REVIEW
TMR Modern Herbal Medicine 2022;5(4):20. https://doi.org/10.53388/MHM2022B0816001

Role of traditional herbal medicine in the treatment of malaria

Virender Kumar [1], Vandana Garg [1]*, Harish Dureja [1]*

[1]Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, Haryana 124001, India.

***Corresponding to** Vandana Garg, Department of Pharmaceutical Sciences, Maharshi Dayanand University, NH-10, Rohtak (Haryana) 124001, India. E-mail: vandugarg@rediffmail.com. Harish Dureja, Department of Pharmaceutical Sciences, Maharshi Dayanand University, NH-10, Rohtak (Haryana) 124001, India. E-mail: harishdureja@gmail.com.

Author contributions
Virender Kumar was responsible for writing original draft; Vandana Garg was responsible for review and editing; Harish Dureja was responsible for supervision and methodology.

Competing interests
All authors declare no conflicts of interest.

Acknowledgments
The authors thank Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, Haryana for providing the necessary facilities.

Abbreviations
WHO, World Health Organization; GDP, Gross domestic product; EMP-1, Epithelial Membrane Protein -1; HRP-1, Histidine-rich protein-1; PfCRT, Plasmodium falciparum chloroquine resistance; IC_{50}, Half-maximal inhibitory concentration.

Peer review information
TMR Modern Herbal Medicine thanks all anonymous reviewers for their contribution to the peer review of this paper.

Citation
Kumar V, Garg V, Dureja H. Role of traditional herbal medicine in the treatment of malaria. *TMR Modern Herb Med*. 2022;5(4):20. doi:10.53388/MHM2022B0816001

Executive editor: Chao-Yong Wu.
Received: 16 August 2022;
Accepted: 11 November 2022;
Available online: 30 November 2022.

Abstract
Malaria is one of the world's major public health concerns and numerous medicinal plants are commonly used for treating malaria. Traditional health care uses medicinal plants widely, but no scientific documentation is available and, there is a growing risk of losing this knowledge. Thus, this study aims to document the traditional use of medicinal plants in treating malaria and related conditions. In this review, numerous herbal medicines for antimalarial potential are explained. The literature survey was done using keywords i.e., malaria, herbal, herbal, traditional use, antimalarial, quinine, artemisinin, and traditional medicine by using PubMed, Science Direct, Google Scholar, and HINARI database. This review discusses the life cycle of the malarial parasite, what makes you attractive to mosquitoes, and the role of traditional herbal medicine in malaria.

Keywords Artemisinin; Antimalarial; Herbal; Malaria; Quinine

Highlights

The article provides a list of medicinal plants that are believed to be useful in the treatment of malaria.

The role of Quinine, Chloroquine, Artemisinin, *Acanthospermum hispidum*, *Byrsocarpus coccineus*, *Carpolobia lutea*, *Dialium guineense*, Heliotropium indicum, *Keetia leucantha*, *Pupalia lappacea*, *Sansevieria liberica*, *Strychnos spinosa* and Ananas comosus has been described in treatment of malaria.

Introduction

Malaria is one of the most vulnerable, widespread, life-threatening infectious diseases that cause millions of deaths across the globe [1]. The disease malaria not only affects the population in an area, but also disposes significant loss to the national economy and financial condition Malaria is considered a threat to a country's socioeconomic development, as it affects children's schooling with the disease and destroys the productive days of employees for work. The recorded number of people suffering from malaria cases was 241 million in 2020, as per the WHO report, and that too, maximum from Africa itself [2]. According to one report estimation, it has been stated that there will be a fall in the growth of GDP by 0.41% if there is a rise in the morbidity rate of malaria by 1% [3]. Charles Louis Alphonse Laveran first diagnosed the malarial parasites (plasmodium), a French army surgeon, from a patient's blood sample in 1907; he received a Nobel prize [4]. The literal meaning of malaria is “bad air” derived from medieval Italian words [5].

In humans, mainly four types of plasmodium species are known to cause malaria viz [6].

- Plasmodium falciparum
- Plasmodium vivax
- Plasmodium ovale
- Plasmodium malariae

These belong to the *Apicomplexa* phylum, *plasmodium* genus, are strict intracellular protozoan (plasmodium) parasites [7]. The parasite mainly propagates in the stagnant water of ditches, ponds, etc., as they easily lay eggs and develops into larvae afterward. The life cycle of the malarial parasite is very versatile, as it depends upon two hosts viz. female anopheles mosquito (also the vector of the same disease) and human being. Out of these, an infection caused by *Plasmodium falciparum* is fatal. Various reports state a close relationship exists between humans and African apes’ malarial parasites [8]. In India, the most cases of malaria were found in Odisha, Chhattisgarh, Jharkhand, Meghalaya and Madhya Pradesh [9]. There are four main problems for managing malaria in a population viz [10].

- Development of resistance in malarial parasites sooner for easily affordable, safest, effective, and first-line drugs like Chloroquine.
- Mosquitoes which are vectors for this disease, are also getting resistant to various insecticides used to control them.
- Introduction of fake antimalarial drugs in the market, for example, artesunate blister packs for malaria management contained no active ingredient in the samples obtained from mainland south-east Asia [11].
- Lack of infrastructure and resources for managing malaria and its control in developing and underdeveloped countries.

As per WHO, two approaches [2] are used for controlling, treating and preventing malarial infection which are:

- Prevention: reduction in human-vector contact and lifespan of mosquitoes by using insecticidal nets, indoor residual spraying and administration of entire course of antimalarial drugs in the population at high risk in due course of time.
- Case management: treatment of affected individuals with chemotherapy (currently, ACTs are used, which are artemisinin-based combination therapies).

However, many chemical drugs have been developed to treat malaria patients. They were adequate for a more extended period, but slowly, the parasite developed resistance against them which posed a challenging task for treating malaria. Since the parasite life cycle is dependent on two hosts, so, with such a versatile life cycle and the continuous alteration in metabolic pathways in the parasite during its life cycle make it more cumbersome and arduous task for scientists to develop a vaccine against the malarial parasite. Due to this, no vaccine has been created, so it isn't easy to control its spread. So, this is high time to scrutinize and develop newer drugs that can tackle this major problem of drug resistance and helps in curing malaria [12].

Malaria patients are advised to follow a nutritionally balanced diet that includes cereals, pulses, vegetables, fruits, milk, milk products, fish, chicken soups/stews, sugar, honey, etc. that provides adequate nutrition and maintains fluid balance [13].

Since nature is full of enormous surprising things about the maximum of which human beings are unaware [14]. Hence, a shift has occurred for searching herbal plants with certain compounds as their secondary metabolites, potent enough against the malarial parasite and can help cure patients of malaria. This led to the evolution of a newer branch of science i.e., ethnopharmacology, which aims to find out those plant-based products rationally which were traditionally used for the treatment of malaria and were more prevalent in a local tribal community based on cultural values. This focuses on finding out those plant species have medicinal value and using them as a template for synthesizing newer drugs that are more effective [15]. Pineapple is one of the most consumed members of the family Bromeliaceae growing in several tropical and subtropical countries [16]. It contains substantial amounts of bioactive compounds, minerals, dietary fiber, nutrients, and enzymes. Bromelain is the proteolytic enzyme derived from the stem portion of the pineapple and showed various antiedematous, anti-inflammatory fibrinolytic, anti-inflammatory and antimalarial activity [17]. In this review, we summarized the antimalarial effect of pineapple from the previous studies and proposed it as an herbal drug for treating malaria. Further, pineapple and bioactive compounds can be designed as a novel drug delivery system to deliver the drug efficiently and prevent resistance. The life cycle of the malarial parasite is very versatile as it depends upon two hosts, viz. female Anopheles mosquito (also the vector of the same disease) and the human being. First, the female anopheles mosquito bites a healthy human being to suck blood and accidentally delivers sporozoites into the human body. From this point onwards, the malarial infection gets initiated and propagates further. After that, the sporozoites infect the liver by migrating and invading hepatocytes, where they undergo schizogony (exo-erythrocytic schizogony) and form schizonts. The moment the hepatocyte ruptures, merozoites are released outwards and enter the bloodstream, infecting normal erythrocytes and invading after that. In some species like *P. vivax* and *P. ovale* a dormant stage (hypnozoites) can persist in the liver and cause infection relapse by invading the bloodstream even weeks or years later. To complete the life cycle, the malarial parasite must invade the host’s erythrocytes [18]. They again undergo schizogony or asexual multiplication (erythrocytic schizogony) in a similar way as in hepatocytes. In this way, it produces around 8-32 merozoites. Generally, four factors are responsible for controlling and governing the entry of merozoite into the RBCs, which are mentioned below [19]:

- Host cell- merozoite interaction.
- Reorientation of merozoite to expose apical prominence which, aids in contact with the host cell surface.
- Irreversible attachment between merozoite’s apical dominance and host cell surface followed by the formation of an electron-dense junction.
- Formation of parasitophorous vacuole due to invagination of the parasite into host cell.

HRP-1, EMP-1, HRP-2 and EMP-2 are the four major proteins, which are found expressed on infected RBCs [20]. Some of them get differentiated into sexual gametocytes (blood-stage parasites). Whenever at any moment, the erythrocyte ruptures, it gets released outside and starts infecting other surrounding normal erythrocytes as well, hence, creating a vicious cycle responsible for clinical manifestations of the disease. When a female anopheles’ mosquito again bites the infected individual, the male (microgametocytes) and female (macrogametocytes) gametes are ingested along with the blood meal, and the sporogonic cycle (Multiplication of malarial parasite in the mosquito body) commences. Soon, the microgametes fuse with the macrogametes in the mosquito’s stomach leading to the formation of zygotes which in turn, later becomes elongated and motile (ookinetes). They further develop into oocytes while invading the midgut wall. These grow and mature into sporozoites and get released on rupture. Additionally, they migrate toward the mosquito's salivary glands, where they are stored. Whenever the mosquito bites another healthy individual to suck blood meal, in turn, it transmits these stored sporozoites into that person's body, infecting him with malaria and this cycle continues further [21]. The Malaria Asexual Reproduction Cycle is shown in Figure 1 and gametocyte development is shown in Figure 2.

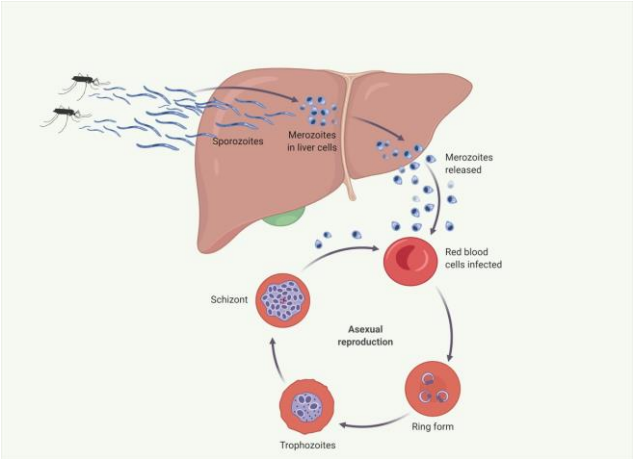

Figure 1 Malaria Asexual Reproduction Cycle [22]

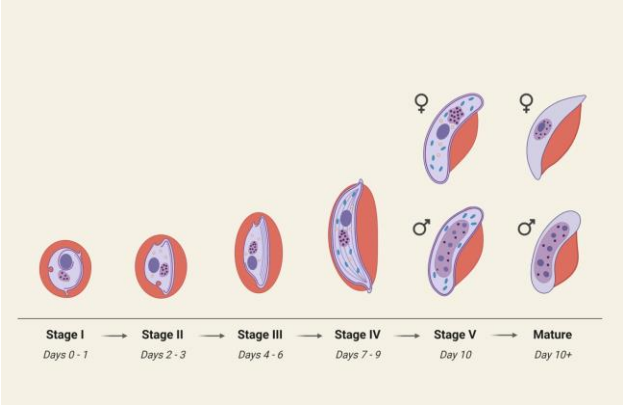

Figure 2 *P. falciparum* Gametocyte Development [22]

What makes you attractive to mosquitoes?

Research in the past has shown mosquitoes to be selective predators. Much research has been done on what makes mosquitoes attracted to their prey, from genetic factors such as blood group to characteristics such as clothing color and body temperature.. The most important factor that attracts mosquitoes to humans is the scent of our bodies, but the smell of our bodies is influenced at least in part by our genes [23]. The carbon dioxide we exhale is highly attractive to mosquitoes, and it has been noticed that adults are more likely to get bitten by, mosquitos than children because of the larger amount of carbon dioxide they exhale.

These mosquitoes have thermosensors that can detect the heat of the body. Pregnant women's increased body temperature and carbon dioxide production make them more attractive to mosquitoes. What makes you attractive to mosquitoes is shown in Figure 3.

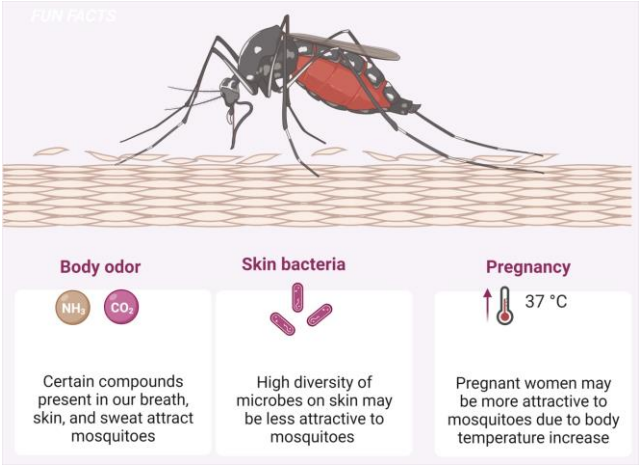

Figure 3 What makes you attractive to mosquitoes? [24]

Traditional medicine used for the treatment of malaria:

Quinine

Quinine is obtained from the cinchona tree. It was first discovered in the 17th century and used to treat malaria. It was also called Sacred bark, Jesuit's, and Cardinal bark [25]. The food vacuole gets swelled by quinine which leads to the lysis of the cell by an increase in the granularity of the cell [26]. On the other hand, this traditional medicine did not gain resistance quickly to the parasite. Cinchona has been used as a medicine since the 1600s, and various studies have been conducted on the cinchona to study its medicinal properties. It has been used as a medicine for a long time. This medicine has shown favorable effects in the treatment of malaria till now.

Chloroquine

This traditional medicine causes a toxic effect on the parasite and results in the death of the malarial parasite. It acts by inhibiting the detoxification of hematin in the parasite's digestive vacuole [27]. The resistance to chloroquine in malarial parasite is mainly due to mutation at position 76 (K76T) in PfCRT (*Plasmodium falciparum* chloroquine resistance) [28]. Chloroquine is a doc for malaria due to its low toxicity to the host, cost-effectiveness, ease of use, and best clinical efficacy. However, the parasite has gained resistance due to its heavy usage 29]. The combination of the pyrimethamine-sulfadoxine act on Dihydropteroate synthase & Dihydrofolate reductase.

Artemisinin

Artemisinin is obtained from the sweet herb wormwood and used as a first -line treatment for *Plasmodium falciparum*. It is a widely used anti-malarial drug [30]. The chemical structure responsible for the anti-malarial activity is tetracyclic 1,2,4-trioxane. Several studies show that it also contains anti-cancer properties [31]. The resistance is caused mainly due to mutation in the Kelch protein, present on the chromosome 13. The mechanism of action is now specified, but it acts in two ways. Firstly, by direct attack on mitochondria and interacts with Fe of hemoglobin which leads to the synthesis of ROS and attacks the protein of parasites [32]. This herbal medicine is used as anti-malarial as well as anti-cancer.

Acanthospermum hispidum

Various experimental studies have been conducted on the *Acanthospermum hispidum*. A study showed that it contains an anti-plasmodial property on W2 & 3D7 strain (IC = 4.8 g/mL & 7.5 g/mL) [33]. These values are in the limit for the anti-malarial activity (IC 50 ~ 10 g/mL); this extract showed moderate cytotoxicity (IC 50 > IC 30 g/mL) on two cell lines. This plant also contains sesquiterpene lactones of the germacranolide group [34]. The molecules obtained from the Asteraceae have the most substantial anti-malarial properties. *Byrsocarpus coccineus*

Clinical studies have been conducted on the *Byrsocarpus coccineus* to study anti-malarial properties.The extract of *Thonn* & *Byrsocarpus coccineus* does not show good anti-malarial properties . The methanolic and dichloromethane extract showed moderate activity (IC_{50} = 54.7 & 41.6 g/mL respectively). It also contains tannins, glycosides, sugars, alkaloids and saponins. Anti-inflammatory properties have also been shown by the *Byrsocarpus coccineus*, which helps treat malaria [35].

Carpolobia lutea

This traditional medicine shows various properties like anti-diarrheal, anti-ulcer and anti-malarial. The lipophilic extract of *Carpolobia lutea*, showed a more favorable effect on W2 strain (IC_{50} = 8.1 g/mL) than on 3D7 strain (IC_{50} = 19.4 g/mL) [36]. It consists of phytoconstituents like triterpenic saponins (roots), tannins, anthraquinones, cardiotonic glycosides and alkaloids. This was the first time the plants were used as anti-malarial agents, further the researcher's attack towards herbal agents. A clinical study on mice showed that a 2450 mg/kg dose was safe for traditional use [37].

Dialium guineense

Only the dichloromethane extract of *Dialium guineense* showed moderate activity on the malarial parasite. The aqueous extract showed low activity (IC_{50} = 65.5 g/mL) compared to the dichloromethane extract (IC_{50} = 42.1 g/mL). A study showed that the molluscicidal activity of leaves & fruits was due to triterpenoid glycosides [38].

Heliotropium indicum

This traditional herb is used to treat symptoms of malaria, such as colics or hyperthermia. So, it can be used as an adjuvant in malaria medicine. It also shows

anti-leukemic, ganglion-blocking, and anti-tumor activity. It doesn't show significant anti-plasmodial activity [39].

Keetia leucantha

The dichloromethane extract of twigs and leaves showed good anti-plasmodial activity, mainly chloroquine-sensitive strain (IC_{50} = 11.3 & 13.8 g/mL resp. on 3D7 and IC_{50} = 15.8 & 26.5 g/mL resp. on W2). The selectivity index of twigs & leaves was found to be 8.8 & 4.8, respectively [40]. The anti-plasmodial activity was shown by the aerial part of the *Keetia leucantha* same as Canthium species (Rubiaceae), which was used as a traditional medicine for the treatment of malaria.

Pupalia lappacea

Pupalia lappacea does not show anti-plasmodial activity except for the dichloromethane extract, indicating moderate activity (IC_{50} = 50.29 g/mL). Traditionally, it was used for different purposes like vomiting, abdominal colic, and cephalgia, which were malaria symptoms. Then, further, it was investigated for treating malarial symptoms [41].

Sansevieria liberica

First ever used herb for the study of anti-plasmodial activity in-vitro. The dichloromethane extract of *Sansevieria liberica* leaves showed moderate activity (IC_{50} = 44.5 g/mL), but its selectivity index was very low. The twigs and leaves of the *Sansevieria guineensis* (L.) Willd. from Guatemala showed antiplasmodial activity [42].

Strychnos spinosa

Strychnos spinosa consists of alkaloids that were used as anti-plasmodial agents. The dichloromethane extract of leaves showed high antiplasmodial activity (IC_{50} = 15.6 and 8.9 on 3D7 and W2, respectively). It has a higher selectivity index than 6.4. A study showed that the stem and bark showed low or no activity. This is the first time when the leaves of *Strychnos spinosa* were used for the in-vitro study [43].

Other herbal parts or fruits in malaria

Modern antimalarial drugs are made from two subgroups of traditional medicines (artemisinin and quinines), both of which have been used for thousands of years to treat malaria. Traditional medicine is an important and sustainable source of treatment in areas where drug resistance levels are increasing, and access to effective antimalarial drugs is difficult [44]. The traditional belief is that *A. comosus* has important antimalarial properties and often contains abundant polyunsaturated fatty acids (linoleic acid). Phillip et al. evaluated *in vivo* antimalarial effect of the fruit peel of *A. comosus*. In this study, using methanol as the extraction solvent, the fruit peel of the plant was fractionated with successive amounts of n-hexane, dichloromethane, ethyl acetate, methanol, and water. A curative antimalarial model using artemisinin combination therapy (ACT) as a reference drug was performed on mice infected with *Plasmodium berghei* and treated orally 9 with three doses of the plant extract and one dose of each of its fractions and subtractions. Extracts from the plant exhibited significant non-dose dependent parasite inhibition ($P < 0.001$) between 44.84 and 76.09 %. The dichloromethane fraction showed the highest inhibitory effect (87.58%) among all fractions. Significant inhibitory effects were observed for the subtractions in the 84.14 to 92.54 % ranges. The inhibitory effect of ACT was found to be substantial, i.e., 83.92%. Hence, its strong antimalarial properties support the folkloric use of *A.comosus* for malaria treatment [45]. In another study, Abayomi et al. investigated the antimalarial effect of methanol -extracted *A. comosus* peel extract (PEAC). They administered the extract at a dose of (100, 200, and 400 mg/kg) in mice using Peter's 4-day suppressive test. Biological progression of infection in mice infected with 1 X 10^6 parasitized red blood cells. Parasite levels in the animals steadily increased throughout the course of the 14-day experiment. PEAC did not differ significantly from the untreated control group for infected individuals and the treated group for infected individuals. Mice t infected with *P. beighei* and treated with chloroquine and artemether-lumefantrine did not show signs of parasitemia. The PEAC (400 mg/kg) prolongs the survival of mice by almost 20% by day 21, but the chloroquine extends it by nearly 80% by day 28. The survival rate of artemether-lumefantrine was 100% on day 28 [24]. Among the aryl amino alcohols, quinine is an alkaloid present in cinchona. Different preparations exist, including hydrochlorides, dihydrochlorides, sulphates, bisulphates, and gluconates; dihydrochloride is the most commonly used preparation. In intra-erythrocytic malaria parasites, quinine has schizonticidal properties. Age, pregnancy, immunity, and disease severity affect quinine pharmacokinetic properties and therapeutic responses [46]. Plasmodium falciparum infections are rapidly controlled with artemisinin and derivatives (collectively known as ARTs). The effectiveness of ART combination therapy is highly dependent on the rapid reduction of parasite burden. In addition to killing parasites through protein damage, dihydroartemisinin (DHA) also compromises parasite proteasome activity [47]. The use of artemisinin has been associated with reduced malaria transmission because they are active against gametocytes, the parasite form transmitted by mosquitoes [48,49]. But resistance to the existing drug therapy has been reported. As a result, there is a great need for novel antimalarials, especially those derived from medicinal plants. Pineapple and its bioactive compounds can be used in treating malaria, as suggested by the reported literature. I In many countries, pineapple is used as a folkloric treatment for malaria. Form ancient times, pineapple and related compounds were used in the treatment of malaria in comparison to the existing therapy.

Herbals drugs used in the treatment of malaria

Numerous herbal plants are used in the treatment of malaria. Some of the important plants with their metabolites, which are responsible for antimalarial effects are enumerated in Table 1.

Table 1 Herbal drugs used in the treatment of malaria

No.	Plant	Family	Metabolite	Ref.
1	Adhatoda vasica	Acanthaceae	Vasicine	[50]
2	Aloe vera L.	Xanthorrhoeaceae	Aloin (barbaloin), arabinose, aloe-emodin	[51]
3	Andrographis paniculate	Acanthaceae	Andrographolide, andropanolide, andrographic acid	[52,53]
4	Anthemis auriculata Boiss	Asteraceae	Sesquiterpene lactone	[53,54]
5	Artemisia annua	Asteraceae	Artemisinin	[55]
6	Artemisia gorgonum Webb	Asteraceae	Terpenoid (germacranolide)	[56]
7	Artocarpus champeden	Moraceae	Prenylated flavones, Prenylated flavonoids	[57]
8	Artocarpus rigidus	Moraceae	Flavonoids	[58]
9	Atropa belladonna	Solanaceae	Hyoscyamine, atropine	[59]
10	Azadirachta indica A. Juss.	Meliaceae	Azadirachtin, nimbin	[60,61]
11	Bauhinia purpurea L.	Leguminosae	Flavonoid derivatives, Quinones	[62]
12	Bowdichia nitida Spruce ex Benth.	Leguminosae	Diterpene	[63]
13	Bulbine frutescens Willd.	Asphodelaceae	Phenylanthraquinones	[64]
14	Caesalpinia bonduc L. Roxb.	Caesalpinia- ceae	Furanoditerpenoids	[65]
15	Cannabis sativa L.	Cannabaceae	Quinones	[66]
16	Capsicum annuum	Solanaceae	Capsaicin, capsicosides EG	[67]
17	Carpesium rosulatum Miq.	Asteraceae	Sesquiterpene lactones	[68]
18	Cassia siamea Lam.	Leguminosae	Alkaloid	[69]
19	Cathranthus roseus	Apocynaceae	Vincristine, vinblastine	[70]
20	Chisocheton siamensis Craib	Meliaceae	Limonoids	[71]
21	Cinchona succirubra	Rubiaceae	Quinine, quinidine, cinchonine	[72]
22	Cratoxylum cochinchinense Blume	Clusiaceae	Prenylated xanthone	[73]
23	Croton lobatus L.	Euphorbiaceae	Diterpene	[74]
24	Cymbopogon citratus	Poaceae	Citral, citronellal, geranial	[75]

25	Diospyros quaesita Thwaites	Ebenaceae	Triterpene	[76]
26	Erythrina subumbrans Merr.	Leguminosae	Flavonoid derivatives	[77]
27	Garcinia polyantha Oliv.	Clusiaceae	Xanthone	[78]
28	Grewia bilamellata Gagnep.	Tiliaceae	Coumarinolignan	[76]
29	Guiera senegalensis J. F. Gmel.	Combretaceae	Naphthyl butenone	[79]
30	Harungana madagascariensis Poir.	Clusiaceae	Triterpene	[80]
31	Heimia salicifolia Link & Otto	Lythraceae	Alkaloid	[58]
32	Holarrhena antidysentrica	Apocynaceae	Norconessine, isoconessine	[81]
33	Hyptis suaveolens (L.) Poit.	Lamiaceae	Abietane-type diterpenoid endoperoxide	[82]
34	Mangifera indica	Anacardiaceae	Mangiferin, ambolic acid, ambonic acid, arabinan, mangiferonic acid	[83]
35	Mimosa pudica	Fabaceae	Mimosine, 2-hydroxymethylchroman-4-one	[84]
36	Ocimum sanctum	Lamiaceae	Eugenol, methyl eugenol, carvacrol	[85]
37	Papever somniferum	Papaveraceae	Morphine, codeine, papaverine	[86]
38	Parthenocissus tricuspidata Planch.	Vitaceae	Stilbene glycoside	[87]
39	Phyllanthus niruri L.	Euphorbiaceae	Coumarin	[88]
40	Piptadenia pervillei Vatke	Leguminosae	Phenolic derivatives Flavonoid derivatives	[89]
41	Polyalthia cerasoides (Roxb.) Bedd.	Annonaceae	Dimeric aporphine alkaloid	[90]
42	Polyalthia viridis Craib	Annonaceae	Quinone	[58]
43	Psorospermum glaberrimum Hochr.	Clusiaceae	Bianthrone	[58]
44	Punica granatum L.	Lythraceae	Tannins	[88]
45	Ricinus communis	Euphorbiaceae	Ricinoleic acid, ricinine, ferulic acid	[91]
46	Rourea minor (Gaertn.) Aubl.	Connaraceae	Lignan	[92]
47	Sarcococca hookeriana Baill.	Buxaceae	Steroidal alkaloids	[93]
48	Strychnos nuxvomica	Loganiaceae	Strychnine, brucine	[94]
49	Styrax benzoin	Styracaceae	Cinnamic acid, benzoic acid	[94]
50	Terminalia bellirica	Combretaceae	Ellagic acid, gallic acid	[95]
51	Vernoniopsis caudate (Drake) Humbert	Asteraceae	Helenanolide sesquiterpene lactones	[96]
52	Wedelia trilobata Hitchc.	Asteraceae	Sesquiterpene lactones	[97]
53	Zanthoxylum flavum Vahl.	Rutaceae	Coumarin	[98]
54	Zanthoxylum flavum Vahl.	Rutaceae	Tryptophane derivative	[98]
55	Zanthoxylum rhoifolium Lam.	Rutaceae	Alkaloid	[98]
56	Zingiber officinalis	Zingiberaceae	Gingerol, zingiberene	[99]

Future perspective

Despite the increasing use of traditional medicine in treating malaria and the fact that it is usually more affordable and more readily accessible than Western medicine, it has limitations. The safety and efficacy of the drug are unknown, first of all. It also requires more work to pinpoint which plants, preparations, or dosages offer the best results, even among traditional healers. Several factors determine the concentration of active ingredients in a plant species. Despite these limitations, research can resolve all of them. Several systematic reviews, summarized here, have been published by the Research Initiative on Traditional Antimalarial Methods as well as guidelines to improve the quality of future research. Reviewing and updating these guidelines is still a long way to go. It is more appropriate to consider them as stepping stones for further research than as final products.

Conclusion

The world needs to control and eradicate malaria, which threatens humankind. Malaria has evolved into a complex multistage parasite in mosquitoes and their human hosts. To develop a malaria vaccine, one must thoroughly understand its biology. In traditional medicine, plants have remained an essential source of lead compounds, which have been used to develop drugs. Developing effective and promising combination treatments would provide an effective means of controlling malaria resistance, but to confirm the outcomes of the animal studies needed, further studies would need to be conducted using Plasmodium falciparum strains, as well as human volunteers.

References

1. Miller LH, Ackerman HC, Su XZ, Wellems TE. Malaria biology and disease pathogenesis: insights for new treatments. *Nat Med*. 2013;19(2):156–67. https://www.doi.org/10.1038/nm.3073.
2. Malaria [Internet]. [cited 2022 May 9]. https://www.who.int/health-topics/malaria#tab=tab_1
3. Nonvignon J, Aryeetey GC, Malm KL, et al. Economic burden of malaria on businesses in Ghana: a case for private sector investment in malaria control. *Malar J*. 2016;15(1):454. https://pubmed.ncbi.nlm.nih.gov/27599835/
4. Hay SI, Cox J, Rogers DJ, Randolph SE, Stern DI, Shanks GD, Myers MF, Snow RW. Climate change and the resurgence of malaria in the East African highlands. Nature. 2002 Feb 21;415(6874):905-9. https://pubmed.ncbi.nlm.nih.gov/415905a.
5. A Brief History of Malaria - Saving Lives, Buying Time - NCBI Bookshelf [Internet]. [cited 2022 May 9]. https://www.ncbi.nlm.nih.gov/books/NBK215638/
6. Cox FE. History of the discovery of the malaria parasites and their vectors. *Parasit Vectors*. 2010;3(1):5. https://pubmed.ncbi.nlm.nih.gov/20205846/
7. O'Donnell RA, Blackman MJ. The role of malaria merozoite proteases in red blood cell invasion. *Curr Opin Microbiol*. 2005;8(4):422–7. https://pubmed.ncbi.nlm.nih.gov/16019257/
8. Dunn FL. Patterns of parasitism in primates: phylogenetic and ecological interpretations, with particular reference to the hominoidea. *Folia Primatol* (Basel). 1966;4(5):329–45. https://pubmed.ncbi.nlm.nih.gov/5333744/
9. Figure 1, [The malaria parasite life cycle.]. - Coffee Break - NCBI Bookshelf [Internet]. [cited 2022 Jun 17]. https://www.ncbi.nlm.nih.gov/books/NBK5951/figure/malaria_LifeCycle/
10. WL K. Ethical perspective on malaria research for Africa. *Acta Trop*. 2005;95(3). https://pubmed.ncbi.nlm.nih.gov/16023987/
11. Newton PN, McGready R, Fernandez F, et al. Manslaughter by fake artesunate in Asia--will Africa be next?. *PLoS Med*. 2006;3(6):e197. https://pubmed.ncbi.nlm.nih.gov/16752952/
12. Takala SL, Plowe CV. Genetic diversity and malaria vaccine design, testing and efficacy: preventing and overcoming 'vaccine resistant malaria'. *Parasite Immunol*. 2009;31(9):560-573. https://pubmed.ncbi.nlm.nih.gov/19691559/
13. Paras Hospitals [Internet]. [cited 2022 Jun 17]. https://www.parashospitals.com/blogs/foods-eat-avoid-treating-malaria

14. Chinsembu KC. Plants as antimalarial agents in Sub-Saharan Africa. *Acta Trop*. 2015;152:32–48. https://pubmed.ncbi.nlm.nih.gov/26297798/
15. Bero J, Frédérich M, Quetin-Leclercq J. Antimalarial compounds isolated from plants used in traditional medicine. *J Pharm Pharmacol*. 2009;61(11):1401–33. https://pubmed.ncbi.nlm.nih.gov/19903367/
16. Mondal S, Bhattacharya S, Pande JN, Biswas Moulisha B. Evaluation of acute anti-inflammatory effect of Ananas comosus leaf extracts in rats. *Pharmacologyonline*. 2011;3: 1312-1315. https://www.researchgate.net/publication/221963482_Evaluation_of_acute_anti-inflammatory_effect_of_Ananas_comosus_leaf_extracts_in_rats
17. Pavan R, Jain S, Shraddha, Kumar A. Properties and therapeutic application of bromelain: a review. *Biotechnol Res Int.* 2012;2012:976203. https://pubmed.ncbi.nlm.nih.gov/23304525/
18. Schmidt CQ, Kennedy AT, Tham WH. More than just immune evasion: Hijacking complement by Plasmodium falciparum. *Mol Immunol*. 2015;67(1):71-84. https://pubmed.ncbi.nlm.nih.gov/25816986/
19. Cowman AF, Berry D, Baum J. The cellular and molecular basis for malaria parasite invasion of the human red blood cell. *J Cell Biol*. 2012;198(6):961–971. https://pubmed.ncbi.nlm.nih.gov/22986493/
20. Aikawa M. Morphological changes in erythrocytes induced by malarial parasites. *Biol Cell*. 1988;64(2):173–181. https://pubmed.ncbi.nlm.nih.gov/3228621/
21. Bhutta ZA, Darmstadt GL, Haws RA, Yakoob MY, Lawn JE. Delivering interventions to reduce the global burden of stillbirths: improving service supply and community demand. *BMC Pregnancy Childbirth*. 2009;9 Suppl 1(Suppl 1):S7. https://pubmed.ncbi.nlm.nih.gov/19426470/
22. Figure 1, [The malaria parasite life cycle.]. - Coffee Break - NCBI Bookshelf [Internet]. [cited 2022 May 9]. https://www.ncbi.nlm.nih.gov/books/NBK5951/figure/malaria_LifeCycle/
23. Verhulst NO, Qiu YT, Beijleveld H, et al. Composition of human skin microbiota affects attractiveness to malaria mosquitoes. *PLoS One*. 2011;6(12):e28991. https://pubmed.ncbi.nlm.nih.gov/22216154/
24. McBride CS. Genes and Odors Underlying the Recent Evolution of Mosquito Preference for Humans. *Curr Biol*. 2016;26(1):R41–R46. https://pubmed.ncbi.nlm.nih.gov/26766234/
25. Achan J, Talisuna AO, Erhart A, Yeka A, Tibenderana JK, Baliraine FN, et al. Quinine, an old anti-malarial drug in a modern world: Role in the treatment of malaria. *Malar J*. 2011;10(1):1–12. https://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-10-144
26. Jacobs GH, Oduola AMJ, Kyle DE, Milhous WK, Martin SK, Aikawa M. Ultrastructural study of the effects of chloroquine and verapamil on Plasmodium falciparum. *Am J Trop Med Hyg*. 1988;39(1):15–20. https://pubmed.ncbi.nlm.nih.gov/3041853/
27. Wicht KJ, Mok S, Fidock DA. Molecular Mechanisms of Drug Resistance in *Plasmodium falciparum* Malaria. *Annu Rev Microbiol*. 2020;74:431. https://pubmed.ncbi.nlm.nih.gov/32905757/
28. Warhurst DC. A molecular marker for chloroquine-resistant falciparum malaria. *N Engl J Med*. 2001;344(4):299–302. http://www.ncbi.nlm.nih.gov/pubmed/11172160
29. Winstanley PA, Ward SA, Snow RW. Clinical status and implications of antimalarial drug resistance. *Microbes Infect*. 2002;4(2):157–64. https://www.doi.org/10.1016/s1286-4579(01)01523-4
30. Krishna S, Bustamante L, Haynes RK, Staines HM. Artemisinins: their growing importance in medicine. *Trends in Pharmacological Sciences*. 2008;29(10):520–527. https://www.doi.org/10.1016/j.tips.2008.07.004
31. O'Neill PM, Barton VE, Ward SA. The Molecular Mechanism of Action of Artemisinin—The Debate Continues. *Molecules*. 2010;15(3):1705–21. https://www.mdpi.com/1420-3049/15/3/1705/htm
32. Cragg GM, Newman DJ. Natural products: a continuing source of novel drug leads. *Biochim Biophys Acta*. 2013;1830(6):3670–95. https://pubmed.ncbi.nlm.nih.gov/23428572/
33. Koukouikila-Koussounda F, Abena AA, Nzoungani A, Mombouli JV, Ouamba JM, Kun J, et al. In Vitro Evaluation of Antiplasmodial Activity of Extracts of *Acanthospermum hispidum* DC (Asteraceae) and Ficus Thonningii Blume (Moraceae), Two Plants Used in Traditional Medicine in the Republic of Congo. *Afr J Tradit Complement Altern Med*. 2013;10(2):270. https://pubmed.ncbi.nlm.nih.gov/24146450/
34. Cartagena E, Bardon A, Catalan CAN, de Hernadez ZNJ, Hernandez LR, Joseph-Nathan P. Germacranolides and a new type of guaianolide from *Acanthospermum hispidum*. *J Nat Prod*. 2000;63(10):1323–8. https://pubmed.ncbi.nlm.nih.gov/11076545/
35. Akindele AJ, Adeyemi OO. Antiinflammatory activity of the aqueous leaf extract of *Byrsocarpus coccineus*. *Fitoterapia*. 2007;78(1):25–8. https://pubmed.ncbi.nlm.nih.gov/17118572/
36. Nwafor PA, Bassey AIL. Evaluation of anti-diarrhoeal and anti-ulcerogenic potential of ethanol extract of *Carpolobia lutea* leaves in rodents. *J Ethnopharmacol*. 2007;111(3):619–24. https://pubmed.ncbi.nlm.nih.gov/17296280/
37. Mitaine-Offer AC, Miyamoto T, Khan IA, Delaude C, Lacaille-Dubois MA. Three new triterpene saponins from two species of Carpolobia. *Journal of Natural Products*. 2002;65(4):553–7. https://kyushu-u.pure.elsevier.com/en/publications/three-new-triterpene-saponins-from-two-species-of-carpolobia
38. Molluscicidal triterpenoid glycosides of *Dialium guineense* [Internet]. [cited 2022 Aug 9]. https://agris.fao.org/agris-search/search.do?recordID=US9619751
39. Sarkar C, Mondal M, Khanom B, Hossain MM, Hossain MS, Sureda A, et al. Heliotropium indicum L.: From Farm to a Source of Bioactive Compounds with Therapeutic Activity. *Evid Based Complement Alternat Med*. 2021;e9965481. https://pubmed.ncbi.nlm.nih.gov/34158818/
40. Bero J, Hérent MF, Schmeda-Hirschmann G, Frédérich M, Quetin-Leclercq J. In vivo antimalarial activity of *Keetia leucantha* twigs extracts and in vitro antiplasmodial effect of their constituents. *J Ethnopharmacol*. 2013;149(1):176–83. https://pubmed.ncbi.nlm.nih.gov/23792125/
41. Naidu, P.P., & Rajesh, B.N. *PUPALIA LAPPACEA* JUSS [L]: A REVIEW OF PHYTOCHEMISTRY AND THERAPEUTIC APPLICATION. *Asian Journal of Pharmaceutical and Clinical Research*, 2014;7:15-18. https://www.semanticscholar.org/paper/PUPALIA-LAPPACEA-JUSS-%5BL%5D%3A-A-REVIEW-OF-AND-Naidu-Rajesh/4c7f156d49fd6b8209f245aef9fcd832ecda2335
42. Orabueze IC, Uzor SC, Ndiaye B, Uba D, Ota DA, Agbedahusi J. Antimalarial, Antioxidant Activities and Chemoprofile of *Sansevieria liberica* Gerome and Labroy (Agavaceae) Leaf Extract. *Adv Pharmacol Pharm Sci*. 2021;2021:9053262. https://pubmed.ncbi.nlm.nih.gov/34913035/
43. Isa AI, Awouafack MD, Dzoyem JP, et al. Some *Strychnos spinosa* (Loganiaceae) leaf extracts and fractions have good antimicrobial activities and low cytotoxicities. *BMC Complement Altern Med*. 2014;14:456. https://pubmed.ncbi.nlm.nih.gov/25428165/
44. Murambiwa P, Masola B, Govender T, Mukaratirwa S, Musabayane CT. Anti-malarial drug formulations and novel delivery systems: a review. *Acta Trop*. 2011;118(2):71–79. https://pubmed.ncbi.nlm.nih.gov/21439929/
45. Uzor PF, Ishiwu BU, Nwodo NJ. In vivo antimalarial effect of Ananas comosus (L) Merr (Bromeliaceae) fruit peel, and gas chromatography-mass spectroscopy profiling: A possible role for polyunsaturated fatty acid. *Tropical Journal of Pharmaceutical Research*. 2020;19(1):137–45. https://www.doi.org/10.4314/tjpr.v19i1.21
46. Achan J, Talisuna AO, Erhart A, Yeka A, Tibenderana JK, Baliraine FN, et al. Quinine, an old anti-malarial drug in a modern world: role in the treatment of malaria. *Malar J*. 2011;10:144. https://pubmed.ncbi.nlm.nih.gov/21609473/
47. Bridgford JL, Xie SC, Cobbold SA, et al. Artemisinin kills malaria parasites by damaging proteins and inhibiting the proteasome. *Nat Commun*. 2018;9(1):3801. https://pubmed.ncbi.nlm.nih.gov/30228310/
48. Artesunate combinations for treatment of malaria: meta-analysis. Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews - NCBI Bookshelf [Internet]. [cited 2022 Jun 17]. https://www.ncbi.nlm.nih.gov/books/NBK70990/
49. Nosten F, Van Vugt M, Price R, Luxemburger C, Thway KL, Brockman A, et al. Effects of artesunate-mefloquine combination on incidence of

Plasmodium falciparum malaria and mefloquine resistance in western Thailand: a prospective study. *Lancet*. 2000;356(9226):297–302. https://pubmed.ncbi.nlm.nih.gov/11071185/

50. Sampath Kumar KP, Bhowmik D, Tiwari P, Kharel R. Indian traditional herbs Adhatoda vasica and its Medicinal application. *Journal of Chemical and Pharmaceutical Research*. 2010;2(1):240–5. https://www.semanticscholar.org/paper/Indian-traditional-herbs-Adhatoda-vasica-and-its-Kumar-Bhowmik/b028d58a0db2c2ef8995435b0426ef031a01ddee
51. Rajasekaran S, Ravi K, Sivagnanam K, Subramanian S. Beneficial effects of aloe vera leaf gel extract on lipid profile status in rats with streptozotocin diabetes. *Clin Exp Pharmacol Physiol*. 2006;33(3):232–7. https://pubmed.ncbi.nlm.nih.gov/16487267/
52. Trivedi NP, Rawal UM, Patel BP. Hepatoprotective effect of andrographolide against hexachlorocyclohexane-induced oxidative injury. *Integr Cancer Ther*. 2007;6(3):271–80. https://pubmed.ncbi.nlm.nih.gov/17761640/
53. Reyes BAS, Bautista ND, Tanquilut NC, Anunciado R v., Leung AB, Sanchez GC, et al. Anti-diabetic potentials of Momordica charantia and Andrographis paniculata and their effects on estrous cyclicity of alloxan-induced diabetic rats. *J Ethnopharmacol*. 2006;105(1–2):196–200. https://pubmed.ncbi.nlm.nih.gov/16298503/
54. Babaei G, Aliarab A, Abroon S, Rasmi Y, Aziz SG. Application of sesquiterpene lactone: A new promising way for cancer therapy based on anticancer activity. *Biomed Pharmacother*. 2018;106:239-246. https://pubmed.ncbi.nlm.nih.gov/29966966/
55. Batista R, de Jesus Silva Júnior A, de Oliveira AB. Plant-derived antimalarial agents: new leads and efficient phytomedicines. Part II. Non-alkaloidal natural products. *Molecules*. 2009;14(8):3037–72. https://pubmed.ncbi.nlm.nih.gov/19701144/
56. Ortet R, Prado S, Regalado EL, Valeriote FA, Media J, Mendiola J, et al. Furfuran lignans and a flavone from Artemisia gorgonum Webb and their in vitro activity against Plasmodium falciparum. *J Ethnopharmacol*. 2011;138(2):637–40. https://pubmed.ncbi.nlm.nih.gov/21982788/
57. Widyawaruyanti A, Subehan, Kalauni SK, Awale S, Nindatu M, Zaini NC, et al. New prenylated flavones from Artocarpus champeden, and their antimalarial activity in vitro. *J Nat Med*. 2007;61(4):410–3. https://doi.org/10.1007/s11418-007-0153-8
58. Noronha M, Pawar V, Prajapati A, Subramanian RB. A literature review on traditional herbal medicines for malaria. *South African Journal of Botany*. 2020;128:292–303. https://doi.org/10.1016/j.sajb.2019.11.017
59. Maqbool F, Singh S, Kaloo ZA, Jan M. Medicinal importance of Genus Atropa Royle-A review. *International Journal of Advanced Research*. 2014;2(2):48–54. https://www.journalijar.com/article/790/medicinal-importance-of-genus-atropa-(royle)--a-review/
60. Ogbuehi IH, Ebong OO. Traditional Medicine Treatment of Malaria in Onitsha, South East Nigeria. *Greener Journal of Medical Sciences*. 2015;5(1):011–8. https://www.gjournals.org/GJMS/Publication/2015/January/HTML/051114384%20Ogbuehi%20and%20Ebong.htm
61. Odugbemi TO, Akinsulire OR, Aibinu IE, Fabeku PO. Medicinal plants useful for malaria therapy in Okeigbo, Ondo State, Southwest Nigeria. *Afr J Tradit Complement Altern Med*. 2006;4(2):191-198. https://pubmed.ncbi.nlm.nih.gov/20162091/
62. Boonphong S, Puangsombat P, Baramee A, Mahidol C, Ruchirawat S, Kittakoop P. Bioactive compounds from Bauhinia purpurea possessing antimalarial, antimycobacterial, antifungal, anti-inflammatory, and cytotoxic activities. *J Nat Prod*. 2007;70(5):795–801. https://pubmed.ncbi.nlm.nih.gov/17480099/
63. Matsuno Y, Deguchi J, Hirasawa Y, Ohyama K, Toyoda H, Hirobe C, et al. Sucutiniranes A and B, new cassane-type diterpenes from Bowdichia nitida. *Bioorganic & Medicinal Chemistry Letters*. 2008;18(13):3774–7. https://europepmc.org/article/med/18524584
64. Bringmann G, Mutanyatta-Comar J, Maksimenka K, Wanjohi JM, Heydenreich M, Brun R, et al. Joziknipholones A and B: The First Dimeric Phenylanthraquinones, from the Roots of Bulbine frutescens. *Chemistry – A European Journal*. 2008;14(5):1420–9. https://onlinelibrary.wiley.com/doi/full/10.1002/chem.200701328
65. Pudhom K, Sommit D, Suwankitti N, Petsom A. Cassane furanoditerpenoids from the seed kernels of Caesalpinia bonduc from Thailand. *Journal of Natural Products*. 2007;70(9):1542–4. https://pubs.acs.org/doi/abs/10.1021/np070330y
66. Radwan MM, ElSohly MA, Slade D, Ahmed SA, Wilson L, El-Alfy AT, et al. Non-cannabinoid constituents from a high potency Cannabis sativa variety. *Phytochemistry*. 2008;69(14):2627–33. https://pubmed.ncbi.nlm.nih.gov/18774146/
67. Ribeiro SFF, Carvalho AO, da Cunha M, Rodrigues R, Cruz LP, Melo VMM, et al. Isolation and characterization of novel peptides from chilli pepper seeds: antimicrobial activities against pathogenic yeasts. *Toxicon*. 2007;50(5):600–11. https://pubmed.ncbi.nlm.nih.gov/17572465/
68. Moon HI. Antiplasmodial activity of ineupatorolides A from Carpesium rosulatum. *Parasitol Res*. 2007;100(5):1147–9. https://pubmed.ncbi.nlm.nih.gov/17102985/
69. Morita H, Oshimi S, Hirasawa Y, Koyama K, Honda T, Ekasari W, et al. Cassiarins A and B, novel antiplasmodial alkaloids from Cassia siamea. *Org Lett*. 2007;9(18):3691–3. https://pubmed.ncbi.nlm.nih.gov/17685627/
70. Ueda JY, Tezuka Y, Banskota AH, le Tran Q, Tran QK, Harimaya Y, et al. Antiproliferative activity of Vietnamese medicinal plants. *Biol Pharm Bull*. 2002;25(6):753–60. https://pubmed.ncbi.nlm.nih.gov/12081142/
71. Maneerat W, Laphookhieo S, Koysomboon S, Chantrapromma K. Antimalarial, antimycobacterial and cytotoxic limonoids from Chisocheton siamensis. *Phytomedicine*. 2008;15(12):1130-1134. https://pubmed.ncbi.nlm.nih.gov/18617378/
72. Andrade-Neto VF, Brandão MGL, Stehmann JR, Oliveira LA, Krettli AU. Antimalarial activity of Cinchona-like plants used to treat fever and malaria in Brazil. *J Ethnopharmacol*. 2003;87(2–3):253–6. https://pubmed.ncbi.nlm.nih.gov/12860318/
73. Laphookhieo S, Syers JK, Kiattansakul R, Chantrapromma K. Cytotoxic and antimalarial prenylated xanthones from Cratoxylum cochinchinense. *Chem Pharm Bull (Tokyo)*. 2006;54(5):745–7. https://pubmed.ncbi.nlm.nih.gov/16651783/
74. Attioua B, Weniger B, Chabert P. Antiplasmodial Activity of Constituents Isolated from *Croton lobatus*. *Pharmaceutical Biology*. 2008;45(4):263–6. https://www.tandfonline.com/doi/abs/10.1080/13880200701214607
75. Acaricidal activity of volatile oil from lemon and citronella grasses on tropical cattle ticks [Internet]. [cited 2022 Aug 8]. https://agris.fao.org/agris-search/search.do?recordID=TH2001000804
76. Ma CY, Musoke SF, Tan GT, Sydara K, Bouamanivong S, Southavong B, et al. Study of antimalarial activity of chemical constituents from Diospyros quaesita. *Chem Biodivers*. 2008;5(11):2442–8. https://pubmed.ncbi.nlm.nih.gov/19035573/
77. Rukachaisirikul T, Innok P, Suksamrarn A. Erythrina alkaloids and a pterocarpan from the bark of Erythrina subumbrans. *J Nat Prod*. 2008;71(1):156–8. https://pubmed.ncbi.nlm.nih.gov/18171023/
78. Lannang AM, Louh GN, Lontsi D, Specht S, Sarite SR, Flörke U, et al. Antimalarial compounds from the root bark of Garcinia polyantha Olv. *J Antibiot (Tokyo)*. 2008;61(8):518–23. https://pubmed.ncbi.nlm.nih.gov/18997392/
79. Fiot J, Sanon S, Azas N, Mahiou V, Jansen O, Angenot L, et al. Phytochemical and pharmacological study of roots and leaves of Guiera senegalensis J.F. Gmel (Combretaceae). *J Ethnopharmacol*. 2006;106(2):173–8. https://pubmed.ncbi.nlm.nih.gov/16443341/
80. Ndjakou Lenta B, Ngouela S, Fekam Boyom F, et al. Anti-plasmodial activity of some constituents of the root bark of Harungana madagascariensis LAM. (Hypericaceae). *Chem Pharm Bull (Tokyo)*. 2007;55(3):464-467. https://pubmed.ncbi.nlm.nih.gov/17329893/
81. Exploring antibacterial potential of some ayurvedic preparations to control bacterial enteric infections. [Internet]. [cited 2022 Aug 8]. https://www.cabdirect.org/cabdirect/abstract/20113030295
82. Chukwujekwu JC, Smith P, Coombes PH, Mulholland DA, van Staden J. Antiplasmodial diterpenoid from the leaves of Hyptis suaveolens. *J Ethnopharmacol*. 2005;102(2):295–7. https://pubmed.ncbi.nlm.nih.gov/16213121/

83. Ojewole JAO. Antiinflammatory, analgesic and hypoglycemic effects of Mangifera indica Linn. (Anacardiaceae) stem-bark aqueous extract. *Methods Find Exp Clin Pharmacol*. 2005;27(8):547–54. https://pubmed.ncbi.nlm.nih.gov/16273134/
84. Robinson RD, Williams LA, Lindo JF, Terry SI, Mansingh A. Inactivation of strongyloides stercoralis filariform larvae in vitro by six Jamaican plant extracts and three commercial anthelmintics. *West Indian Med J*. 1990;39(4):213-217. https://pubmed.ncbi.nlm.nih.gov/2082565/
85. Mittal R, Kumar R, Chahal H. Antimicrobial activity of Ocimum sanctum leaves extracts and oil. *Journal of Drug Delivery and Therapeutics*. 2018;8(6):201–4. http://jddtonline.info/index.php/jddt/article/view/2166
86. Jackson DE. A note on the pharmacological action of opium alkaloids. *Journal of Pharmacology and Experimental Therapeutics.* 1914;6(1):57–72. https://jpet.aspetjournals.org/content/6/1/57
87. Son IH, Chung IM, Lee SJ, Moon HI. Antiplasmodial activity of novel stilbene derivatives isolated from Parthenocissus tricuspidata from South Korea. *Parasitol Res*. 2007;101(1):237–41. https://pubmed.ncbi.nlm.nih.gov/17211658/
88. Subeki S, Matsuura H, Takahashi K, et al. Anti-babesial and anti-plasmodial compounds from Phyllanthus niruri. *J Nat Prod*. 2005;68(4):537-539. https://pubmed.ncbi.nlm.nih.gov/15844943/
89. Ramanandraibe V, Martin MT, Rakotondramanana DL, et al. Pseudoguanolide sesquiterpene lactones from Vernoniopsis caudata and their in vitro antiplasmodial activities. *J Nat Prod*. 2005;68(5):800-803. https://pubmed.ncbi.nlm.nih.gov/15921436/
90. Kanokmedhakul S, Kanokmedhakul K, Lekphrom R. Bioactive constituents of the roots of Polyalthia cerasoides. *J Nat Prod*. 2007;70(9):1536-1538. https://pubmed.ncbi.nlm.nih.gov/17845001/
91. Ilavarasan R, Mallika M, Venkataraman S. Anti-inflammatory and free radical scavenging activity of Ricinus communis root extract. *J Ethnopharmacol*. 2006;103(3):478–80. https://pubmed.ncbi.nlm.nih.gov/16310994/
92. Pan WH, Xu XY, Shi N, Tsang SW, Zhang HJ. Antimalarial Activity of Plant Metabolites. *Int J Mol Sci*. 2018;19(5):1382. https://pubmed.ncbi.nlm.nih.gov/29734792/
93. Devkota KP, Lenta BN, Choudhary MI, et al. Cholinesterase inhibiting and antiplasmodial steroidal alkaloids from Sarcococca hookeriana. *Chem Pharm Bull (Tokyo)*. 2007;55(9):1397-1401. https://pubmed.ncbi.nlm.nih.gov/17827771/
94. Guo R, Wang T, Zhou G, et al. Botany, Phytochemistry, Pharmacology and Toxicity of Strychnos nux-vomica L.: A Review. *Am J Chin Med*. 2018;46(1):1–23. https://pubmed.ncbi.nlm.nih.gov/29298518/
95. Sharif A, Nawaz H, Rehman R, Mushtaq A, Rashid U. A review on bioactive potential of Benzoin Resin. *IJCBS*. 2016;10:106–110. https://www.researchgate.net/publication/336825434_A_review_on_bioactive_potential_of_Benzoin_Resin
96. Ramanandraibe V, Grellier P, Martin MT, Deville A, Joyeau R, Ramanitrahasimbola D, et al. Antiplasmodial phenolic compounds from Piptadenia pervillei. *Planta Medica*. 2008;74(4):417–21. http://www.thieme-connect.com/products/ejournals/html/10.1055/s-2008-1034328
97. That QT, Jossang J, Jossang A, Kim PP, Jaureguiberry G. Wedelolides A and B: novel sesquiterpene delta-lactones, (9R)-eudesman-9,12-olides, from Wedelia trilobata. *J Org Chem*. 2007;72(19):7102-7105. https://pubmed.ncbi.nlm.nih.gov/17705534/
98. Ross SA, Krishnaven K, Radwan MM, Takamatsu S, Burandt CL. Constituents of Zanthoxylum flavum and their antioxidant and antimalarial activities. *Natural Product Communications*. 2008;3(5):791–4. https://doi.org/10.1177/1934578X0800300521
99. Riyazi A, Hensel A, Bauer K, Geißler N, Schaaf S, Verspohl EJ. The effect of the volatile oil from ginger rhizomes (Zingiber officinale), its fractions and isolated compounds on the 5-HT3 receptor complex and the serotoninergic system of the rat ileum. *Planta Med*. 2007;73(4):355–62. https://pubmed.ncbi.nlm.nih.gov/17511060/