Advances of natural product in the control of malarial parasite

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Abstract

A dangerous protozoan parasite disease called malaria, which is spread by female Anopheles mosquitoes in tropical areas, is brought on by a species of Plasmodium. Of the entire world population, an estimated 3.3 billion people reside in regions where malaria is common and kills 660,000 people annually. Natural substances made from plants have been crucial in the fight against malaria. Synthetic medications are risky and have a wide range of negative effects. Different ailments have been treated with medicinal herbs. Chemicals that come from plants have some positive effects on the body. The bark of the South American native Chinchona tree contains the first anti-malarial medication, quinine. The pure medication Artemisinin, which is isolated from the Artemisia annua plant and is effective against all malarial parasites, was also found in China. In different countries different plant parts extract derived herbal remedies used in control of malaria which are affordable, safer and effective than any chemical compound. In this review I discussed region wise plants used for anti plasmodial activity.

Keywords: Malaria, Malarial Parasite, Quinine, Artemisinin, Chloroquine, Antimalarial drugs, Antiplasmodial activity, Medicinal Plants, Plant extract

Introduction

Due to the early link of the disease with marshy environments, the term malaria is derived from the Italian "mal'aria," which means "bad air" (Tuteja, 2007). A protozoan parasite that usually infects a particular species of mosquito that feeds on humans can cause malaria, a dangerous and occasionally fatal disease (https://www.cdc.gov). In tropical and subtropical regions, notably in sub-Saharan Africa, malaria is one of the most prevalent diseases spread by mosquitoes (Karunamoorthi and Ilango, 2010). More than 400,000 people die from malaria each year, infecting close to 290 million people worldwide (mayoclinic.org). By 2022, over half of the world's population will be at risk from malaria. The most recent global malaria report estimates that there were 241 million cases of malaria in 2020, up from 227 million cases in 2019. (https://www.who.int).

The female Anopheles mosquito is the means through which the species is spread. The transmission of numerous diseases, including malaria, filariasis, dengue, Japanese encephalitis, chikungunya, and yellow fever, which result in millions of deaths each year in nearly all tropical and subtropical nations as well as many other parts of the world, makes this one of the most significant groups of insects in terms of public health issues (Ghosh et al. 2012). According to the Mayo Clinic, the parasite is transmitted through mosquito bites (mayoclinic.org). Malaria often causes severe disease, including high fevers, shivering chills, and flu-like symptoms (https://www.cdc.gov). In the endemic regions, malaria continues to be one of the most important issues and the main cause of mortality and morbidity. 109 countries and territories are currently

considered dangerous, of which 45 are on the World Health Organization (WHO) list.

Therefore, it's important to keep an eye on Plasmodium growth inside the host's body in order to control the malaria infection. Affordable and efficient anti-malarial medications are urgently needed for this purpose (Rajakumar & Rahuman, 2011). Natural substances made from plants have been extremely important in the fight against malaria. According to Inbaneson et al. (2012), medicinal plants are a reliable source of both conventional and modern medicine. Due to their potential pharmacological properties, medicinal plants have been used to treat a variety of diseases. These properties include antineoplastic, antimicrobial, antioxidant, anti-inflammatory, analgesic, anti-diabetic, anti-hypertensive, antidiarrheal, and other activities (Shaikh and Patil, 2020). Examples include artemisinin, obtained from *Artemisia annua* discovered by Tu Youyou, and quinine, which was the first anti-malarial drug of plant origin and was isolated from the bark of Cinchona tree (Rubiaceae) by Pierre Joseph Pelletier and Joseph Caventou (Achan et al. 2011). The choice of plants for testing for antimalarial activity is based on the traditional perception of a given plant's effects. People typically prefer using herbal remedies because they are widely accepted by the community and are readily available. Compared to contemporary medicine, herbal medicines are said to be more accessible, reliable, and cost-effective. Most regions of the world are finding it difficult to control malaria due to treatment resistance (Nguta et al. 2010a). Since the early 1960s, chloroquine, the best and most widely used drug to treat malaria, has lost its potency against parasites. As a result, it is urgently necessary to develop new information, goods, equipment, and medications in order to properly control malaria (Omulokoli et al. 1997). An efficient vaccination would be the most successful and cost-effective way to treat malaria, and its potential long-term effects could potentially lead to its eventual eradication. Despite significant advancements, a malaria vaccine is still far from being developed (Nguta et al. 2010). Drug discovery could have a head start thanks to natural products. For many years, the development of anti-malarial lead compounds has been based on traditional herbal medicines.

About malarial parasites

According to Tuteja (2007) and Igweh (2012), malaria parasites are eukaryotic single-celled microorganisms that belong to the class Sporozoa, phylum Apicomplexa, and genus Plasmodium. Only five Plasmodium species can infect humans naturally: *Plasmodium vivax, Plasmodium ovale, Plasmodium malariae*, and the deadly *Plasmodium falciparum* that causes malaria, whereas *Plasmodium knowlesi* hardly poses a threat to people (Tu, 2016). There are more than 100 species of Plasmodium, which can infect many animal species, including reptiles, birds, and various mammals (Igweh, 2012). These species differ from one another in terms of morphology, immunology, geographic distribution, relapse patterns, and treatment responses (Tuteja, 2007). Additionally, one species that infects macaques normally has recently been linked to zoonotic malaria

in people (there are other species that may occasionally or under experimental settings, infect humans).

Types of Human Malarial Parasites

P. falciparum, which can be found globally in tropical and subtropical regions, is the cause of severe, potentially fatal malaria. Since *P. falciparum* multiplies quickly in the blood, it can result in anaemia and serious blood loss. Small blood arteries may become blocked by the infected parasites. The result is cerebral malaria, which can be lethal when it affects the brain.

A species called *P. vivax* is mainly prevalent in Asia, Latin America, and a small portion of Africa. It is most likely the parasite that causes malaria in humans. Both *P. vivax* and *P. ovale* have latent liver stages known as "hypnozoites" that can stay in this organ for weeks to many years, causing malaria infections to recur.

Mostly in West Africa, *P. ovale* is a species that is found in Africa.It is linked to *P. vivax* physiologically and morphologically, but not in the same way. This explains why *P. ovale* is more common throughout most of Africa than *P. vivax*.

The sole species of the human malaria parasite, *P. malariae*, is present throughout the world and has a quartan cycle (a three-day cycle). It results in a chronic, long-lasting infection that, in some circumstances, can last a lifetime if left untreated. *P. malaria* can result in serious complications like the nephritic syndrome in some patients who have a chronic infection.

Long-tailed and pig-tailed macaques are naturally infected by *P. knowlesi*, which is widespread in Southern Asia. Due to *P. knowlesi's* 24-hour reproduction cycle, an infection can go from mild to severe very quickly.

A few rodent species, particularly lab mice and rats, are susceptible to *P. berghei's* malaria. 22 to 24 hours are needed for the erythrocytic cycle. Infections with *P. berghei* may also impact the brain and result in cerebral complications in experimental mice.

Plant extraction and their use in the control of malarial parasites

Extraction of specific components from plants is the aim of plant processing. A solid object (the plant) is brought into contact with a liquid (the solvent) in this method for separating solids from liquids. The plant parts are then contained within the solvent after being solubilized (https://www.berkem.com). The most urgent sources of biomolecules, which can be screened from plant parts, are thought to be plant extracts. (https://www.sciencedirect.com).

Plants have always been thought of as a potential substitute and a rich source of new medications. Traditional

medicine frequently combines the use of several herbs. Instead of individual chemicals, whole plants or combinations of plants are employed. Crude plant extracts exhibit stronger anti plasmodial efficacy in vitro or in vivo at equivalent doses than separated ingredients. It is conveniently offered. Compared to chemical chemicals, it has less adverse effects. Products made from plants are inexpensive.

Materials and Method

Data was taken 10-15 years ago from the present year and was gathered by scanning published literature in the databases Google Scholar, Research Gate, and Pub Med for research articles, reviews, books, and other publications. Various key word searches, including those employing the terms "malaria," "malarial parasite," "quinine," and "artemisinin," were used to identify published publications.

Role of plant extracts in the control of malarial parasites

The two main antimalarial medications, quinine and artemisinin, are used to treat malaria around the world (Wright and Phillipson 1990; Thomson, 1993). Traditional medicinal herbs have historically been the primary source of antimalarial medications. The bulk of antimalarial drugs currently in use, such as quinine and artemisinin, were either produced using chemical models of compounds derived from plants or were directly taken from plants. (2006) Schwikkard et al. These drugs include artemisinin-based combination treatments (ACTs), mefloquine (Lariam), lumefantrine, sulfadoxine/pyrimethamine, quinoline compounds, and doxycycline (Tu, 2016).

Quinine

Before 1820, the cinchona bark was first dried, ground to a fine powder, and then mixed with a liquid (typically wine) before being consumed. Quinine, as a component of the bark of Cinchona (quina-quina) tree, was the first drug used effectively to treat malaria, from as early as the 1600s, when it was referred to as the "Jesuit's bark," "Cardinal bark," or "Sacred bark" (Achan, 2011) (https://www.britannica.com).

The cinchona alkaloid quinine is a member of the pharmacological class known as aryl amino alcohols. According to Chan (2011), quinine quickly kills intra-erythrocytic malaria parasites. For *Plasmodium vivax* and *Plasmodium malariae*, it is also gametocytocidal, but not for *Plasmodium falciparum*.

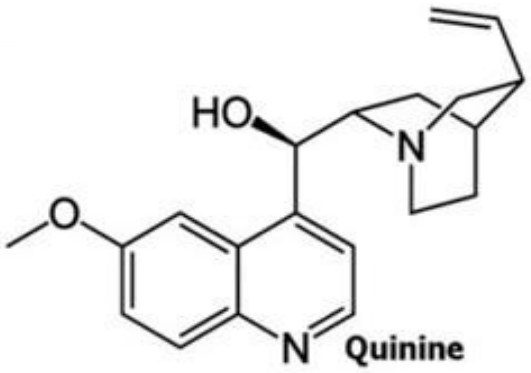

Fig 1: Chemical Structure of Quinine

However, quinine's use is constrained by its high level of toxicity and brief pharmacological half-life (Camargo et al. 2009; Muregi, 2010). Malaria can be prevented or treated using quinine and other cinchona alkaloids such quinidine, cinchonine, and cinchonidine (NCBI). Quinine also possesses analgesic properties, however they are not antipyretic. It is unknown how quinine works to prevent malaria (Achan, 2011).

The Peru tree Cinchona (*Cinchona succiruba*) [Rubiacae] plant is the source of pure quinine. Synthetic quinine substitutes emerged in the 20th century (Karunamoorthi et al. 2013). In 1940, chloroquine, another antimalarial medication, was created using quinine as a model. Quinine, a natural substance derived from the bark of the South American tree *Cinchona calisaya*, was the first extensively used antimalarial medication. Synthetic quinine derivatives, such as 8- aminoquinoline primaquine and 4- aminoquinoline choloroquine, date back to Ehrlich's groundbreaking work on methylene blue in the late 19th century.

By preventing the poisonous by-product of haemoglobin degradation, heme, from polymerizing into insoluble and harmless pigment granules, these medications can lead to parasitic mortality by causing cell lysis and parasite cell autodigestion (Olliaro and Yuthavong, 1999). The World Health Organization (WHO, 2010) recommendations recommend quinine plus doxycycline, tetracycline, or clindamycin as a second-line treatment for uncomplicated malaria (advised when the first-line medication fails or is unavailable), as well as quinine plus clindamycin for treating malaria in the first trimester of pregnancy. In India, Kolar district in Karnataka and the north-eastern regions have seen the emergence of quinine resistance (Farooq and Mahajan, 2004). Quinine has a low therapeutic index and significant side effects when used (WHO). Tinnitus, minor hearing loss, headaches, and nausea are examples of the cinchonism side effects that are frequently seen at therapeutic dosages. According to Karlsson et al. (1990), hearing loss is typically concentration-dependent and treatable. Vertigo, nausea, vomiting, back pain, diarrhoea, pronounced auditory loss, and visual abnormalities, including vision loss, are some of the more severe symptoms (White, 1996).

Artemisinin

Artemisia annua L., *Artemisia apiacea* Hance, *Artemisia scoparia* Waldst. et kit., *Artemisia capillaries*

Thunb., *Artemisia japonica* Thunb., and *Artemisia eriopoda* Bunge are among the six species that make up the Artemisia family, according to plant classification. However, only *Artemisia annua* L. has a significant amount of artemisinin in it (Tu et al. 2009). Artemisinin was discovered as a pure medicine isolated from the plant *Artemisia annua* in the 1970s. Antimalarial medication artemisinin, sometimes referred to as qinghaosu, is extracted from the sweet wormwood plant. Purified from the dried leaves or flower clusters of *Artemisia annua*, artemisinin is a sesquiterpene lactone, or a chemical made up of three isoprene units bonded to cyclic organic esters (https://www.britannica.com). The active constituent was filtered in 1972 and given the names qinghaosu (essence of qinghao) and artemisinin, respectively (Meshnick, 2002).

All Plasmodium species, which cause malaria, have been shown to be effectively treated with artemisinin. The medication is very helpful in treating infections caused by multidrug-resistant *P. falciparum*, the deadliest of the malaria protozoans, and chloroquine-resistant parasites (https://www.britannica.com). The World Health Organisation (WHO) has officially approved artemisinin-based combination treatments as the first-line treatment for uncomplicated falciparum malaria in all locations where malaria is endemic (WHO, 2006). In China by the 1980s, derivatives of artemisinin were being used. As drug-resistant *Plasmodium falciparum* strains increased, particularly in Southeast Asia, Western interest in these drugs grew. Artemisinin derivatives were commonly utilised in Thailand, Burma, and Vietnam by the early 1990s (McIntosh and Olliaro, 1998). The morbidity and mortality caused by malaria have decreased as a result of replacing ineffective, failed medicines (chloroquine and sulfadoxine-pyrimethamine) with artemisinin-based combination therapy. For the fight against malaria worldwide, artemisinin resistance would be terrible (Ramani, 2016).

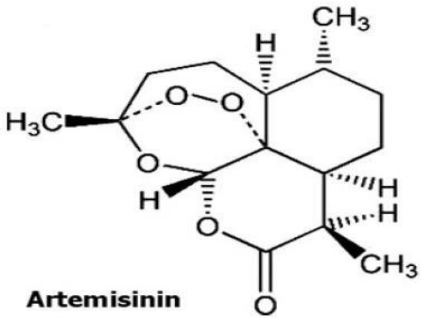

Fig 2: Chemical Structure of Artemisinin

The globe is using artemisinin and its derivatives more and more frequently since they represent a very significant new class of antimalarials. The most important artemisinin derivatives are artesunate, artemether, arteether, and dihydroartemisinin. Rapid action and eradication characterise the artemisinin derivatives. They are particularly efficient against malaria because of their quick onset (Meshnick, 2002). Initially, artemisinin and its derivatives were used as monotherapies, but it gradually became recognised that antimalarial medications, like those for tuberculosis and HIV, should be used in combination. A semi-synthetic artemisinin

derivative known as atelinate was developed, however it was never used for anything other than animal testing. A new artemisone is currently being developed.

In clinical testing, the structurally different peroxide known as artiflene proved to be a successful antimalarial, but because to high production costs and a lack of clear advantages over artemisinin derivatives, it was eventually abandoned (White, 2008).

Plasmodium organisms in the schizont stage of development are the focus of artemisinin. The parasite form that is transmitted to humans in the saliva of Anopheles mosquitoes, sporozoites, grow into schizonts, which contain hemozoin, an insoluble form of iron. As schizonts consume the haemoglobin found in the cytoplasm of human red blood cells, hemozoin is created within the schizonts. It is thought that the peroxide group in artemisinin combines with hemozoin to produce radicals that target the proteins in parasites and kill the organisms (https://www.britannica.com).

Most likely, artemisinin was given orally, intravenously, or as a suppository. Within hours of delivery, the medication reaches its peak plasma levels and begins to work swiftly, considerably lowering the parasite burden within the first few days of treatment. Among the drugs made from artemisinin, artesunate is distinctive. It enables the medication to start working right away. When cerebral malaria is neglected, it can quickly spread to the brain and result in death within 72 hours. Artesunate is used to treat this condition. According to Britannica, artemisinin appears to have little adverse effects in humans.

Chloroquine

Malaria caused by *Plasmodium falciparum* is a serious health issue, especially in sub-Saharan Africa. In the latter part of the 20th century, chloroquine was the antimalarial drug of choice since it was risk-free, inexpensive, and very effective against susceptible malaria parasites. Chloroquine is no longer often used as a treatment for falciparum malaria in Southeast Asia and South America since the advent of chloroquine resistance more than 40 years ago (Djimdé et al. 2001). Due to its great efficiency against all species of malaria parasites and its high tolerance, chloroquine was considered to be a close substitute for the perfect antimalarial medicine and was utilised for decades (Krettli et al. 2001). Escalating levels of chloroquine resistance are a factor in Africa's escalating malaria morbidity and fatality rates. Chloroquine continues to be the primary antimalarial medication in the majority of African nations due to the lack of accessible alternatives.

Chloroquine was the most significant of these medications and was widely utilised, especially starting in the 1940s (Yakoub et al. 1995). Chloroquine resistance slowly evolved with prolonged use. By the late 1950s,

sections of Southeast Asia and South America had *P. falciparum* resistant to chloroquine, and by the 1980s, this resistance had spread to practically all regions with falciparum malaria (Achan, 2011).

Despite this, chloroquine's widespread use and easy accessibility helped reduce the disease's morbidity and death, particularly in sub-Saharan African villages where almost every kid contracts the parasite every year. Because of chloroquine's remarkable success and extensive use over the years, the two parasite species that are most commonly responsible for human malaria infections, *Plasmodium falciparum* and *Plasmodium vivax*, have acquired chloroquine resistance (Wellems and Plowe, 2001).

The effectiveness of chloroquine is assumed to be due to its capacity to inhibit malaria parasites' hematin detoxification while they develop inside the red blood cells of their hosts (Chou, 1980; Dorn, 1998). As the parasite consumes and breaks down haemoglobin in its digestive food vacuole, a significant amount of hematin is expelled. According to Zhang et al. (1999), hematin is detoxified via polymerization into harmless crystals of the hemozoin pigment and maybe also by a glutathione-mediated process of destruction. Chloroquine interferes with detoxification and kills the parasite by binding with hematin in its -oxodimer form and adhering to the developing faces of the hemozoin crystals (Dorn et al. 1998; Sullivan et al. 1996; Pagola et al. 2000). According to Verdier et al. (1985), P. falciparum that is resistant to chloroquine lives by reducing the amount of drug accumulating in the digestive vacuole. The mechanism underlying this survival tactic is yet unknown.

Table 1: Information on anti-malarial plants, their families, used plant parts, IC_{50} Value, target organism from different countries with references

Country	**Family**	**Plant name**	**Used plant parts**	**IC_{50} value**	**Target organism**	**References**
Angola	Annonaceae	*Hexalobus crispiflous*	Stem bark	2.0 µg/mL	in vitro activity against *P. falciparm*	Boyom et al. 2003
		Pachypodantium confine	Stem bark	16.6 µg/mL		
	Euphorbiaceae	*Euphorbia hirata*	Whole plant	6 µg/mL	In vitro activity against *P. falciparm*	Tona et al., 2016
		Bridelia ferruginea	Bark	400 mg/kg	In vivo in mice *P. berghei*	Kolawole and Adesoye, 2010
Benin	Asteraceae	*Acanthospermum hispidum*	Aerial parts	7.5 µg/mL	Dichlorometh ane extracts In	Bero et al.,
	Rubiaceae	*Keetia leucantha*	Leaves	13.8 µg/mL		
			Twigs	11.3		

				µg/mL	vitro activity against *P. falciparum*	2009
	Polygalace ae	*Carpolobia lutea*	Aerial Parts	19.4 µg/mL		
	Loganiace ae	*Strychnos spinosa*	Leaves	15.6 µg/mL		
Burkina Faso	Asteraceae	*Dicoma tomentosa*	Whole plant	7.90 µg/mL	Dichlorometh ane extracts In vitro activity against *P. falciparum*	Jansen et al. 2010
	Clusiaceae	*Psorospermum senegalense*	Leaves	10.03 µg/mL		
	Rubiaceae	*Gardenia sokotensis*	Leaves	14.01 µg/mL		
	Euphorbia ceae	*Achromanes difformis*	Leaves	7.0 µg/mL	In vitro activity against *P. falciparum*	Bidla et al. 2004
	Cleomaceae	*Cleome rutidosperma*	Leaves	9.2 µg/mL		
Cameroon	Annonaceae	*Annona muricata*	Leaves	20 µg/mL	In vitro activity against *P. falciparu m*	Titanji et al., 2008
		Hexalobus crispiflorus	Essential oil	2 µg/mL	In vitro activity against *P. falciparum*	
	Apocynac eae	*Picralia nitida*	Roots	0.2 µg/mL	Dichlorometh ane extracts In vitro activity against *P. falciparum*	
			Stem bark	0.5 µg/mL		
			Fruit rind	1.5 µg/mL	Aqueous extracts. In vitro activity against *P. falciparum*	
	Euphorbia ceae	*Alchorn ea cordifol ia*	Leaves	0.2- 0.5 µg/mL	In vivo in mice *P. berghei*	
	Lamiaceae	*Holshund ia opposit e*	Root bark	5.6 µg/mL	Hexane extracts. In vitro activity against *P. falciparum*	
	Poaceae	*Cymbopog on citratus*	Leaves	6- 9.5 µg/mL	In vivo in mice *P. berghei*	

Ghana	Poaceae	*Bambusa vulgaris*	Leaves	0.49µg/mL	Ethyl acetate extracts In vitro activity against *P. falciparum*	Komlaga et al. 2016
	Phyllanthaceae	*Phyllanthus fraternus*	Whole plant	0.44 µg/mL	Methanol extracts In vitro activity against *P. falciparum*	
	Leguminosae	*Senna siamea*	Root	22.89 µg/mL		
	Lamiaceae	*Tectona grandis*	Leaves	0.92 µg/mL		
	Combretaceae	*Terminalia ivorensis*	Leaves	5.70 µg/mL		
India	Lamiaceae	*Ocimum sanctum*	Leave	35.58 µg/mL	Ethanol extracts In vitro activity against *P. falciparum*	Inbaneson et al. 2012
		Ocimum canum		53.50 µg/mL		
		Ocimum basilicum		43.81 µg/mL		
	Apocynaceae	*Catharanthus roseus*	Leaves	49.63 µg/mL	Ethanol extracts In vitro activity against *P. falciparum*	Ravikumar et al. 2012
		Thevetia peruviana	Seeds	58.83 µg/mL		
	Cucurbitaceae	*Coccinea grandis*	Leaves	69.00 µg/mL		
	Fabaceae	*Prosopis juliflora*	Leaves, bark and flower	>100 µg/mL		
		Acacia nilotica	Bark	59.80 µg/mL		
	Meliaceae	*Azadirachta indica*	Bark	29.77 µg/mL		
	Rubiaceae	*Morinda pubescns*	Leaves	62.70 µg/mL		
	Asteraceae	*Parthenium hysterophous*	Whole plant	6 µg/mL	Ethanol extracts In vitro activity against *P.falciparm*	Singh et al. 2014
	Apocynaceae	*Holarrhena pubescens*	Leaves	7 µg/mL		
	Myrtaceae	*Corymbia citriodora*	Leaves	5 µg/mL		
	Annonaceae	*Annona squamosa*	Leaves	2.1µg/mL		
		Wrightia arborea	Leaves	25		

	Apocynaceae			µg/mL	In vitro activity against *P. falciparum*	Simonsen et al. 2001
	Boraginaceae	*Heliotropium europaeum*	Root	43 µg/mL		
			Stem	35 µg/mL		
	Flacourtiaceae	*Casearia elliptica*	Leaves	9 µg/mL		
	Lythraceae	*Ammannia multiflora*	Root	18 µg/mL		
	Mimosaceae	*Prosopis juliflora*	Fruit and Flower	24 µg/mL		
	Moraceae	*Ficus benghalesis*	Stem	26 µg/mL		
Kenya	Euphorbiaceae	*Phyllanthus reticulats*	Leaves	10.0 µg/mL	In vitro activity against *P. falciparum*	Omulokoli et al. 1997
		Suregada zanzibariesis		1.5 µg/mL		
	Rubiaceae	*Pentas longiflora*	Roots	20.0 µg/mL	Methanol extracts In vitro activity against *P. falciparum*	Wanyoie et al. 2004
	Amaranthaceae	*Cyathula polycephla*	Roots	47.2 µg/mL		
		Cyathula cylindrial	Leaves	49.0 µg/mL		
Mozambique	Euphorbiaceae	*Bridelia cathartca*	Roots, stem	0.05 µg/mL	Ethanol and aqueous extract In vitro activity against *P. falciparum*	Silva et al. 2011
	Cucurbitaceae	*Momordica balsamina*	Aerial parts	4.6 µM	In vitro activity against *P. falciparum*	
	Fabaceae	*Senna occidentais*	Leaves	19.3 µg/mL	Hexane extract In vitro activity against *P. falciparum*	
		Senna abbreviata	Leaves	111.0 mg/kg/ wt	In vivo in mice *P. berghei*	
	Rubiaceae	*Crossopteryx*	Stem bark	>10 µg/mL	Methanol	

		febrifuga			extract In vitro activity against *P. falciparum*	
Peru	Menispermaca e	*Abuta rufescens*	Bark	2.3 µg/mL	Dichloromet h ane extract In vitro activity against *P. falciparum*	Roumy et al. 2007
			Leaves	7.9 µg/mL		
	Solanaceae	*Cyphomandra hartwegii*	Leaves	10.0 µg/mL		
	Lacistemaceae	*Lacistema aggregatm*	Bark	7.4 µg/mL		
Sierra Leone	Menispermace ae	*Triclisia patens*	Woodand bark	8 µg/mL	Ethanol extracts In vitro activity against *P. falciparum*	Marsha ll et al. 1990
	Apocynaceae	*Landolphia dulcis*	Wood	31 µg/mL		
	Annonaceae	*Xylopia aethiopca*	Wood	31 µg/mL		
	Amaranthaceae	*Cyathula prostrata*	Leaves	50 µg/mL		
São Tomé and Príncipe	Asteraceae	*Ageratum conyzoides*	Aerial parts and leaves	55 µg/mL	Dichlorometh ane fraction In vitro activity against *P. falciparum*	Silva et al. 2011
		Struchium sparganophorm	Leaves	< 10 µg/mL	Petroleum ether fraction In vitro activity against *P. falciparum*	
		Tithonia diversifolia	Aerial parts	15 µg/mL	Ethanol extract In vitro activity against *P. falciparum*	
	Meliaceae	*Cedrela odorata*	Wood, leavs, stem barks	1.37 µg/mL	Ethanol extract In vitro activity against *P. falciparm*	
	Solanaceae	*Cestrum laevigatum*	Leaves	50 µg/mL	Dichlorometh ane fraction In vitro activity against *P. falciparum*	

Uganda	Asteraceae	*Microglossa pyrifolia*	Leaves	1.24 µg/mL	Ethyl acetate extract against *P. falciparum*	Adia et al. 2015
	Lamiaceae	*Clerodendrm rotundifolium*	Leaves	1.98 µg/mL	Aqueous extract against *P. falciparum*	
Yamen	Euphorbiaceae	*Acalypha fruticosa*	Leaves	1.6 µg/mL	Aqueous extract against *P. falciparum*	Alshawsh et al. 2009
	Meliaceae	*Azadirachta indica*	Leaves	2.0 µg/mL		
	Cucurbitaceae	*Dendrosicyos socotrana*	Leaves	2.3 µg/mL		
	Burseraceae	*Boswellia elongate*	Bark	26.7 µg/mL	Methanol extract against *P. falciparum*	

Conclusion

The worrisome rise in drug resistance, the prevalence of malaria, and the scarcity of current effective treatments make this a serious global public health issue. One potential source for such affordable medicines is the use of traditional herbal remedies. Traditional herbal medicines have been used by humans for thousands of years. The effectiveness of two key plant-derived chemicals, quinine and artemisinin, in treating malaria has prompted scientists to look for additional plant-based antimalarial medications. For many decades, traditional antimalarial phytotherapy has been derived from more than 1000 plant species. Researchers have been looking for novel plants that are effective against the malarial parasite in many nations. We employ a variety of plant parts, including leaves, roots, stems, bark, flowers, fruits, and aerial parts. It has occasionally been used to combine two or more plants from different families. Different plant components extracts are employed to create herbal malaria treatments that are more inexpensive, safe, and effective than any chemical product in different nations. Herbal medicines are preferable than synthetic ones in terms of the adverse effects they can cause when used to treat human illnesses. Further study of the medicinal plants covered in this review may result in the creation of novel medications and improved malaria treatment strategies.

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