

Prospective Plants with Corroborated Antimalarial Actions: A Review

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(Received: May 15, 2021; Accepted: July 6, 2021; Published (Web): July 15, 2021)

Abstract

Malaria is a serious illness resulted from parasites that are communicated to people through the bites of infected female Anopheles mosquitoes. Malaria is still in a worrying trend, particularly in tropical and subtropical climates although it is curable and preventable. In spite of a noteworthy abatement in incidence and death rates caused by malaria, even in 2017, a big number of people (219 million) have been affected by it along with 435 thousand confirmed death cases. Though a lot of synthetic drugs have been commercialized to treat malaria, those are compromised with some serious side effects. On the contrary, plant sources are always getting a big focus to develop novel and effective therapeutics in the treatment of different ailments *i.e.* quinine and artemisinin to treat malarial complications. The usage of herbal plants against malaria has also a very ancient root. Several families of plant species have showed potential antimalarial activities in previous research works. In this review work, families of these plants have been compiled so that prospective researchers can find a hint to discover more effective and safer plant-derived therapeutic options against malaria.

Keywords: Malaria, Plants, Antiplasmodial, Ethnobotany, *Plasmodium falciparum*.

Introduction

Malaria is a generic word for protozoa of the *Plasmodium* genus that is frequently used in conjunction with the term "Malaria parasites". It is defined as an ailment or disease state resulted from parasites of this genus in the blood or tissues of a person. Presence of the parasites at any stage in the human body suggests the existence of malarial infection (Hempelmann *et al.*, 2013). Mosquitoes preserved in amber dating back 30 million years ago provided the first proof of the presence of malaria (Poinar, 2005). During the Middle Ages, the disease continued to be a problem, when malaria epidemics caused the coastal plains of Italy and England to lose their global dominance (Dobson, 1994). Though, between 2000 and 2015, the incidence and death rates

declined by 37% and 60%, respectively worldwide (WHO, 2016). It causes deaths of around one million people per year in the tropical and subtropical zones (Mojarrab *et al.*, 2014). Eventually, around 90% of cases of malaria have been ascertained in Sub-Saharan Africa, (Nguta *et al.*, 2010). Even in 2017, Africa still has the highest burden of malaria calamity, with 200 million cases which attribute to 92% of total cases (WHO, 2018). Research showed that, the disease affects 4 to 5 million Ethiopians each year (Ayele *et al.*, 2012) with 70,000 mortalities (PMI, 2008). 219 million cases of malaria recorded globally in 2017 with an increment of almost 2 million cases than the previous year, resulting in 435 thousand deaths, which attributes to 1190 death per day (WHO, 2018). WHO stated that malaria caused

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DOI: <https://doi.org/10.3329/bpj.v24i2.54716>

by *P. falciparum* was responsible for 99% case of all malaria associated deaths (WHO, 2015; Alebie et al., 2017). Even in Bangladesh, malaria is endemic in 13 of 64 Bangladeshi districts and a total of 14 million individuals are in danger. But with a ray of hope like other countries, malaria incidences are in a declining phase in Bangladesh too (6.2 per 1000 people in 2008 to 2.1 per 1000 people in 2012) (Haque et al., 2014).

Many synthetic drugs like chloroquine, mefloquine, atovaquone–proguanil, doxycycline, and artemisinin derivatives are used for malaria treatment (Grabias and Kumar, 2016). However, several neuropsychiatric adverse effects including nausea, headache, vertigo, loss of balance, depression, sleep disturbances, psychoses have been recorded for these antimalarial drug options. Moreover, neurotoxic, gastrointestinal, and genitourinary adverse effects like vomiting, abdominal pain, and vaginitis along with teratogenic adverse effects were also observed from those drugs (Grabias and Kumar, 2016). These conventional antimalarial drugs are often expensive and/or unavailable in many malaria-affected populations. Besides, developing drug resistance by the malaria parasite *P. falciparum* is another major issue which becomes a major concern nowadays (Greenwood and Mutabingwa, 2002). For these reasons, the urge to discover novel and effective antimalarial drugs with unique modes of action has become more pronounced (Ogbuehi et al., 2013).

Plants are very good sources of therapies to treat different kinds of illness from the ancient age (Alam et al., 2020; Emon et al., 2020). Natural products derived from plants have recently become the focus of attention as a primary source of innovative, safer, and more effective secondary bioactive metabolites with therapeutic capabilities (Emon et al., 2021; Rudra et al., 2020; Ogbuehi et al., 2013). Almost 80% of all drug products are either directly derived from plants or their modified forms (Alam et al., 2021). The history of plant products against malaria has a very ancient root (Muthaura et al., 2007). Based on ethnobotanical leads, initially, antimalarial drugs like artemisinin and quinine were derived from the herbaceous plants *Artemisia annua* L. and *Cinchona*

pubescens Vahl., respectively (Wongsrichanalai, 2002). Till 2004, almost 1277 plants from 160 families have been reported with promising antimalarial activities (Rasoanaivo et al., 2011; Uzor et al., 2020). In different studies, various phytochemicals including alkaloids, indole alkaloids, naphthoisoquinolines, furoquinolines, acridones, amides, cryptolepines, terpenoids, clerodane and labdane diterpenoids, bisnorterpenes, acyclic triterpenes, cassane furanoditerpenes, abietane diterpenes, coloratane sesquiterpenes, beilshmiedic acid derivatives, pentacyclic triterpenes were found active against the disease (Onguéné et al., 2013). In this review article, we have classified plants based on their family who have showed antimalarial properties in previous researches so that prospective researchers, drug developers and other related personnel can find a contemporary clue in order to facilitate the discovery of novel and effective antimalarial therapeutics.

Materials and Methods

Article search strategy: An extensive literature search was conducted using several online databases including Web of Science, Scopus, PubMed/Medline, ScienceDirect, Wiley Online Library, and Google Scholar during this review. We have used ‘Antimalarial’, ‘Antiplasmodial’, ‘Malaria’, ‘Plasmodium’, ‘Plant products’ and ‘Herbal’ as key words to gather the related information. Considering peer reviewed and published articles only, describing malaria and role of plants and plant products against malarial complications as inclusion criteria, 118 out of 253 distinct articles were included in this review.

Notable plant families with antimalarial actions

Annonaceae

Enantia chlorantha Oliv. is an ornamental tree with thick leaf and a spreading crown and grows to a height up to 30m. It is found in densely wooded forests in east and south part of Cameroon, as well as in the south section of Nigeria, Angola, Gabon and the Democratic Republic of the Congo (Tcheghebe et al., 2016). In Cameroon, the stem bark of *E.*

chlorantha was commonly used to cure malaria, jaundice and various fevers (Adjanohoun *et al.*, 1996). The aqueous extract of *E. chlorantha* was shown to be efficient to ameliorate *P. yoelii* infection in mice after administered orally in drinking fluid at 0.2–150 mg/ml, but no effect was seen when administered via oral cannulation or subcutaneously. The ethanol extract of *E. chlorantha* also exhibited effective result in eliminating the parasites after being administered subcutaneously in doses of 0.05–0.5 mg/g (Agbaje and Onabanjo, 1991).

Annona muricata L., an evergreen tree which is typically 5–10m tall, has low branches with a diameter of 15–83cm. It is seen in Central and South America's tropical areas, as well as Southeast Asia and Western Africa (Coria-Télez *Et al.*, 2018). *A. muricata* aqueous leaf extract demonstrated strong LC₅₀ and LC₉₀ values against third instar larvae of *Aedes aegypti* (LC₅₀ 51.13µg/ml and LC₉₀ 82.08µg/ml) *Culex quinquefasciatus* (LC₅₀ 88.72µg/ml and LC₉₀ 151.30µg/ml) and *Anopheles stephensi* (LC₅₀ 61.38µg/ml and LC₉₀ 156.55µg/ml) (Santhosh *et al.*, 2015.)

Xylopiya parviflora Spruce is a small tree with a height of up to 3m. It is native to East Africa (Woguem *et al.*, 2014). The methanol extracts of leaves and stem from *X. parviflora* had a strong antiplasmodial activity with IC₅₀ values ranging from 1.07 to 5.83g/ml (Boyom *et al.*, 2011).

Apocynaceae

Rauvolfia vomitoria Afzel. is a small tree that grows to around 15m in height and can be found widely all over the world, especially in Asia and West-African countries (Olatokunboh *et al.*, 2009). Water, hexane, dichloromethane and methanol extracts from leaves of *R. vomitoria* demonstrated a very effective antimalarial activity against chloroquine-sensitive NF54 strains of *P. falciparum* with IC₅₀ values ranging from 0.63 to 20.19µg/ml (Cynthia, 2018).

Holarrhena floribunda (G.Don) T.Durand & Schinz, called faux rubber tree, is a 4.5-15m tall shrub to a medium-sized tree (Ahmed 2017). The leaf

extract of *H. floribunda* decreased parasitaemia caused by *P. berghei* with 6.96%, 29.06%, and 37.71%, respectively at 100, 250, and 500 mg/kg body weight doses (Hoekou *et al.*, 2017).

Tithonia diversifolia (Hemsl.) A.Gray, generally termed as Mexican sunflower, is a perennial or annual shrub which typically grows to a height of 1.2–3m. It is native to North and Central America, but has been naturalized in Africa, Australia, and Asia too (Ajao and Moteetee, 2017). The aqueous and methanol extracts of leaves of *T. diversifolia* were 50% and 74% effective against *P. berghei* and the LC₅₀ of the aqueous extract was found to be 1.2ml/100g body weight in mice (Oyewole *et al.*, 2008).

Asteraceae

Artemisia annua L., commonly known as sweet wormwood, sweet annie or sweet sagewort is an annual herb growing more than 2m. This herb is native to Asia mainly China, but has been naturalized all across the world including the United States (Das, 2012). Based on previous research work, 72g of *A. annua* crude alcohol extract was 100% effective against *P. vivax* and *P. falciparum*, while 20g and 35 g aqueous infusions of *A. annua* were 100% and 93% effective against *P. falciparum*, accordingly. *A. annua* aqueous decoction was also 92% effective at 20g amount against *P. falciparum* (Willcox *et al.*, 2004). Artemisinin, extracted from the leaves of this Chinese plant has a very pronounced antimalarial application (Tajuddeen and Heerden, 2019). Co-administration of artemisinin with other drugs or its derivative *i.e.* artesunate has been considered as effective combination therapy to treat multi-drug resistant malaria (Batista *et al.*, 2009).

Bignoniaceae

Spathodea campanulata P.Beauv., popularly known as the African tulip tree, is broadly spread throughout Africa and found numerously in Cameroon also. (Ngouela *et al.*, 1991). The hexane and chloroform extracts of *S. campanulata* exhibited inhibitory action against *P. berghei* and suppressed malaria in mice models (Amusan *et al.*, 1996).

Capparidaceae

The evergreen perennial shrub, *Buchholzia coriacea* Engl. commonly known as "Wonderful kola" is found in African nations such as Nigeria, Ghana, and Liberia. *B. coriacea* seeds were found to decrease parasitemia levels substantially. The seed extracts (20, 40, and 600 mg/kg body weight dose) were administered for four days continuously to find the desired actions (Enechi et al., 2021).

Cleome rutidosperma DC. is a low-growing shrub with trifoliolate foliage and tiny violet-blue blooms that become pinks with the age. It is found in waste grounds and grassy areas. The plant is native to West Africa, but it has been naturalized in many regions of tropical America and Southeast Asia including Malaysia and India (Ghosh et al., 2019). Ethanol extract of the plant had shown moderate effect against *P. falciparum* strain with IC₅₀ value of 34.4µg/ml whereas diethyl ether extract demonstrated a good antiplasmodial effect with IC₅₀ value of 8.1µg/ml (Bose et al., 2010).

Clusiaceae

Allanblackia monticola Mildbr. ex Engl. is a big forest tree that occurs in Cameroon's West and South regions. The methanol extract of *A. monticola* had IC₅₀ ranging from 0.6 to 8.9 g/ml on *P. falciparum* F32 and FcM29 strains (Azebaze et al., 2007).

Combretaceae

Terminalia superba Engl. & Diels is a large deciduous tree with a stem diameter of 120 cm and a height of 30-50m. *T. superba* is native to West and Central Africa (Kuate et al., 2010). The aqueous extract from leaves of *T. superba* showed a very good antiplasmodial activity and selectivity with IC₅₀ values ranging from 0.57µg/ml and 1.26µg/ml on PfINDO and Pf3D7 strains of *P. falciparum*, respectively (Mbouna et al., 2018).

Euphorbiaceae

Alchornea cordifolia (Schumach. & Thonn.) Müll.Arg. often known as Schum-Thron, is a shrubby plant that grows throughout coastal regions of West Africa (Osadebe and Okoye, 2003). Ethanol

extract of *A. cordifolia* leaves had moderate *in vitro* activity over *P. falciparum* in the mice model though chloroform and ether extracts didn't show any promising action (Banzouzi et al., 2002).

Euphorbia hirta L. is a reddish or purplish-colored, slender-stemmed, annual plant with many branches from the ground to the top reaching a height of up to 40 m. *E. hirta* is found in landfill areas along roadsides in the hotter areas of India and Australia (Kumar et al., 2010). The methanol extract of *E. hirta* aerial parts exhibited major active chromatographic fractions that inhibited *P. falciparum* growth by 90% at 5 g/ml concentration (Liu et al., 2007).

Fabaceae

Cajanus cajan (L.) Millsp. is a perennial or annual leguminous plant which is broadly distributed in tropical and subtropical portions of the world including Asia, Africa and South America (Kong et al., 2010). *C. cajan* leaf extract inhibited the growth of *P. falciparum* at IC₅₀ value of 2.0µg/ml (Ajaiyeoba et al 2013).

Leguminosae

Guibourtia coleosperma (Benth.) Leonard or giant false mopanie, is a tree native to southern Africa which can be found in Namibia, Zambia, Zaire, Zimbabwe and Angola also (Bekker et al., 2006). *G. coleosperma* aqueous and organic extracts both had moderate antimalarial activity, with IC₅₀ values of 31.61 and 28.17g/ml, respectively (du Preez et al., 2020).

Liliaceae

Allium sativum L. is a fragrant herbaceous plant that grows up to 30 to 80cm tall (Sendl., 1995). *A. sativum* is thought to have evolved in Central Asia 600 years ago and has subsequently expanded over Southwest Asia and the Mediterranean (Malik et al., 2020). *A. sativum* was tested against larvae of *Anopheles stephensi* and the LC₅₀ values for hexane extract were 7.5 ppm after 24 hours and 7.6 ppm after 48 hours of exposure. Moreover, the LC₉₀ values were 22.1 ppm after 24 hours, and 15.4 ppm after 48 hours of exposure (Shrankhla et al., 2012).

Malvaceae

Sida acuta Burm. f. familiar as as Kurumthotti, is a weedy perennial shrubby plant having a smooth bark (Sreedevi et al., 2009). The shrub is native to Central America and Mexico, although it has since spread throughout the tropics and subtropics (Karou et al., 2007). Ethanol fraction of *S. acuta* was found to have a significant action against *P. falciparum* at the IC₅₀ value 4.37µg/ml during a study of *in vitro* antimalarial test (Karou et al., 2003).

Meliaceae

Khaya grandifoliola C.DC. is a large-leaved evergreen tree that is also known as African mahogany, Benin mahogany or Senegal mahogany. Benin, Ghana, the Democratic Republic of the Congo, Sudan, Ivory Coast, Guinea, Togo, Nigeria, and Uganda are all home to it (Ojokuku et al., 2010). Antimalarial activity of *K. grandifoliola* stem and bark against *P. berghei* was investigated in mice by a group of researchers. Based on the study, the n-hexane extract, the crude and purified fractions provided very good antimalarial activities with around 91% chemosuppression *in vivo* and IC₅₀ values of 1.4µg/ml (for multi-drug resistant clone of *P. falciparum*) and 0.84 µg/ml (for Nigerian *P. falciparum* isolates). (Agbedahunsi et al., 1998).

Meliantaceae

Bersama engleriana Gürke is a small to medium-sized tree that reaches a height of 6 to 9m, hardly surpassing 25m. It's often found throughout tropical Africa, Senegal to Zaire, Southern Africa as well as areas of favoring areas with more rainfall or evergreen woods (Watcho et al., 2014). The methanol extract of *B. engleriana* leaves displayed a prospective antiplasmodium effect, with an IC₅₀ of 2.7g/ml against *P. falciparum* (Ngemenya et al., 2005).

Menispermaceae

Penianthus longifolius Miers is a tall shrub reaching up to 3–4.4m which is native to the rain forests of Cameroon, Nigeria, Gabon, Equatorial Guinea, Central African Republic, Congo and Angola

(Tabekoueng et al., 2019). *P. longifolius* methanol extract had shown promising *in vitro* activity on two *P. falciparum* malarial clones designated as Indochina (W-2) and Sierra Leone (D-6) types with IC₅₀ values of 350.066 and 284.377ng/ml, respectively (Tane et al., 2005).

Myrtaceae

Eucalyptus robusta Sm., popular as swamp mahogany, is a medium to large tree that typically grows of 20 to 30 m having a width of approximately 1m (Boland et al., 2006). It is widely distributed to Australia's east coast. However, it has propagated itself in other nations and is said to cover a total area of 2.3 million hectares globally (Vuong et al., 2015). Aqueous extracts of *E. robusta* stem and bark demonstrated promising antimalarial activity by suppressing *P. falciparum* D10 strain with IC₅₀ values of 10–20µg/ml in parasite lactate dehydrogenase (pLDH) assay (Nundkumar and Ojewole, 2002).

Poaceae

Cymbopogon citratus (DC.) Stapf is a perennial aromatic plant native to southern India and Sri Lanka that grows up to 2m tall with a 1.2m wide and a thick clump. It is currently cultivated all over the world, especially in tropical, subtropical and Savannah countries (Machraoui et al., 2018). *C. citratus* has notable antimalarial efficacy, as evidenced by a study that found dosages of 200 to 1600mg/kg dry powder of *C. citratus* suppressed parasitaemia against *P. berghei* ANKA strain by 91.89% to 96.61% (Chukwuocha et al., 2016). The essential oils from the extract of *C. citratus* leaves exhibited antimalarial activity against *P. berghei* in mice models with IC₅₀ values ranging from 6 to 9.5µg/ml (Tchoumboungnang et al., 2005).

Piperaceae

Peperomia vulcanica Baker & C. H. Wright, an herbaceous plant, is seen around the world in subtropical and tropical areas, although they are most common in Central and Northern South America. The hexane and methylene chloride extracts of *P.*

vulcanica demonstrated potential antimalarial activity with IC_{50} ranging from 0.89 - 3.23 μ g/ml against *P. falciparum* (Ngemenya et al., 2015). Crude extract of *P. vulcanica* also demonstrated moderate antimalarial activity against *P. falciparum* (70% inhibition by 40 μ g/ml crude extract) (Titanji et al., 2008; Ngemenya et al., 2004).

Rubiaceae

Morinda lucida Benth. is a medium-sized tree with short branches and dazzling leaves that reaches up to 15m and is native to West and Central Africa (Chithambo et al., 2017). Ethanol extract of *M. lucida* had a good antimalarial efficacy against *P. berghei* while 400, 600 and 800mg doses inhibited 0.40 \pm 0.20, 1.40 \pm 0.24 and 1.20 \pm 0.58 % parasitaemia on 5th day of treatment in mice, respectively (Afolabi and Abejide, 2020).

Cinchona barks from Rubiaceae family are very popular sources of antimalarial therapeutics (Batista et al., 2009). They are found in mainly South America, particularly the Andes. It is also spread in Vietnam, India, Cameroon, Java, and a few more African and Asian nations (Raza et al., 2021). Quinine isolated from the barks is one of the very first antimalarial drugs used in early ages (Fernandez et al., 2008). It was discovered in 1820 by Pelletier and Caventou and used as lead antimalarial moiety for almost three centuries (Batista et al., 2009). Besides, quinine conjugates and its analogues can also serve promising antimalarial efficacies (Jones et al., 2015).

Rutaceae

Citrus sinensis (L.) Osbeck, a short evergreen tree of 7.5 to 15m height, is widely cultivated in tropical, semi-tropical and some warm temperate regions. This tree is native to China, Southeast Asia, Malay Archipelago, New Caledonia and Australia (Etebu and Nwauzoma, 2014). Petroleum ether and methanol extract of ripe fruit rind of *C. sinensis* possessed antimalarial activity against *P. falciparum* FCK2 strain with IC_{50} values of 51.06 and 53.61 μ g/ml respectively (Bhat et al., 2001). In another study, the crude extracts of *C. sinensis* peels

were found active against *Anopheles subpictus* larva that causes malaria with LC_{50} of 58.25 ppm and LC_{90} of 298.31 ppm (El-Akhal et al., 2015).

Scrophulariaceae

Scoparia dulcis L., also known as sweet broom weed, is a branching perennial herb with wiry stems that may reach a height of one meter. It is extensively distributed throughout tropical and subtropical areas of India, West Indies, America, Brazil and Myanmar (Paul 2017). The ethyl acetate extract of *S. dulcis* inhibited the growth of *P. falciparum* with the IC_{50} value 19.5 μ g/ml (Ngemenya et al., 2004).

Simaroubaceae

Quassia amara L. is a South American rain forest small tree, with a height of 2-6 m (Cachet et al., 2009). The hexane extract of *Q. amara* leaves exhibited promising antimalarial activity against *P. berghei* by suppressing the parasite density of 0.16 \pm 0.001% in the laboratory mouse. Methanol extract of *Q. amara* leaf also suppressed the parasite density of 0.05 \pm 0.03% at the dose of 200mg/kg (Ajaiyeoba et al., 1999).

Zingiberaceae

Renealmia alpinia (Rottb.) Maas is an herb with gregarious and simple leaves that generally grows up to 2-6 m in height. This plant is native to tropical moist lowland rainforests but widely distributed in Mexico, Peru, Brazil, Antilles, French Guiana, Guyana, Suriname and Venezuela (Gómez-Betancur & Benjumea 2014). Aqueous rhizome extract of *R. alpinia* demonstrated antimalarial activity against *P. falciparum* chloroquine-resistant strain with an IC_{50} value of 10 \pm 1.4 μ g/ml (Céline et al., 2009).

Renealmia thyrsoidea (Ruiz & Pav.) Poepp. & Endl. is a herbaceous perennial plant which produces clumps of erect stems around a height of 0.8-5 m (Maas 1977). The species is native to tropical America. Although it is widely spread in Bolivia, Guyana, Colombia, Ecuador, Nicaragua, Panama, Trinidad, Peru, Suriname and Tobago and Venezuela (Noriega et al., 2016). Based on previous research work, aqueous rhizome extract of *R. thyrsoidea* had

shown antimalarial effect against *P. falciparum* chloroquine-resistant strain at the IC₅₀ value of 6.8 ± 1.5 µg/ml (Céline et al., 2009).

Notable Bangladeshi plant families with antimalarial actions

Acanthaceae

Andrographis paniculata (Burm.f.) Nees, popularly known as 'Kalmegh', is a branching annual plant that grows to 60-70cm in height (Nyeem et al., 2017). It is widely common in Asian nations such as Bangladesh, India, Sri Lanka, Pakistan, Malaysia, and Indonesia (Nyeem et al., 2017). The methanol extract of *A. paniculata* whole plant inhibited the chloroquine-sensitive *P. falciparum* strain D10 with the IC₅₀ value of 45.74 µg/ml and the resistant strain Gombak A with the IC₅₀ of 65.06 µg/ml (Najila et al., 2002).

Anacardiaceae

Mangifera indica L. is a local Bangladeshi fruit producing tree and known as 'Aam' that grows as a medium to a large green tree that is generally 10 to 40 m in height (Parvez 2016). *M. indica* is grown in tropical regions around the world, including India, Thailand, China, Bangladesh, Malaysia and Indonesia (Pierson et al., 2014). *M. indica* aqueous extract exhibited IC₅₀ of 18.11, 20.08, and 10.23 µg/ml against NF54, CamWT_C580Y, and FA08 parasite strains of *P. falciparum*, respectively (Jibira et al., 2020).

Apocynaceae

Rauvolfia serpentina (L.) Benth. ex Kurz, locally known as 'Sarpagandha' is a climbing evergreen perennial shrub (Chenniappan and Kadarkarai, 2010). The species is native to India, Bangladesh and other regions of Asia including Himalayas, Myanmar, Indonesia and Sri Lanka (Kumari et al., 2013). Based on a previous study, methylene chloride extract of *R. serpentina* bark exhibited notable antimalarial activity against chloroquine-resistant *P. falciparum* MRC-PF-43 strain along with IC₅₀ value of 8.32 µg/ml and 59% inhibition (Chenniappan and Kadarkarai, 2010). In another study, 200 mg/kg of *R. serpentina*

leaf ethanol extract showed antimalarial activity in *P. berghei* NK65 strain infected mice model with 84.14% chemo suppression, while 400 mg/kg *R. serpentina* leaf hot water extract showed 82.53% chemo suppression (Omoya et al., 2019). In another *in vivo* study, a dose of 500 mg/kg of cyclohexane and methylene chloride extracts of *R. serpentina* root displayed moderate antiplasmodial activity against chloroquine-resistant *P. berghei* NK65 strain with 20% survival on 9th day of post-infection (Samy and Kadarkari, 2011).

Areaceae

Areca catechu L., commonly called 'Supari', is a 15-25m tall megaphanerophyte with a single stem (Peng et al., 2015; Nath et al., 2011). It is also known as 'Areca nut' and widely consumed with *Piper Betle* leaf (locally known as 'Pan') in many Asian countries. It is commonly found in the tropical Pacific, Asian and few east African Countries (Garg et al., 2014). Butanol fraction of *A. catechu* nut extract exhibited remarkable antimalarial activity against *P. falciparum* showing the IC₅₀ value of 18 µg/ml (Boniface et al., 2014).

Fabaceae

Erythrina variegata L. is a branched, deciduous medium-sized woody tree growing up to 25m and is used by various tribes of Bangladesh (Rahmatullah et al., 2012). It is known as 'Mafang' in Bangladesh and also available in Taiwan, southern China, Philippines, Indonesia, Thailand, Myanmar, Malaysia, India, and Indian Ocean islands (Lim 2014; Rahmatullah et al., 2012). Methanol extract of the *E. variegata* leaves showed strong antimalarial activity over *P. falciparum* K1 strain with IC₅₀ value of 6.8 µg/ml (Herlina et al., 2011).

Lamiaceae

Ocimum gratissimum L. is a branching shrub that grows up to 1.9m tall which is locally known as 'Ram Tulsi' in Bangladesh (Prabhu et al., 2009). The species is native to tropical regions, including India, West Africa, Savannah, coastal areas of Nigeria, Srilanka, Nepal, and Bangladesh (Prabhu et al.,

2009). Essential oils from the leaves of *O. gratissimum* were shown to be extremely potent over *P. falciparum*, with IC₅₀ ranging from 6.9 to 14.9 g/ml (Ngemenya et al., 2004).

Meliaceae

Azadirachta indica A.Juss., known as 'Neem' in Bangladesh, is a fast-growing evergreen tree having wide branches and may reach a height of 15-20m (Maithani et al., 2011). Alongside Bangladesh, it can also grow in India and Myanmar though it can grow abundantly in tropical and subtropical areas (Maithani et al., 2011). Based on a previously conducted study, *A. indica* leaves extract had antiplasmodial activity against *P. falciparum* with the LD₅₀ of 7.52 µg/ml, 6.76 µg/ml, and 5.96 µg/ml for ethanol, methanol and acetone extracts respectively (Deshpande et al., 2014).

Myrtaceae

Syzygium cymosum (Lam.) DC., locally known as 'Khudijam' in Bangladesh, can grow up to a height of 15-20m and has plain wide leaves (Hossainey et al., 2020). Tropical and subtropical regions including India, Singapore, Myanmar and Malacca are also home to this plant (Dhar et al., 2016). The crude methanol extract of *S. cymosum* leaves exhibited remarkable efficacy against chloroquine-sensitive 3D7, chloroquine-resistant Dd2 and mild efficacy against artemisinin-resistant IPC 4912 Mondulkiri strains of *P. falciparum* with the IC₅₀ value of 6.28µg/ml, 13.42µg/ml and 17.47µg/ml, respectively (Hossainey et al., 2020).

Conclusion

Herbal plants are always great wellsprings of novel therapeutics which offer more efficacy and lesser side effects against various disease states compared to other synthetic drugs. In parallel, to treat malarial complications, medicinal plants and plant products have been also documented from the very old ages in different countries, cultures and tribes. Thus, to discover novel drug therapies against malaria and related complications, researchers can consider these herbal plants although further studies

are still recommended to figure out the exact phytochemicals responsible for displayed antimalarial actions and their accurate mechanism of actions.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

SA and TBK conceptualized and designed the review work. ATO, AZ, HH and TBK gathered the previous works. ATO, SA, AZ and HH wrote the manuscript. TS and MAI critically reviewed the manuscript. SA edited and drafted the final manuscript and supervised the total work.

Declarations

The manuscript was read and approved for submission by all concerned authors. No part of the manuscript has been previously published, and no part of it is currently being considered for publication in any journal.

Conflict of interest

The authors state that they have no conflicting interests that could have appeared to influence the work reported in this paper.

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