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Review

Medicinal plants as a fight against murine blood-stage malaria

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ABSTRACT

Objective: Malaria is an infectious parasitic disease affecting most of countries worldwide. Due to antimalarial 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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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 405,000 cases between 2010 and 2018 (WHO, 2019) (Fig. 2). For malaria prevention and elimination, a total fund of US$ 2.7 billion was being used in 2018.

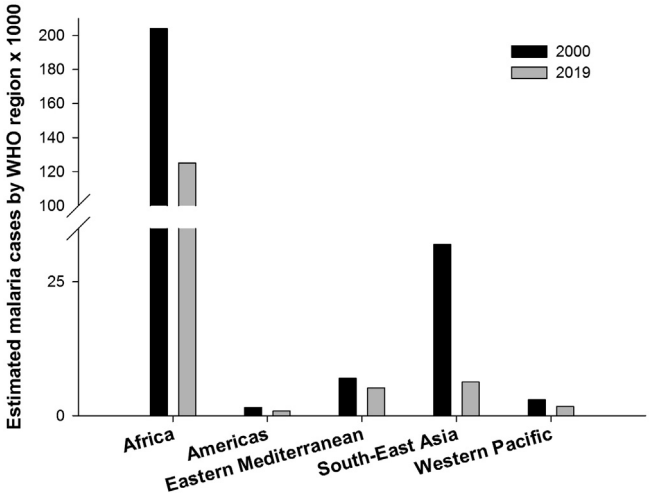

Fig. 1. Regions with malaria cases in 2000 and their status by 2019 (WHO, 2019).

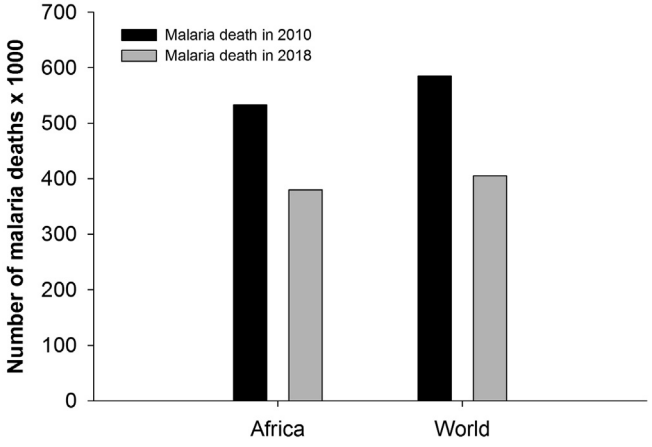

Fig. 2. Estimated number of malaria deaths by WHO region, 2010–2018 (data from World malaria report, 2019).

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	*Leonotis ocymifolia* (Lamiaceae)	NCBI:txid483802	Leaves	Methanol	Ethiopia	Swiss albino	Teklu et al. (2020)
Plasmodium berghe	*Acacia karroo* (Fabaceae)	NCBI:txid138024	Leaves	Methanol	India	BALB/c	Sachdeva et al. (2020)
	Balanites roxburghii (Zygophyllaceae)	NCBI:txid2603000	Leaves				
	Bassia scoparia (Amaranthaceae)	NCBI:txid83154	Leaves				
	Berberis aristata (Berberidaceae)	NCBI:txid659592	Leaves				
	Brassica junea (Cruciferae)	NCBI:txid3705	Leaves				
	Chenopodium album (Amaranthaceae)	NCBI:txid3559	Leaves				
	Chrysanthemum indicum (Asteraceae)	NCBI:txid146995	Leaves				
	Citrullus colocynthis (Cucurbitaea)	NCBI:txid252529	Leaves; Seeds				
	Citrus maxima (Rutaceae)	NCBI:txid37334	Leaves				
	Coriandrum sativum (Apiaceae)	NCBI:txid4047	Leaves				
	Rubus ellipticus (Rosaceae)	NCBI:txid59492	Leaves; Fruits				
	Rumex obtusifolius (Polygonaceae)	NCBI:txid3619	Leaves				
	Salvadora oleoides (Salvadoraeceae)	NCBI:txid1173311	Leaves				
	Saraca asoca (Caesalpiniaceae)	NCBI:txid1073321	Leaves				
	Syngonium podophyllum (Araceae)	NCBI:txid267621	Leaves				
	Syzygium cumini (Myrtaceae)	NCBI:txid260142	Leaves				
	Zanthoxylum acanthopodium (Rutaceae)	NCBI:txid1056460	Leaves				
Plasmodium berghei	*Capsicum frutescens* (Solanaceae)	NCBI:txid4073	Fruits	Methanol	Ethiopia	Swiss albino	Habte and Assefa (2020a)
Plasmodium berghei	*Aloe weloensis* (Aloaceae)	NCBI:txid1593116	Leaves	Leaves	Ethiopia	Swiss albino	Teka et al. (2020)
Plasmodium. Berghei	*Terminalia neotaliala* (Combretaceae)	NCBI:txid1799636	Leaves; Stem	Aqueous, Methanol; Ethanol; Dichloromethane; Hexane	Cameroon	Swiss albino	Tchatat Tali et al. (2020)
Plasmodium berghei	*Bersama abyssinica* (Francoaceae)	NCBI:txid113247	Leaves	Methanol	Ethiopia	Swiss albino	Alehegn et al., 2020.
Plasmodium berghei	*Olea europaea* (Oleaceae)	NCBI:txid4146	Stem	Methanol	Ethiopia	Swiss albino	Hailesilase et al. (2020)
Plasmodium berghei	*Myrica salicifolia* (Myricaceae)	NCBI:txid3509	Roots	Methanol	Ethiopia	Swiss albino	Kifle et al. (2020)
Plasmodium berghei	*Aloe pirottae* (Aloaceae)	NCBI:txid25641	Latex	Aqueous	Ethiopia	Swiss albino	Dibessa et al. (2020)
Plasmodium berghei	*Schinus molle* (Anacardiaceae)	NCBI:txid43851	Seeds	Aqueous	Ethiopia	Swiss albino	Habte et al. (2020b)
Plasmodium berghei	*Daniellia ogea* (Caesalpinioideae)	NCBI:txid162734	Roots	Ehanol	Nigeria	Swiss albino	Ezenyi et al. (2020)
	Andropogon schirensis (Graminaceae)	NCBI:txid2057634	Roots				
	Icacina trichanta (Icacinaceae)	Icacina trichanta	Leaves				
	Chasmanthera dependens (Menispermaceae)	NCBI:txid341015	Stem				
	Triumfetta cordifolia (Tiliaceae)	NCBI:txid2709013	Leaves				
	Celtis durandii (Ulmaceae)	NCBI:txid289393	Roots				
Plasmodium berghei	*Terminalia brownii* (Combretaceae)	NCBI:txid1548809	Stem	Aqueous, Methanolic	Ethiopia	Swiss albino	Biruk et al. (2020)
Plasmodiumberghei	*Helianthus annuus* (Asteraceae)	NCBI:txid4232	Roots; Stems; Seeds; Flowers; Leaves	Ethanol	Indonesia	BALB/c	Ekasari et al. (2019)
Plasmodium berghei	*Terminalia albida* (Combretaceae)	NCBI:txid39992	Stem	Methanol	Guinea	C57BL/6	Camara et al. (2019)
Plasmodium berghei	*Combretum molle* (Combretaceae)	NCBI:txid507414	Stem	Methanol	Ethiopia	Swiss albino	Mulaw et al. (2019)
Plasmodium berghei	*Cordia africana* (Boraginaceae)	NCBI:txid222081	Leaves	Methanol	Ethiopia	Swiss albino	Wondafrash et al. (2019)
Plasmodium berghei	*Fagara zanthoxyloides* (Rutaceae)	wfo-0000685053	Leaves	Methanol	Nigeria	Albino Wistar	Enechi et al. (2019)
Plasmodium berghei	*Paspalum scrobiculatum* (Poaceae)	NCBI:txid173849	Spikelets	Ethanol	Ghana	BALB/C	Laryea and Borquaye (2019)
	Bidens pilosa (Asteraceae)	NCBI:txid42337	Leaves				
	Acridocarpus alternifolius (Malpighiaceae)	NCBI:txid217121	Leaves				
	Clappertonia fcifolia (Triticeae)	NCBI:txid2708755	Leaves				
	Mitragyna ciliate (Rubiaceae)	NCBI:txid170021	Leaves				
	Parinari congensis (Chrysobalanaceae)	NCBI:txid1868823	Stem				
	Monanthotaxis cafra (Annonaceae)	NCBI:txid992735	Leaves				
	Datura stramonium (Solanaceae)	NCBI:txid4076	Leaves				

(*continued on next page*)

Table 1 (*continued*)

Parasite name	Plant (Family)	Plant Taxon ID*	Studied plant part	Extract type	Country of harvest	Mouse strain	References
	Faurea speciose (Proteaceae)	NCBI:txid206258	Leaves				
	Syzygium guineense (Myrtaceae)	NCBI:txid334482	Leaves				
	Croton penduliforus (Euphorbiaceae)	NCBI:txid2708777	Leaves				
Plasmodium berghei	*Euphorbia abyssinica* (Euphorbiaceae)	NCBI:txid316813	Root	Methanol	Ethiopia	Swiss albino	Muluye et al. (2019)
Plasmodium berghei	*Salvadora persica* (Salvadoraceae)	NCBI:txid4326	Roots	Aqueous	Ethiopia	Swiss Albino	Gebrehiwot et al. (2019)
	Balanites rotundifolia (Zygophyllaceae)	NCBI:txid1670835	Leaves				
Plasmodium berghei	*Commiphora Africana* (Burseraceae)	NCBI:txid181237	Stem	Methanol; Dichloromethane	Tanzania	BALB/C	Kweyamba et al. (2019)
	Dichrostachys cinerea (Fabaceae)	NCBI:txid196665					
Plasmodium chabaudi	*Indigofera oblongifolia* (Fabaceae)	NCBI:txid198899	Leaves	Methanol	Saudi Arabia	C57BL/6	Dkhil et al. (2019); Al-Shaebi et al. (2018);Al-Shaebi et al. (2017); Dkhil et al. (2015)
Plasmodium berghei	*Azadirachta indica (Meliaceae)*	NCBI:txid124943	Seeds	Methanol	Burkina Faso	C57BL/6 ; BALB/c	Habluetzel et al. (2019)
Plasmodium Berghei	*Zingiber Officinale* (Zingiberaceae)	NCBI:txid94328	Roots	Methanol	Ethiopia	Swiss Albino	Biruksew et al. (2018)
	Echinops Kebericho (Asteraceae)	NCBI:txid32194	Rhizomes				
Plasmodium berghei	*Aspidosperma pyrifolium* (Apocynaceae)	NCBI:txid141535	Stem	Ethanolic	Brazil	Swiss albino	Ceravolo et al. (2018)
Plasmodium berghei	*Gardenia ternifolia* (Rubiaceae)	NCBI:txid1237590	Roots	Methanol	Ethiopia	Swiss albino	Nureye et al. (2018)
Plasmodium berghei	*Rosa damascene Rosaceae*	NCBI:txid3764	Petals	Phenol rich ethyl acetate	India	Swiss albino	Khare et al. (2018)
Plasmodium berghei	*Picrolemma huberi* (Picramniaceae)	NCBI:txid459142	Leaves	ethanolic	Colombia	BALB/c	Berthi et al. (2018)
	Picramnia latifolia (Simaroubaceae)	NCBI:txid681474	Stem; Leaves Petiole	Ethanol; Hexane			
Plasmodium berghei	*Ziziphus mauritiana* (Rhamnaceae)	NCBI:txid157914	Leaves	Ethanol	Abidjan	Swiss albino	Attemene et al. (2018)
	Anthocleista djalonensis (Loganiaceae)	NCBI:txid26470	Stem barks				
Plasmodium chabaudi; P.berghei	*Terminalia macroptera* (Combretaceae)	NCBI:txid39992	Leaves Roots	Ethanol	Mali	Albino Swiss	Haidara et al. (2018)
Plasmodium berghei	*Lophira alata* (Ochnaceae)	NCBI:txid549775	Leaves	Aquoeus	Nigeria	ND	Falade et al. (2018)
Plasmodium berghei	*Lawsonia inermis* (Lythraceae)	NCBI:txid141191	Leaves; Seeds; Flowers; Stems Roots	Fraxetin; Ehyl acetate	India	BALB/c	Singh et al. (2017a)
Plasmodium. berghei	*Trema orientalis (Cannabaceae)*	NCBI:txid63057	Stem	Methanol	Nigeria	Swiss albino	Olanlokun et al. (2017)
Plasmodium berghei	*Solanum nigrum* (Solanaceae)	NCBI:txid4112	Fruits	Methanol	Iran	Swiss albino	Haddad et al. (2017)
	Teucrium polium (Lamiaceae)	NCBI:txid1117157	Aerial parts				
	Physalis alkekengi (Solanaceae)	NCBI:txid33120	Leaves; Fruits				
	Citrullus colocynthis (Cucurbitaceae)	NCBI:txid252529	Fruits				
	Salix alba (Salicaceae)	NCBI:txid75704	Leaves				
	Achillea millefolium (Compositae)	NCBI:txid13329	Flowers				
	Gossypium herbacum (Malvaceae)	NCBI:txid3633	Leaves				
	Verbena officinalis (Verbenaceae)	NCBI:txid79772	Flowers				
	Portulaca oleracea (Portulacaceae)	NCBI:txid46147	Aerial parts				
	Lavandula angustifolia (Lamiaceae)	NCBI:txid39329	Flowers				
Plasmodium berghei	*Holarrhena floribunda* (Apocynaceae)	NCBI:txid2708850	Leaves	Ethanol	Lomé, Togo	NMRI	Hoekou et al. (2017)
Plasmodium berghei	*Zea mays* (Poacae)	NCBI:txid4577	Peels	Ethanol	Nigeria	Swiss albino	Okokon et al. (2017)
Plasmodium berghei	*Flueggea virosa* (Phyllanthaceae)	NCBI:txid283121	Leaves	Ethanol	India	Swiss albino	Singh et al. (2017b)

Table 1 (*continued*)

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	Ethiopia	Swiss albino	Fentahun et al. (2017)
Plasmodium berghei	*Heinsia crinita* (Rubiaceae)	NCBI:txid61937	Stem; Leaves; Fruits	Ethanol; Dichloromethane; Methanol	Equateur	Swiss mice	Tshisekedi Tshibangu et al. (2017)
Plasmodium chabaudi; P. berghei	*Cymbopogon citratus* (Poaceae)	NCBI:txid66014	Whole plant	Aqueous	México	CBA/Ca	Chukwuocha et al. (2016)
Plasmodium chabaudi	*Punica granatum* (Lythraceae)	NCBI:txid22663	Peels	Methano	Saudi Arabia	Swiss albino	Mubaraki et al. (2016)
Plasmodium berghei	*Chromolaena odorata* (Asteraceae)	NCBI:txid103745	Leaves	Dichloromethane; Methanol	Nigeria	Swiss albino	Afolayan et al. (2016)
	Tithonia diversifolia (Asteraceae)	NCBI:txid684020	Leaves				
	Lawsonia inermis (Lythraceae)	NCBI:txid141191	Leaves				
Plasmodium yoelii	*Vetiver zizanioides* (Poaceae)	NCBI:txid167337	Roots	Hexan	India	Swiss albino	Dhawan et al. (2016)
Plasmodium berghei	*Vernonia amygdalina* (Asteraceae)	NCBI:txid82755	Leaves	Ethanol	Nigeria	Swiss albino	Omoregie and Pal (2016)
Plasmodium berghei	*Erythrina schliebenii* (Fabaceae)	NCBI:txid2590720	Stem	Ethyl acetate; Aqeuous	Tanzania	Swiss albino	Nondo et al. (2016)
	Holarrhena pubescens (Apocynaceae)	NCBI:txid69381	Roots				
	Phyllanthus nummulariifolius (Euphorbiaceae)	NCBI:txid283132	Roots				
	Caesalpinia bonducella (Caesalpiniaceae)	NCBI:txid83961	Roots				
Plasmodium berghei	*Brucea antidysenterica* (Simaroubaceae)	NCBI:txid459111	seeds	aqueous, methanol and chloroform	Ethiopia	Swiss albino	Kefe et al. (2016)
	Ocimum lamiifolium (Nepetoideae)	NCBI:txid39173	leaves				
Plasmodium berghei	*Alnus nepalensis* (Betulaceae)	NCBI:txid109066	Leaves	Methanol	India	BALB/c	Saxena et al. (2016)
Plasmodium berghei	*Gongronema latifolium* (Apocynaceae)	NCBI:txid2020314	Leaves	lime juice	Nigeria	Swiss albino	Idowu et al. (2015)
	Alstonia boonei (Apocynaceae)	NCBI:txid84857	Stem bark				
	Picralima nitida (Apocynaceae)	NCBI:txid52846	Seeds				
Plasmodium berghei	*Landolphia owariensis* (Apocynaceae)	NCBI:txid141576	Leaves	Methanol	Nigeria	Swiss albino	Ezike et al. (2016)
Plasmodium berghei	*Cassia alata* (Fabaceae)	NCBI:txid53923	Leaves	Dichloromethane; Methane	Burkina Faso	NMRI	Da et al. (2016)
Plasmodium berghei	*Ocimum suave* (Lamiaceae)	NCBI:txid39173	Leaves	Aqueous; Chloroform;	Kenya	Swiss albino	Kiraithe et al. (2016)
	Plectranthus barbatus (Lamiaceae)	NCBI:txid41228	Roots	Methanol			
	Zanthoxylum chalybeum (Rutaceae)	NCBI:txid1671342	Roots				
Plasmodium berghei	*Ajuga integrifolia* (Lamiaceae)	NCBI:txid38595	Aerial part	Methanol	Ethiopia	Swiss albino	Asnake et al. (2015)
	Clerodendrum myricoides (Lamiaceae)	NCBI:txid54240	Leaves				
	Melia azedarach (Meliaceae)	NCBI:txid155640	Twig				
	Peponium vogelii (Cucurbitaceae)	NCBI:txid387135	Leaves				
	Premna schimperi (Verbenaceae)	NCBI:txid41393	Leaves				
Plasmodium berghei	*Andropogon leucostachyus* (Poaceae)	NCBI:txid15314	Aerial part	Methanol	Brazil	BALB/c	Lima et al. (2015)
	Croton cajucara (Euphorbiaceae)	NCBI:txid323033	Leaves	Chloroform			
	Xylopia amazonica (Annonaceae)	NCBI:txid225838		Aqeuous			
Plasmodium berghei	*Scindapsus hederaceus* (Araceae)	NCBI:txid258317		Ethyl acetate	Malaysia	ICR	Baba et al. (2015)
	Shorea ovalis (Dipterocarpaceae)	NCBI:txid64590	Stem				
	Zingiber spectabile (Zingiberaceae)	NCBI:txid188518					

(*continued on next page*)

Table 1 (*continued*)

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					
	Trichilia heudelotii (Meliaceae)	NCBI:txid43894	Stem				
Plasmodium berghei	*Vernonia amygdalina* (Asteraceae)	NCBI:txid82755	Leaves	Aqueous; Ethanol	Ethiopia	BALB/c	Abay et al. (2015)
Plasmodium berghei	*Alhagi camelorum* (Fabaceae)	NCBI:txid47037	Whole plant	Methanol	Iran	Swiss albino	Esmaeili et al. (2015)
	Alhagi camelorum (Fabaceae)	NCBI:txid47037	Whole plant				
	Althaea officinalis (Malvaceae)	NCBI:txid145745	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)
Plasmodium berghei	*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)
Plasmodium chabaudi	*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	Stem; Leaves				
Plasmodium berghei	*Echinops kebericho* (Asteraceae)	wfo-0000133310	Roots	Ethanol	Ethiopia	Swiss albino	Toma et al. (2015)
Plasmodium berghei	*Maytenus senegalensis* (Celastraceae)	NCBI:txid256095	Root	Ethanol	Tanzania	Swiss albino	Malebo et al. (2015)

Table 1 (*continued*)

Parasite name	Plant (Family)	Plant Taxon ID*	Studied plant part	Extract type	Country of harvest	Mouse strain	References
Plasmodium berghei	*Citrus limetta* (Rutacaea)	NCBI:txid414735	Fruits; Peels	Ethanol	India	Swiss albino	Mohanty et al. (2015)
Plasmodium berghei	*Psidium acutangulum* (Myrtaceae)	NCBI:txid2478882	Stems; Leaves; Fruits	Aqueous	Framce	Swiss albino	Houël et al. (2015)
Plasmodium berghei	*Grewia trichocarpa* (Tiliaceae)	NCBI:txid2601743	Roots	Aqueous	Kenya	Swiss Albino	Mwangi et al. (2015)
	Dicrostachys cinerea (Mimosaceae)	NCBI:txid196665	Roots				
	Tamarindus indica (Caesalpiniaceae)	NCBI:txid58860	Stem				
	Azadirachta indica (Meliaceae)	NCBI:txid124943	Roots				
	Acacia seya l(Mimosaceae)	NCBI:txid138044	Roots				
Plasmodium berghei	*Conyza sumatrensis* (Asteraceae)	NCBI:txid212787	Leaves	Methanol	Cameroon	Swiss albino	Boniface et al. (2015)
Plasmodium berghei	*Carica papaya* (Caricaceae)	NCBI:txid3649	Leaves	Methanol; Ethanol; Ethyl acetate; Ether	Switzerland	NMRI	Julianti et al. (2014)
Plasmodium berghei	*Telfairia occidentalis* (Cucurbitaceae)	NCBI:txid370897	Leaves	Aqueous	Nigeria	Swiss albino	Adegbolagun et al. (2014)
Plasmodium berghei	*Fuerstia Africana* (Lamiaceae)	NCBI:txid204226	Roots	Methanol	Rwandan	SPF	Muganga et al. (2014)
	Terminalia mollis (Combretaceae)	NCBI:txid507438		Methanol; Aqueous			
	Zanthoxylum chalybeum (Rutaceae)	NCBI:txid1671342		Methanol; Aqueous			
Plasmodium berghei	Telfaria occidentalis (Cucurbitaceae)	NCBI:txid370897	Leaves	Aqueous	Nigeria	Swiss albino	Adegbolagun et al. (2013)
Plasmodium berghei	*Azadirachta indica* (Meliaceae)	NCBI:txid124943	Leaves	Aqueous	Nigeria	Swiss albino	Anagu et al. (2014)
Plasmodium berghei	*Phyllantus amarus* (Phyllanthaceae)	NCBI:txid293060	Leaves	Aqueous	Nigeria	Swiss albino	Kabiru et al. (2013)
Plasmodium yoelii	*Phlomis nissolii (*Labiatae)	NCBI:txid997732	ND	Chloroform, Ethanol; Aquoeus	Turkey	BALB/C	Ozbilgin et al. (2014)
	*Phlomis leucophracta (*Labiatae)	NCBI:txid997725	ND	Chloroform; Ethanol; Aquoeus			
	*Phlomis bourgaei (*Labiatae)	NCBI:txid997703	ND	Chloroform; Ethanol; Aquoeus			
	Centaurea hierapolitana (Asteraceae*)*	NCBI:txid1436092	ND	*H*exane, Chloroform; Methanol			
	Centaurea Lydia (Asteraceae*)*	NCBI:txid145506	ND	*n*-hexane, chloroform; Methanol			
	Centaurea polyclada (Asteraceae*)*	NCBI:txid1530336	ND	*n*-hexane, chloroform; Methanol			
	*Scrophularia floribunda (*Scrophulariace)	NCBI:txid1357615	ND	Chloroform; Ethanol; Aquoesr			
	*Scrophularia depauperata (*Scrophulariace)	NCBI:txid1970690	ND	Chloroform; Ethanol; Aquoeus			
	*Scrophularia cryptophila (*Scrophulariace)	NCBI:txid1970660	ND	Chloroform; Ethanol; Aquoeus			
	*Lavandula stoechas (*Labiatae)	NCBI:txid39333	ND	Ethanol; Aquoeus			
	Rubia davisiana (Rubiaceae)	NCBI:txid25473	ND	Methanol; Ethanol; Aquoeus			
	*Alkanna tinctoria (*Boraginaceae)	NCBI:txid543564	ND	Methanol, Ethanol; Aquoeus			
Plasmodium berghei	*Markhamia obtusifolia* (Sapotaceae)	NCBI:txid1237616	Stem	Ethyl acetate (EtOAc)	South Africa	Swiss albino	Simelane et al. (2013)
	Hypoxis colchicifolia (Hypoxidaceae)	NCBI:txid16123	Bulb				
	Mimusops caffra (Sapotaceae)	NCBI:txid362720	Leaves	Dichloromethane			
Plasmodium berghei	Pluchea lanceolata (Asteraceae)	NCBI:txid1950228	Aerial part	Methanol	India	Swiss albino	Mohanty et al. (2013)
Plasmodium berghei	*Melissa officinalis* (Labiatae)	NCBI:txid39338	Aerial part	Ethanol	Iran	Swiss albino	Sangian et al. (2013)
	Althea officinalis (Malvaceae)	NCBI:txid145745	Flowers				
	Borago officinalis (Boraginaceae)	NCBI:txid13363	Flowers				
	Glycyrrhiza glabra (Papilionaceae)	NCBI:txid49827	Roots				
	Anthemis nobilis (Compositae)	NCBI:txid99037	Flowers				
	Eremostachys laciniata (Lamiaceae)	NCBI:txid694356	Roots				
	Plantago major (Plantaginaceae)	NCBI:txid29818	Seeds				
	Myrtus communis (Myrtaceae)	NCBI:txid119949	Aerial part				
	Stachys lavandulifolia (Labiatae)	NCBI:txid193339	Flowers				
	Arctium lappa (Compositae)	NCBI:txid4217	Roots				

(*continued on next page*)

Table 1 (*continued*)

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)
Plasmodium berghei	*Azadirachta indica* (Meliaceae)	NCBI:txid124943	Root	Aqueous	Kenya	Swiss mice	Nguta and Mbaria (2013)
	Dichrostachys cinerea (Mimosaceae)	NCBI:txid196665	Root				
	Tamarindus indica(Caesalpiniaceae)	NCBI:txid58860	Stem				
	Acacia seyal (Mimosaceae)	NCBI:txid138044	Root				
	Grewia trichocarpa (Tiliaceae)	NCBI:txid2601743	Root				
Plasmodium berghei	*Holarrhena antidysenterica* (Apocynaceae)	NCBI:txid69380	Stem	Aqueous	India	Swiss albino	Priyanka et al. (2013)
	Azadirachta indica (Meliaceae)	NCBI:txid124943	Leaves; Stem				
Plasmodium berghei	*Nyctanthes arbortristis* (Oleaceae)	NCBI:txid41398	Leaves	Ethanol; Aqueous	India	Swiss albino	Agrawal et al. (2013)
Plasmodium berghei	*Rumex crispus* (Polygonaceae)	NCBI:txid174649	Whole plant	Ethanol	Korea	C57BL/6	Lee and Rhee (2013)
Plasmodium berghei	*Otostegia integrifolia* Benth. (Lamiaceae)	NCBI:txid483857	Leaves	Methanol	Ethiopia	Swiss albino	Endale et al. (2013)
Plasmodium. berghei	*Adansonia digitata* (Malvaceae)	NCBI:txid69109	Whole plant	Methanol: Chloroform	Kenya	Swiss albino	Musila et al. (2013)
	Canthium glaucum (Rubiaceae)	NCBI:txid258739					
	Launaea cornuta (Rubiaceae)	NCBI:txid381723					
	Zanthoxylum chalybeum (Rutaceae)	NCBI:txid1671342					
Plasmodium chabaudi	*Artemisia annua* (Asteraceae)	NCBI:txid35608	Leaves	Whole plant	USA	C57BL/6	Elfawal et al. (2012)
Plasmodium berghei	*Sorindeia juglandifolia* (Anacardiaceae)	NCBI:txid1317886	Fruits	Methanol	Cameroon	Swiss albino	Kamkumo et al. (2012)
Plasmodium berghei	*Acanthospermum hispidum* (Asteraceae)	NCBI:txid182999	Aerial part	Hexan	Benin	NMRI	Ganfon et al., (2012)
Plasmodium. berghei	*Azadirachta indica* (Meliaceae)	NCBI:txid124943	Leaves	Ethanol	Ethiopia	Swiss albino	Mesfin et al. (2012)
Plasmodium berghei	*Xanthium strumarium* (Asteraceae)	NCBI:txid318068	Leaves	Ethanol	India	BALB/c; Swiss albino	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					
Plasmodium chabaudi	*Caesalpinia pluviosa* (Fabacaea)	NCBI:txid191898	Stem	Ethanol	Brazil	C57BL/6	Kayano et al. (2011)
Plasmodium berghei	*Terminalia bellerica* (Combretaceae)	NCBI:txid155021	Fruits	Aquoeus	Thailand	ICR	Pinmai et al. (2010)
	Terminalia chebula (Combretaceae)	NCBI:txid155022					
	Phyllanthus emblica (Phyllanthaceae)	NCBI:txid296036					
Plasmodium berghei	*Holarrhena antidysenterica* (Apocynaceae)	NCBI:txid69380	ND	Ether;Chloroform; Methanol; Aquoeus	India	Swiss albino	Verma et al. (2011)
	Viola canescens (Violaceae)	NCBI:txid509528					
Plasmodium berghei	*Grewia plagiophylla* (Tiliaceae)	NCBI:txid82407	Stem; Leaves	Methanol	Kenya	BALB/c	Gathirwa et al. (2011)
	Combretum padoides (Combretaceae)	NCBI:txid507418	Roots; Leaves				
	Hoslundia opposita (Labietaceae)	NCBI:txid204228	Roots; Leaves				
	Rhus natalensis (Anacardiaceae)	NCBI:txid4012	Root; Leaves				
	Combretum illairii (Combretaceae)	NCBI:txid99434	Roots; Leaves				
	Lannea schweinfurthii (Anacardiaceae)	NCBI:txid289717	Leaves; Stem				
	Premna chrysoclada (Verbenaceae)	NCBI:txid41393	Roots, Leaves				
	Allophylus pervillei (Sapindaceae)	NCBI:txid1972007	Roots Stem bark, Leaves				
	Abrus precatorius (Leguminosae)	NCBI:txid3816	Leaves				
	Aganthesanthemum bojeri (Rubiaceae)	NCBI:txid58372	Whole plant				
	Uvaria acuminata (Annonaceae)	NCBI:txid672960	Roots, Leaves				

Table 1 (*continued*)

Parasite name	Plant (Family)	Plant Taxon ID*	Studied plant part	Extract type	Country of harvest	Mouse strain	References
	Azadirachta indica (Meliaceae)	NCBI:txid124943	Leaves				
	Flueggea virosa (Euphorbiaceae)	NCBI:txid283121	Roots				
Plasmodium berghei	Boerhavia elegans (Nyctaginaceae)	NCBI:txid122399	ND	Ethanol	Iran	BALB/C	Ramazani et al. (2010)
	Solanum surattense (Solanaceae)	NCBI:txid4107	ND				
	Prosopis juliflora (Fabaceae)	NCBI:txid13230	ND				
Plasmodium berghei	*Zanthoxylum usambarense* (Rutaceae)	NCBI:txid2562172	Stem	Aquoeus	Kanya	BALB/C	Were 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 palustre (Meliaceae)	NCBI:txid155635	Stem				
	Melia azedarach (Meliaceae)	NCBI:txid155640	Leaves				
Plasmodium berghei	*Aphloia theiformis* (Aphloiaceae)	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:txid1054601	Leaves				
	Justicia gendarussa (Acanthaceae)	NCBI:txid714472	Aerial part				
	Lantana camara (Verbenaceae)	NCBI:txid126435	Leaves; Flowers				
	Nuxia verticillata (Loganiaceae)	NCBI:txid69069	Leaves				
	Psiadia arguta (Asteraceae)	NCBI:txid1225821	Leaves				
	Terminalia bentzoe (Combretaceae)	NCBI:txid1908415	Leaves				
Plasmodium berghei	*Carpesium ceruum* (Asteraceae)	NCBI:txid119171	Whole plant	Ethanol	South Korea	ICR	Kim et al. (2009)
Plasmodium berghei	*Ampelozyziphus amazonicus* (Rhamnaceae)	NCBI:txid106660	Roots	Ethanolic	Brazil	CD1	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)
	Lannea schweinfurthii (Meliaceae)	NCBI:txid289717					
	Sclerocarya birrea (Anacardiaceae)	NCBI:txid289766					
Plasmodium vinckei	*Chrozophora senegalensis* (Euphorbiaceae)	NCBI:txid316752	Leaves, stems	Ether; Acetone; Ethanol	Senegal	Swiss albino	Benoit-Vical et al. (2008)
Plasmodium berghei	*Phyllanthus niruri* (Phyllanthaceae)	NCBI:txid296034	Whole plant	Aqueous, Methanol; Chloroform	Indonesia	Swiss albino	Mustofa (2007)
Plasmodium. berghei	*Flueggea virosa* (Euphorbiaceae)	NCBI:txid283121	Leaves, Stems, Roots	Aqueous	Kenya	Swiss albino	Muthaura et al. (2007a)
	Warburgia stuhlmannii (Canellaceae)	NCBI:txid549618					
	Harungana madagascariensis (Guttiferae)	NCBI:txid198768					
	Maytenus putterlickioides (Celastraceae)	NCBI:txid123430					
	Maytenus undata (Celasteraceae)	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)

(*continued on next page*)

Table 1 (*continued*)

Parasite name	Plant (Family)	Plant Taxon ID*	Studied plant part	Extract type	Country of harvest	Mouse strain	References
	Fuerstia africana (Lamiaceae)	NCBI:txid204226					
	Ludwigia erecta (Onagraceae)	NCBI:txid1620136					
Plasmodium berghei	*Toddalia asiatica* (Rutaceae)	NCBI:txid159068	Root	Aqueous	Kenya	ICR	Muregi et al. (2007a)
	Rhamnus prinoides (Rhamnaceae)	NCBI:txid280022	Leaves; Roots				
	Vernonia lasiopus (Asteraceae)	NCBI:txid83961	Rooots				
Plasmodium berghei	*Caesalpinia volkensii* s (Caesalpinaceae)	NCBI:txid1387603	Leaves; Seeds	Methanol	Kenyan	ICR	Muregi et al. (2007b)
	Maytenus acuminata (Celastraceae)	NCBI:txid1237617	Leaves; Roots				
	Maytenus heterophylla (Celastraceae)	NCBI:txid123430	Roots				
	Maytenus senegalensis (Celastraceae)	NCBI:txid256095	Leaves; Roots				
	Vernonia lasiopus (Compositae)	NCBI:txid83961	Leaves; Roots; Stem				
	Ajuga remota Benth. (Labiatae)	NCBI:txid38595	Whole plant				
	Ekebergia capensis. (Meliaceae)	NCBI:txid124949	Leaves; Roots; Stem				
	Azadirachta indica (Meliaceae)	NCBI:txid124943	Leaves				
	Albizia gummifera (Mimosaceae)	NCBI:txid1561840	Leaves; Stem				
	Ficus sur (Moraceae)	NCBI:txid100575	Leaves; Roots; Stem				
	Rhamnus prinoides (Rhamnaceae)	NCBI:txid280022	Leaves; Roots				
	Rhamnus staddo (Rhamnaceae)	NCBI:txid280026	Leaves; Roots				
	Toddalia asiatica (Rutaceae)	NCBI:txid159068	Leaves; Roots				
	Withania somnifera (Solanaceae)	NCBI:txid126910	Roots				
	Clerodendrum myricoides (Verbenaceae)	NCBI:txid54240	Leaves; Roots				
Plasmodium yoelii	*Pseudoxandra cuspidate* (Annonaceae)	NCBI:txid235824	Leaves; Stem	Aqueous	France	Swiss albino	Bertani et al. (2005)
	Zanthoxylum rhoifolium (Rutaceae)	NCBI:txid549434					
	Tinospora crispa (Menispermaceae)	NCBI:txid285591					
	Quassia amara (Simaroubaceae)	NCBI:txid43725					
	Picrolemma pseudocoffea (Simaroubaceae)	NCBI:txid459142					
	Irlbachia alata (Gentiananceae)	NCBI:txid82716					
Plasmodium berghei	*Striga hermonthica* (Orobanchaceae)	NCBI:txid68872	Whole plant	Methanolic	Nigeria	ND	
	Tapinanthus sessilifolius (Loranthaceae)	NCBI:txid50164	Leaves				
Plasmodium berghei	*Bidens pilosa* (Asteraceae)	NCBI:txid42337	Roots	Ethanol	Brazil	Swiss albino adult mice Swiss albino adult mice Swiss albino adult mice Swiss albino	Andrade-Neto et al. (2004)
Plasmodium vinckei	*Iris germanica* (Iridaceae)	NCBI:txid34205	Rhizome	Ethanol	France	Swiss albino	Benoit-Vical et al. (2003)

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 Céu de Madureira et al. (2002)
	Vernonia amygdalina (Asteraceae)	NCBI:txid82755	Leaves				
	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 (Meliaceae)	NCBI:txid124947	Stem				
	Premna angolensis (Verbenaceae)	NCBI:txid289394	Stem				
	Pycnanthus angolensis (Myristicaceae)	NCBI:txid224864	Stem				
	Morinda lucida (Rubiaceae)	NCBI:txid339305	Stem				
	Morinda lucida (Rubiaceae)	NCBI:txid339305	Leaves				
	Cestrum laevigatum (Solanaceae)	NCBI:txid1237510	Leaves				
	Canna bidentata (Canaceae)	NCBI:txid4627	Roots				
Plasmodium yoelii	*Hydrangea macrophylla* (Hydrangeaceae)	NCBI:txid23110	Leaves	Aqeuous	Japan	ICR	Ishih et al. (2001)
Plasmodium berghei	*Phyllanthus niruri* (Phyllanthaceae)	NCBI:txid296034	Whole plants	Ethanol; Dichloromethane;	Congo	Swiss albino	Tona et al. (2001)
	Morinda morindoides (Rubiaceae)	NCBI:txid659048	Leaves	Aqueous			
	Cassia occidentalis (Fabaceae)	NCBI:txid126820	Roots				
Plasmodium berghei	*Hydrangea macrophylla* (Hydrangeaceae)	NCBI:txid23110	Leaves	Aqueous	Japan	ddY	Kamei et al. (2000)
Plasmodium berghei	*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)
	Pothomorphe umbellate (Piperaceae)	wfo-4000031037	Leaves				
Plasmodium chabaudi	*Ziziphus spina-christi* (Rhamnaceae)	NCBI:txid72171	Leaves	Methanol	Saudi Arabia	Swiss albino	Hafiz et al. (2019)
Plasmodium. berghei	*Ziziphus spina-christi* (Rhamnaceae)	NCBI:txid72171	Leaves	Methanol	Saudi Arabia	C57BL/6	Mubaraki et al. (2017)
Plasmodium chabaudi	*Punica granatum* (Lythraceae)	NCBI:txid22663	Peels	Methano	Saudi Arabia	Swiss albino	Hafiz et al. (2016)

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

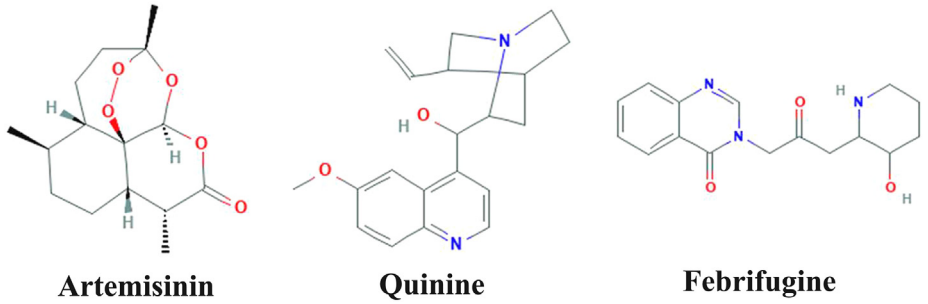

Fig. 3. Documented drugs from plant source.

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 2
Biosynthesized nanoparticles from plant source used for the experimental murine malaria research

Parasite name	Plant (Family)	Plant Taxon ID*	Studied plant part	Country of harvest	Mouse strain	Nanoparticle	References
Plasmodium chabaudi	*Indigofera oblongifolia* (Fabaceae)	NCBI: txid198899	Leaves	Saudi Arabia	C57Bl/6	Silver	Al-Quraishy et al. (2020); Murshed et al. (2020); Dkhil et al. (2020)
Plasmodium berghei	*Vernonia cinerea* (Asteraceae)	NCBI: txid13753	ND	India	Swiss albino	Gold	Jyotshna et al. (2016).
Plasmodium berghei	*Azadirachta indica* (Meliaceae)	NCBI: txid124943	Seed	India	Swiss albino	Silver	Murugan et al. (2016)

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

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 extracts and compounds 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-friendliness, 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 efficacy of medicinal plants should be further investigated.

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