago officinalis (Boraginaceae) | NCBI:txid13363 | Flowers | Ethanol | South Africa | Swiss albino | Mwangi et al. (2015) |
| *Plasmodium* berghei | Glycerrhiza glabra (Papilionaceae) | NCBI:txid49827 | Roots | Ethanol | South Africa | Swiss albino | Mwangi et al. (2015) |
| *Plasmodium* berghei | Anthemis nobilis (Compositae) | NCBI:txid90937 | Flowers | Ethanol | South Africa | Swiss albino | Mwangi et al. (2015) |
| *Plasmodium* berghei | Eremostachys lucinata (Lamiaceae) | NCBI:txid694356 | Roots | Ethanol | South Africa | Swiss albino | Mwangi et al. (2015) |
| *Plasmodium* berghei | Plantago major (Plantaginaceae) | NCBI:txid29818 | Seeds | Ethanol | South Africa | Swiss albino | Mwangi et al. (2015) |
| *Plasmodium* berghei | Myristica communis (Myrtaceae) | NCBI:txid119949 | Aerial part | Ethanol | South Africa | Swiss albino | Mwangi et al. (2015) |
| *Plasmodium* berghei | Stoechas lavandulifolia (Labiatae) | NCBI:txid193339 | Flowers | Ethanol | South Africa | Swiss albino | Mwangi et al. (2015) |
| *Plasmodium* berghei | Arctium lappa (Labiatae) | NCBI:txid4217 | Roots | Ethanol | South Africa | Swiss albino | Mwangi et al. (2015) |

(continued on next page)
| Parasite name         | Plant (Family)                                                                 | Plant Taxon ID* | Studied plant part | Extract type | Country of harvest | Mouse strain | References                  |
|-----------------------|--------------------------------------------------------------------------------|-----------------|--------------------|--------------|--------------------|--------------|-----------------------------|
| *Plasmodium berghei*  | *Bergenia ciliate* (Saxifragaceae)                                              | NCBI:txid23238  | leaves             | Ethanol      | India              | Swiss albino | Walter et al. (2013)         |
|                       | *Azadirachta indica* (Meliaceae)                                                | NCBI:txid124943 | Root               | Aqueous      | Kenya              | Swiss albino | Nguta and Mbaria (2013)      |
|                       | *Dichrostachys cinerea* (Mimosaceae)                                            | NCBI:txid196665 | Root               | Root         | India              | Swiss mice   | (2013)                      |
|                       | *Tamarindus indica* (Caesalpinaceae)                                             | NCBI:txid58860  | Stem               | Root         | India              | Swiss albino | Priyanka et al. (2013)       |
|                       | *Acacia seyal* (Mimosaceae)                                                      | NCBI:txid138044 | Root               | Root         | India              | Swiss albino | Yal et al. (2013)            |
|                       | *Grewia triochocarpa* (Tiliaceae)                                                | NCBI:txid2601743| Roots              | Aqueous      | Kenya              | Swiss albino | Musila et al. (2013)         |
|                       | *Holarrhena antidysenterica* (Apocynaceae)                                       | NCBI:txid69380  | Stem               | Aqueous      | India              | Swiss albino | Agrawal et al. (2013)        |
|                       | *Nyctanthes arboristis* (Oleaceae)                                              | NCBI:txid41398  | Leaves             | Ethanol;     | India              | Swiss albino | Lee and Rhee (2013)          |
| *Plasmodium berghei*  | *Azadirachta indica* (Meliaceae)                                                | NCBI:txid124943 | Leaves             | Ethanol;     | Kenya              | Swiss albino | Endale et al. (2013)         |
|                       | *Rumex crispus* (Polygonaceae)                                                   | NCBI:txid174649 | Whole plant        | Ethanol      | Korea              | C57BL/6      | Mesfin et al. (2012)         |
|                       | *Osteoglossum integrifolia* (Lamiaceae)                                          | NCBI:txid483857 | Leaves             | Methanol     | Ethiopia           | Swiss albino | Chandel et al. (2012)        |
|                       | *Adansonia digitata* (Malvaceae)                                                 | NCBI:txid69109  | Whole plant        | Methanol;    | Kenya              | Swiss albino | (2013)                      |
|                       | *Launaea cornuta* (Rubiaceae)                                                    | NCBI:txid381723 | Aerial part        | Chloroform   | Switzerland        | Swiss albino | (2013)                      |
|                       | *Zanthoxylum chalybeum* (Rutaceae)                                               | NCBI:txid1671342| Leaves             | Ethanol      | India              | Swiss albino | (2013)                      |
|                       | *Artemisia annua* (Asteraceae)                                                    | NCBI:txid35608  | Leaves             | Whole plant  | USA                | C57BL/6      | Elfwal et al. (2012)         |
| *Plasmodium berghei*  | *Sorindeia juglandifolia* (Anacardiaceae)                                         | NCBI:txid1317886| Fruits             | Methanol     | Cameroon           | Swiss albino | Kamkumo et al. (2012)        |
|                       | *Acanthus pyreus* (Asteraceae)                                                    | NCBI:txid182999 | Aerial part        | Hexan        | Benin              | NMRI         | Ganon et al. (2012)          |
|                       | *Azadirachta indica* (Meliaceae)                                                 | NCBI:txid124943 | Leaves             | Ethanol      | Ethiopia           | Swiss albino | Mesfin et al. (2012)         |
|                       | *Xanthium strumarium* (Asteraceae)                                                | NCBI:txid118068 | Leaves             | Ethanol      | India              | BALB/c       | Chandel et al. (2012)        |
| *Plasmodium berghei*  | *Khaya ivorensis* (Meliaceae)                                                     | NCBI:txid486173 | Stem               | Aqueous      | Kenya              | BALB/c       | Tepongning et al. (2011)     |
|                       | *Alstonia boonei* (Apocynaceae)                                                   | NCBI:txid84857  | Fruits             | Ethanol      | Brazil             | C57BL/6      | Kayano et al. (2011)         |
|                       | *Caesalpinia pulvissa* (Fabaceae)                                                | NCBI:txid191898 | Stern              | Ethanol      | Brazil             | C57BL/6      | Pinmai et al. (2010)         |
| *Plasmodium berghei*  | *Terminalia bellerica* (Combretaceae)                                             | NCBI:txid155021 | Fruits             | Ethanol      | Thailand           | ICR          | (2010)                      |
|                       | *Terminalia chebula* (Combretaceae)                                               | NCBI:txid155022 | Fruits             | Ethanol      | Switzerland        | Swiss albino | (2011)                      |
|                       | *Phyllanthus emblica* (Phyllanthaceae)                                            | NCBI:txid296036 | Fruits             | Ethanol      | India              | Swiss albino | Verma et al. (2011)          |
|                       | *Holarrhena antidysenterica* (Apocynaceae)                                       | NCBI:txid69380  | ND                  | Ether;Chloroform; Methanol; Aqueous | Ethiopia | Swiss albino | (2011)                      |
|                       | *Vostra congensis* (Violaceae)                                                    | NCBI:txid509528 | Roots; Stem; Leaves | Methanol     | Kenya              | BALB/c       | Gathirwa et al. (2011)       |
| *Plasmodium berghei*  | *Crematocarpus palliatus* (Tiliaceae)                                             | NCBI:txid296036 | Stem; Leaves       | Methanol     | Kenya              | Swiss albino | (2011)                      |
|                       | *Combretum padoi* (Combretaceae)                                                   | NCBI:txid507418 | Roots; Leaves      | Methanol     | Kenya              | Swiss albino | (2011)                      |
|                       | *Hosulindia opposita* (Labiateae)                                                | NCBI:txid204228 | Roots; Leaves      | Methanol     | Kenya              | Swiss albino | (2011)                      |
|                       | *Rhus natalensis* (Anacardiaceae)                                                | NCBI:txid4012   | Roots; Leaves      | Methanol     | Kenya              | Swiss albino | (2011)                      |
|                       | *Combretum iliarii* (Combretaceae)                                                | NCBI:txid589534 | Roots; Leaves      | Methanol     | Kenya              | Swiss albino | (2011)                      |
|                       | *Lannea schweinfurthii* (Anacardiaceae)                                           | NCBI:txid289717 | Roots; Leaves      | Methanol     | Kenya              | Swiss albino | (2011)                      |
|                       | *Prema chrysocladia* (Verbenaceae)                                               | NCBI:txid41393  | Roots; Leaves      | Methanol     | Kenya              | Swiss albino | (2011)                      |
|                       | *Allrophytus perriva* (Sapindaceae)                                              | NCBI:txid1972007| Roots; Leaves      | Methanol     | Kenya              | Swiss albino | (2011)                      |
|                       | *Abras precatorius* (Leguminosae)                                                 | NCBI:txid3816   | Roots; Leaves      | Methanol     | Kenya              | Swiss albino | (2011)                      |
|                       | *Agathisanthemum bojeri* (Rubiaceae)                                              | NCBI:txid58372  | Whole plant        | Methanol     | Kenya              | Swiss albino | (2011)                      |
|                       | *Uvaria acuminata* (Annonaceae)                                                   | NCBI:txid672960 | Roots; Leaves      | Methanol     | Kenya              | Swiss albino | (2011)                      |
| Parasite name | Plant (Family) | Plant Taxon ID* | Studied plant part | Extract type | Country of harvest | Mouse strain | References |
|---------------|---------------|----------------|-------------------|--------------|-------------------|-------------|------------|
| Plasmodium berghei | Azadirachta indica (Meliaceae) | NCBI:txid124943 | Leaves | | | | |
| | Flueggea virosa (Euphorbiaceae) | NCBI:txid283121 | Roots | | | | |
| | Boerhavia elegans (Nyctaginaceae) | NCBI:txid4107 | ND | Ethanol | Iran | BALB/C | Ramazani et al. (2010) |
| | Solanum surattense (Solanaceae) | NCBI:txid13230 | ND | | | | |
| | Prosopis juliflora (Fabaceae) | | | | | | |
| | Plasmodium berghei | | | | | | |
| | Zanthoxylum usambarense (Rutaceae) | NCBI:txid2562172 | Stem | Aquoeus | Kenya | BALB/C | Wore et al. (2010) |
| | Warburgia ugandensis (Canellaceae) | NCBI:txid549619 | | | | | |
| Plasmodium berghei | Anisopappus chinensis (Asteraceae) | NCBI:txid2052862 | Whole plant | Aqueous; Methanol; Dichloromethane | Congo | NMRI | Lusakibanza et al. (2010) |
| | Entandrophragma pallstrae (Meliaceae) | NCBI:txid122399 | ND | | | | |
| | Aplophia thiermis (Aphloioaceae) | NCBI:txid112806 | Leaves | Methanol | France | Swiss albino | Jonville et al. (2008) |
| | Buddleja salvi folia (Loganiaceae) | NCBI:txid168503 | Leaves; Flowers | | | | |
| | Eupatorium triplinerve (Asteraceae) | NCBI:txid1090619 | Aerial part | | | | |
| | Geniostoma borbonicum (Loganiaceae) | NCBI:txid1054603 | Leaves | | | | |
| | Justicia gendarussa (Acanthaceae) | NCBI:txid714472 | Aerial part | | | | |
| | Lantana camara (Verbenaceae) | NCBI:txid126435 | Leaves; Flowers | | | | |
| | Nuxia verticillata (Loganiaceae) | NCBI:txid69069 | Leaves | | | | |
| | Psidium argutu (Asteraceae) | NCBI:txid1225821 | Leaves | | | | |
| | Terminalia bentzoe (Combretaceae) | NCBI:txid1908415 | Leaves | | | | |
| Plasmodium berghei | Carpesium ceraum (Asteraceae) | NCBI:txid119171 | Whole plant | Ethanol | South Korea | ICR | Kim et al. (2009) |
| Plasmodium berghei | Ampelosyphus amanzonicus (Rhamnaceae) | NCBI:txid106660 | Roots | Ethanolic | Brazil | CDI | Andrade-Neto et al. (2008) |
| Plasmodium berghei | Phyllanthus amarus (Euphorbiaceae) | NCBI:txid293060 | Leaves; Stem | Aqueous | Nigeria | Swiss albino | Dapper et al. (2007) |
| Plasmodium berghei | Turraea robusta (Meliaceae) | NCBI:txid1899148 | Stems, Roots | Aqueous | Kenya | Swiss albino | Gathirwa et al. (2008) |
| | Lanrea schweinfurthii (Meliaceae) | NCBI:txid289717 | | | | | |
| Plasmodium vinckei | Sclerochara birrea (Anacardiaceae) | NCBI:txid289766 | Leaves, stems | Ether; Acetone; Ethanol | Senegal | Swiss albino | Benoit-Vical et al. (2008) |
| | Chrozophora senegalensis (Euphorbiaceae) | NCBI:txid316752 | | | | | |
| Plasmodium berghei | Phyllanthus niruri (Phyllanthaceae) | NCBI:txid296034 | Whole plant | Aqueous | Indonesia | Swiss albino | Mustofa (2007) |
| Plasmodium berghei | Flueggea virosa (Euphorbiaceae) | NCBI:txid283121 | Leaves, Stems, Roots | Aqueous; Methanol; Chloroform | Kenya | Swiss albino | Muthaura et al. (2007a) |
| | Warburgia stahlmannii (Canellaceae) | NCBI:txid155635 | | | | | |
| | Harungana madagascariensis (Guttiferae) | NCBI:txid198768 | | | | | |
| | Maytenus putterlickioides (Celastraceae) | NCBI:txid123430 | | | | | |
| | Maytenus undata (Celastraceae) | NCBI:txid123432 | | | | | |
| Plasmodium yoelii | Eurycoma longifolia (Simaroubaceae) | NCBI:txid458531 | Root | Methanol | Malaysia | ND | Mohd Ridzuan et al. (2007) |
| Plasmodium berghei | Schkuhria pinnata (Asteraceae) | NCBI:txid176579 | Whole plant | Aqueous; Methanol | Kenya | Swiss albino | Muthaura et al. (2007b) |
| Parasite name | Plant (Family)                  | Plant Taxon ID* | Studied plant part | Extract type | Country of harvest | Mouse strain | References                        |
|---------------|--------------------------------|-----------------|--------------------|--------------|--------------------|--------------|-----------------------------------|
| *Fuerstia africana* (Lamiaceae) | NCBi:txid204226 | Studied plant part | Aqueous | Kenya | ICR | Muregi et al. (2007a) |
| *Ludwigia erecta* (Onagraceae) | NCBi:txid1620136 | Root | Leaves; Roots | Roots | Roots | Leaves; Seeds | Methanol | Kenyan | ICR | Muregi et al. (2007b) |
| *Maytenus senegalensis* (Celastraceae) | NCBi:txid256095 | Leaves; Roots; Stem | Leaves; Roots | Stem | Roots; Leaves; Roots | Whole plant | 
| *Veronica lasiopis* (Compositae) | NCBi:txid83961 | Leaves | Leaves; Roots | Roots | Roots | Seeds | Aqueous | France | Swiss albino | Bertani et al. (2005) |
| *Maytenus heterophylla* (Celastraceae) | NCBi:txid123440 | Leaves; Roots; Stem | Leaves; Roots | Stem | Roots | Leaves; Roots | Methanol | Kenya | ICR | Muregi et al. (2007b) |
| *Rhamnus prinoides* (Rhamnaceae) | NCBi:txid280022 | Roots | Leaves; Roots | Roots | Roots | Leaves; Seeds | Methanol | Kenya | ICR | Muregi et al. (2007b) |
| *Rhamnus staddo* (Rhamnaceae) | NCBi:txid280026 | Leaves; Roots | Leaves; Roots | Roots | Roots | Roots | Aqueous | France | Swiss albino | Bertani et al. (2005) |
| *M. acuminata* (Rutaceae) | NCBi:txid1237617 | Leaves; Roots | Leaves; Roots | Roots | Roots | Roots | Aqueous | France | Swiss albino | Bertani et al. (2005) |
| *T. asiatica* (Rutaceae) | NCBi:txid1237617 | Leaves; Roots | Leaves; Roots | Roots | Roots | Roots | Aqueous | France | Swiss albino | Bertani et al. (2005) |
| *Clerodendrum myricoides* (Verbenaceae) | NCBi:txid54240 | Leaves; Roots | Leaves; Roots | Stem | Leaves; Roots | Whole plant | 

**Table 1 (continued)**

| Parasite name | Plant (Family)                  | Plant Taxon ID* | Studied plant part | Extract type | Country of harvest | Mouse strain | References                        |
|---------------|--------------------------------|-----------------|--------------------|--------------|--------------------|--------------|-----------------------------------|
| *Plasmodium yoelii* | NCBi:txid235824 | Leaves; Stem | Leaves | Aqueous | France | Swiss albino | Bertani et al. (2005) |
| *Zanthoxylum rhoifolium* (Rutaceae) | NCBi:txid549434 | Leaves; Roots | Leaves | Aqueous | France | Swiss albino | Bertani et al. (2005) |
| *Tinospora crispata* (Menispermaeae) | NCBi:txid285591 | Leaves; Roots | Leaves | Aqueous | France | Swiss albino | Bertani et al. (2005) |
| *Quassia amara* (Simaroubaceae) | NCBi:txid43725 | Leaves; Roots | Leaves | Aqueous | France | Swiss albino | Bertani et al. (2005) |
| *Picrolemma pseudocoffea* (Simaroubaceae) | NCBi:txid459142 | Leaves; Roots | Leaves | Aqueous | France | Swiss albino | Bertani et al. (2005) |
| *Irlbachia alata* (Gentianaceae) | NCBi:txid82716 | Leaves; Roots | Leaves | Aqueous | France | Swiss albino | Bertani et al. (2005) |
| *Pseudoxandra cuspidate* (Annonaceae) | NCBi:txid68872 | Whole plant | Leaves | Methanolic | Nigeria | ND | 
| *Striga hermonthica* (Orobanchaceae) | NCBi:txid50164 | Whole plant | Leaves | Methanolic | Nigeria | ND | 
| *Bidens pilosa* (Asteraceae) | NCBi:txid42337 | Roots | Ethanol | Brazil | Swiss albino | 
| *Iris germanica* (Iridaceae) | NCBi:txid34205 | Rhizome | Ethanol | France | Swiss albino | 

M.A. Dkhil, S. Al-Quraishy, E.M. Al-Shaebi et al. Saudi Journal of Biological Sciences 28 (2021) 1723–1738
The drug research requires an urgent need for new and improved anti-malarial therapeutics, preferably with novel mechanisms of action to avoid, control or minimize parasite resistance. A cheaper, simpler, more sustainable alternative to most synthetic drugs and pharmaceuticals is offered by the use of medicinal plants in therapy. In addition, they were hardly seen to have any side effects and are accepted with less adverse consequences (Nasri and Shirzad 2013).

In 2018, a cumulative funding of US$ 663 million was spent globally in fundamental research and product growth for malaria. This was a small improvement (an increase of US$ 18 million, or 2.8 percent) from the previous year (WHO, 2019).

Table 1 (continued)

| Parasite name | Plant (Family) | Plant Taxon ID* | Studied plant part | Extract type | Country of harvest | Mouse strain | References |
|---------------|----------------|----------------|-------------------|--------------|-------------------|--------------|------------|
| *Plasmodium berghei* | *Struchium sparganophorum* (Asteraceae) | NCBI:txid2067364 | Leaves | Ethanol | Guinea | BALB/c | do Ceu de Madureira et al. (2002) |
| *Vernonia amygdalina* (Asteraceae) | | NCBI:txid68299 | Aerial part | | | | |
| *Ageratum conyzoides* (Asteraceae) | | NCBI:txid68299 | Aerial part | | | | |
| *Cinchona succirubra* (Rubiaceae) | | NCBI:txid43462 | Stem | | | | |
| *Aloe humilis* (Liliaceae) | | NCBI:txid247124 | Leaves | | | | |
| *Tithonia diversifolia* (Asteraceae) | | NCBI:txid684020 | Aerial part | | | | |
| *Cedrela odorata* (Melaceae) | | NCBI:txid124947 | Stem | | | | |
| *Prenna angolensis* (Verbenaceae) | | NCBI:txid289394 | Stem | | | | |
| *Pycnanthus angolensis* (Myristicaceae) | | NCBI:txid224864 | Stem | | | | |
| *Morinda lucida* (Rubiaceae) | | NCBI:txid339305 | Stem | | | | |
| *Morinda lucida* (Rubiaceae) | | NCBI:txid339305 | Leaves | | | | |
| *Cestrum laeavigatum* (Solanaceae) | | NCBI:txid1237510 | Leaves | | | | |
| *Cananga bidentata* (Canaceae) | | NCBI:txid4627 | Roots | | | | |
| *Plasmodium yoelii* | *Hydrangea macrophylia* (Hydrangeaceae) | NCBI:txid23110 | Leaves | Aqueous | Japan | ICR | Ishih et al. (2001) |
| *Phyllanthus niruri* (Phyllanthaceae) | | NCBI:txid296034 | Whole plants | Ethanol; Dichloromethane; Aqueous | Congo | Swiss albino | Tona et al. (2001) |
| *Morinda morindoides* (Rubiaceae) | | NCBI:txid659048 | Leaves | | | | |
| *Cassia occidentalis* (Fabaceae) | | NCBI:txid126820 | Roots | | | | |
| *Plasmodium berghei* | *Hydrangea macrophylia* (Hydrangeaceae) | NCBI:txid23110 | Leaves | Aqueous | Japan | ddY | Kamei et al. (2000) |
| *Erythrina senegalensis* (Fabaceae) | | NCBI:txid157649 | Stem | Aqueous | Nigeria | Swiss albino | Saidu et al. (2000) |
| *Plasmodium berghei* | *Pothomorphe peltata* (Piperaceae) | wfo-4000031037 | Leaves | Hexane; Methanol | Brazil | Swiss albino | de Ferreira-da-Cruz et al. (2000) |
| *Plasmodium berghei* | *Pothomorphe umbellata* (Piperaceae) | wfo-4000031037 | Leaves | | | | |
| *Plasmodium chabaudi* | *Ziphitus spinosa* (Rhamnaceae) | NCBI:txid72171 | Leaves | Methanol | Saudi Arabia | Swiss albino | Hafiz et al. (2019) |
| *Ziziphus spinosa* (Rhamnaceae) | | NCBI:txid72171 | Leaves | Methanol | Saudi Arabia | Swiss albino | Mubaraki et al. (2017) |
| *Plasmodium chabaudi* | *Punica granatum* (Lythraceae) | NCBI:txid226663 | Peels | Methanol | Saudi Arabia | Swiss albino | Hafiz et al. (2016) |

*Identification number of the source species, derived from the NCBI Taxonomy database. ND: not determined.

Fig. 3. Documented drugs from plant source.
2. Methodology

This review included all related published scientific articles from January 2000 to November 2020. This article was conducted by searching the electronic databases NCBI, ISI Web of knowledge and ScienceDirect and Saudi digital library to check articles and thesis for M.Sc/Ph.D.

Relevant studies were reviewed through numerous steps. In the first step, target published articles were identified by using general related terms, such as medicinal plants and ‘malaria.’ The second step involved screening the resulting articles by using highly specific keywords, including ‘murine or mice’. The last step of the review focused on selected studies involving the use of medicinal plants against malaria in mice.

We included studies published from January 2000 up to November 2020 on medicinal plants used to treat malaria using mice as animal model. Studies published in the English language were only included.

We excluded papers published before 2000. We excluded in vitro studies, review articles, personal communications and unpublished data.

The reviewers examined each article and independently extracted data on the scientific name, family, local name, and part of the plant used and method of extraction (Tables 1 and Table 2).

Data were entered into Excel datasheet and the frequency distribution of medicinal plants, used Plasmodium species, plant part used, plant Taxon ID, family of the plants, used plant extract and the country were described. The obtained data were presented in tables and Figures.

3. Results and discussion

In this systematic review, medicinal plants from January 2000 to November 2020 have been used for the treatment of murine malaria have been showed. Accordingly, 323 plant species in 170 research articles were identified for treatment of malaria. Only 128 articles were included in this study. The reviewed plants belonged to 83 families. Medicinal plants of the families Asteraceae, Meliaceae Fabaceae and Lamiaceae are the most abundant for use in laboratory animal antimalarial studies with 31, 17, 15 and 12 research papers, respectively (Table 1).

More medicinal plants species with antimalarial activity were from families Asteraceae and Meliaceae due to high prevalence of these families in the studied countries especially in Africa.

Leaves were the most common plant part used for the experimental malaria research due to the availability of several active compounds (Asafo-Agyei et al., 2019).

According to region, published articles from 33 different countries were reviewed. Most of malaria published articles are from Africa especially Nigeria and Ethiopia (Table 1) where the prevalence of the parasite is high in Africa (WHO, 2019) and most of research is directed to solve the problem.

Only 3 review article were found with our search. Memvanga et al. (2015) reported that approximately 120 extracts obtained from Congolese plant species demonstrated strong or fair antiplasmodial activity. A variety of compounds have also been isolated and reported with promising antiplasmodial effects. Many of these compounds were new scaffolds for promising antimalarial drugs to be synthesized. In comparison to mammalian cells, most of these compounds and extracts have high selective activity against Plasmodium parasites. In mice, the efficacy and safety of several plant-based products has been verified and a strong association between in vitro and in vivo antimalarial activity has been observed.

Amoa Onguéné et al. (2013) surveyed the activity of 278 compounds from African flora until the year 2013. In this review, authors reported compounds mainly contained alkaloids and flavonoids with anti-malarial properties. In the review by Adebayo and Krettli (2011), they focused on medicinal plants which are used to treat malaria in Nigeria from 1984 to 2008.

Biosynthetic approaches for nanoparticles would be much more efficient if nanoparticles were created extracellularly utilizing plants or their extracts in a controlled way (Du et al., 2020). Recently, due to its simplicity and eco-friendlyness, plant-mediated biological synthesis of nanoparticles is gaining importance (Du et al., 2020). In general, set of experiments were carried out to evaluate if this analysis would be used to assess the activity of plant crude extracts (Phillipson and O'Neill, 1987).

Murugan et al. (2016) synthesized silver nanoparticles (AgNP) using the Azadirachta indica seed kernel extract as reducing and stabilizing agent. They reported a moderate activity of the nanoparticles against P. berghei in mice (Table 2). Moreover, our group published three articles on the effect of AgNPs synthesized from Indigofera oblongifolia leaf extracts on P. chabaudi induced infection in C57Bl/6 mice. The suppression of parasitemia reached more than 90% (Murshed et al., 2020). Also, the antioxidant and hepatic and spleen protective role of I. oblongifolia extract was investigated in addition to the iron regulatory role of this medicinal plant.

4. Conclusion

In developing countries, malaria is very widespread, particularly in African countries, causing health problems. In many countries, studies using medicinal plants to suppress parasites and as a defensive tool is common and it is advisable to make people aware of the significance of medicinal plants. Moreover, the biochemical
function, protection and efficacious medicinal plants should be further investigated.

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