

EXPLORING THE ANTIMALARIAL POTENTIAL OF MEDICINAL PLANTS: A COMPREHENSIVE REVIEW OF IN-VIVO AND IN-VITRO STUDIES

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Abstract

Background: Malaria is a fatal disease caused by Plasmodium parasites infects millions of people each year Worldwide specifically in tropical and subtropical regions. Despite global control efforts limited access to healthcare persist. **Objectives:** The main aim was to summarize and evaluate antimalarial potential of various plant extracts and their therapeutic potential against Malaria. **Methods:** Databases such as Google Scholar, PubMed, Web of science core collection, Scopus and Scientific Electronic Library Online (SciELO) were thoroughly searched for studies on antimalarial herbs. Keywords such as "medicinal plants," "antimalarial activity," and "ethnomedicine" were used to retrieve specific information. Relevant information like Plant species, parts used, extraction method, solvents used, efficacy, and toxicity were extracted from peer-reviewed papers. **Results:** This study summarizes the antiplasmodial potential of 50 plant families and 124 individual plants through both in-vivo and in-vitro evaluations. Prominent families like Asteraceae, Euphorbiaceae, and Rubiaceae demonstrated the highest antiplasmodial activity. In-vivo, Bidens pilosa achieved 100% suppression, while Euphorbia abyssinica and Strychnos mitis showed significant suppression rates of 93.69% and 95.5%, respectively. Leaves showed the highest recovery, with plants like N sativa and S mitis emphasizing their importance in in-vivo studies. In vitro, Asteraceae, Annonaceae, and Euphorbiaceae stood out, with Annona muricata and Artemisia roxburghiana also exhibited notable IC₅₀ values of 12.2 µg/mL and 0.42 µg/mL respectively, reinforcing their potential for further investigation. The dominance of leaves as the primary plant part used for extraction further highlighted their high recovery rates and broad activity spectrum across both study types. **Conclusion:** This review study emphasizes the potential of medicinal plants as a vital source of antimalarial drugs, citing promising efficacy and safety findings in both traditional and scientific studies. These findings highlight the need for additional research to identify bioactive chemicals and development of low-cost, plant-based treatments for malaria Treatment around the world.

INTRODUCTION

Malaria remains a major global health threat, particularly in underdeveloped countries where it causes high morbidity and mortality. The infection spreads by the bites of infected female *Anopheles* mosquitos and primarily caused by a protozoan parasite that infects red blood cells (RBCs) and liver cells (hepatocytes) (Fikadu & Ashenafi, 2023). This parasite infects humans through several species, including *Plasmodium falciparum*, *Plasmodium ovale*, *Plasmodium vivax*, *Plasmodium malariae*, and *Plasmodium knowlesi*. Malaria is notorious for its extensive influence on human populations, resulting in significant health costs in impacted areas (Oriero et al., 2021).

In 2017, malaria infected an estimated 219 million people and killed 435,000 people worldwide. Worldwide, the mortality rate of malaria ranges from 0.3% to 2.2%, and in tropical areas, the rate can reach up to 30% in cases of severe malaria endemic (Talapko et al., 2019). In 2020, it was predicted that malaria causes 241 million medical incidents and cause around 627,000 fatalities (Patel et al., 2024). In 2021, there were over 247 million cases of malaria globally, resulting in 619 thousand casualties. *Plasmodium falciparum* and *Plasmodium vivax* are the species responsible for the highest rates of mortality and morbidity, respectively, among those that cause malaria in humans. (Cerilo-Filho et al., 2024). According to the World Malaria Report for 2021, over half of the world's population resides in 87 countries and areas at risk of malaria transmission. All these studies show the gradual increase in malaria cases throughout the years worldwide.

Environmental factors like rainfall, climate, topography, humidity and people's socioeconomic status have great impact on malaria growth and transmission. As a result, tropical countries with warm climate, heavy rainfall, and high humidity, such as Ethiopia and Indian subcontinent are ideal for mosquito growth (Dabaro et al., 2021).

Several antimalarial medicines have lost potency due to the development of resistance in parasite specifically in *Plasmodium falciparum*, hindering

malaria treatment efforts. Chloroquine, previously a key component of malaria treatment, is now mostly useless in many areas due to mutations in the PfCRT transporter, which prevent the medication from accumulating in the parasite's digestive vacuole and disrupting its capacity to detoxify heme (Ross & Fidock, 2019),(Martin et al., 2009) . Similarly, amodiaquine has encountered resistance due to PfCRT mutations, and its efficacy varies geographically (Foguim et al., 2020). Piperaquine, which is frequently used in combination with artemisinin derivatives, has also developed resistance, mainly in Southeast Asia, due to changes in drug transport pathways (Blasco et al., 2017) (Tang et al., 2020). Mefloquine and lumefantrine, both heme detoxification drugs, have developed resistance due to changes in the PfMDR1 transporter, which reduces their efficacy (Tang et al., 2020) (Windle et al., 2020).

According to initial findings, the combinations of DHA + piperaquine + mefloquine and artemether + lumefantrine + amodiaquine show promise in delaying the emergence of artemisinin resistance or restoring antimalarial sensitivity in previously artemisinin-resistant regions (van Der Pluijm et al., 2020).

Furthermore, mutations in the DHPS and DHFR genes have reduced the efficacy of the sulfadoxine-pyrimethamine combination, which targets the folate production pathway (Chaturvedi et al., 2021) (Bazie et al., 2020). Finally, mutations in the cytochrome b gene cause resistance to atovaquone, which inhibits mitochondrial activity (Massamba et al., 2020); nevertheless, these resistant parasites may be less transmissible. The evolution of resistance to these medications emphasizes the critical need for continued surveillance and the development of new antimalarial agents with unique modes of action to successfully combat malaria. plant based medicines are proven to be very effective in disease control.

Throughout human history, plant-based remedies have played a critical role in healthcare practices, serving as the principal source of medicine for centuries. Ancient civilizations relied on the

healing properties of plants to treat diseases and maintain health, with their knowledge often passed down through generations. Traditional systems of treatment, such as Ayurveda and Traditional Chinese Medicine (TCM), continue to represent this reliance on plant-based remedies (Elendu, 2024). These systems emphasize a general approach, integrating plant-derived compounds to restore balance and treat a wide range of diseases. Despite advances in synthetic pharmaceuticals, plant-based treatments remain highly applicable, contributing to modern drug discovery and establishing the foundation of traditional practices that persist in various cultures today. This dependence highlights the value of plants as an essential resource of medicine for human health and well-being (Chaachouay & Zidane, 2024).

The current article contained data from diverse studies worldwide, summarizing the antimalarial efficacy of plant extracts, and highlight Global relevance of traditional medicine against strains of *Plasmodium* species, specifically including *P. berghei* and *P. falciparum*.

MATERIAL AND METHOD

Literature Search Literature was Searched about antimalarial potential of plant extracts, specifically in relation to their efficacy against *Plasmodium berghei* and other strains. Databases like PubMed, Scopus, Web of Science (WoS),

Scientific Electronic Library Online (SciELO) and Google Scholar were utilized. The following keywords were used in search process: “antimalarial activity,” “ethnomedicines,” “plant-based medicines,” “plant extract” “*Plasmodium berghei*,” and “antiplasmodial.” Articles published 2010-2024 were included to ensure up-to-date insights.

Inclusion Exclusion criteria

Studies that focus on plant extracts or compounds evaluated for their antimalarial efficacy through in vitro, and in vivo were included. Experimental data, research without any major findings, and studies not available in English were Excluded. Relevant articles were screened through titles and abstracts, followed by a full-text study. Bibliographies of selected articles were also examined for additional sources.

Data Extraction

Collected data, including anti-malarial efficacy, preparation methods, and phytochemical compositions. Experimental methods such as IC₅₀ and LD₅₀ determination, animal model studies using *P. berghei* or other strains, and histopathological analyses were emphasized. Data extraction included details on plant species and family, plant parts used, extraction methods, active compounds and dosages.

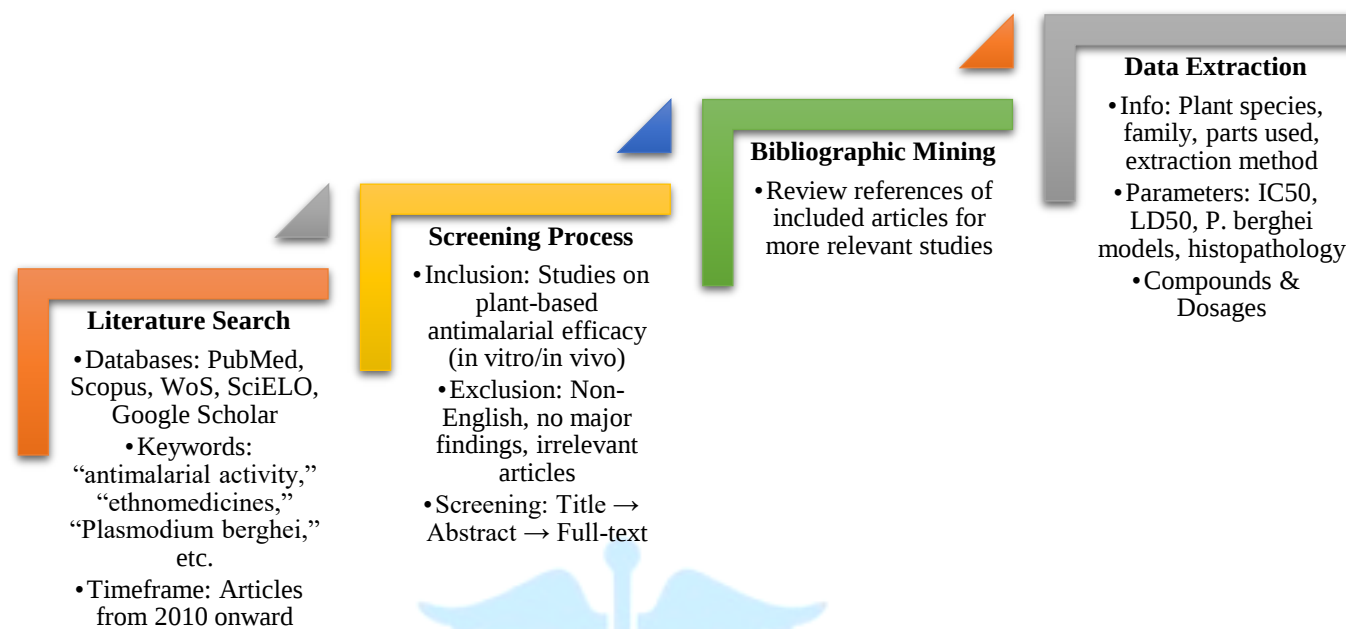


Figure 1 Flowchart for Methodology

RESULTS AND DISCUSSION

Medicinal Plants and Their Antimalarial Potential:

It has long been known that medicinal plants are an important source of antimalarial drugs, especially in areas where drug resistance is becoming a major problem and malaria is still endemic in most parts of the worlds. In Ethiopia, several plants have demonstrated significant antimalarial properties. Among them, *A. remota* and *Ca. frutescens* were particularly effective, reducing parasitemia by 77.34% and 72.65% respectively, at an oral dose of 100 mg/kg, with a safe LD₅₀ of over 2000 mg/kg. *Aloe macrocarpa* latex was even more potent, achieving a 100% reduction in parasitemia at a dose of 400 mg/kg in *P. berghei*-infected mice, with an LD₅₀ also exceeding 2000 mg/kg (Nigussie & Wale, 2022). In India, neem (*Azadirachta indica*) leaf extracts displayed strong antiplasmodial effects by significantly reducing parasitemia and preventing hypoxia in *P. berghei*-infected mice (Atawodi & Atawodi, 2009). Similarly, *Ocimum sanctum* (holy basil) water-soluble extracts reduced parasitemia to 2.80% in treated mice, compared to 25.2% in

control groups, demonstrating promising antimalarial activity (Shivaprasad et al., 2023).

The research identifies the antimalarial activity of different plant extracts, with their ranking according to their suppression activity (Table 1). *Bidens pilosa* (Asteraceae) leaf crude extract and ethyl acetate fraction had the highest suppression at 100%, with complete inhibition at 500 mg/kg and 125 mg/kg, respectively, against *Plasmodium berghei* ANKA, though its toxicity is yet to be determined (Nadia et al., 2020). *Azadirachta indica* (Caricaceae) leaf extract in 96% ethanol also exhibited 100% suppression at 600 mg/kg, with a safety margin of 800 mg/kg, against *P. berghei* NK65 (Afolabi et al., 2021). *Strychnos mitis* leaf aqueous extract and hydroalcoholic fraction exhibited 95.5% and 93.97% suppression, respectively, at 600 mg/kg, with a good safety margin of up to 2000 mg/kg against *P. berghei* ANKA (Fentahun et al., 2017). *Nigella sativa* (Ranunculaceae) seed methanol extract was 94% suppressed at 1250 mg/kg against *P. yoelii nigeriensis* (Okeola et al., 2011). Likewise, *Euphorbia abyssinica* (Euphorbiaceae) root extract in 80% methanol was 93.69% suppressed at 600

mg/kg with a high safety level of 2000 mg/kg against *P. berghei* ANKA (Muluye et al., 2019). *Clerodendrum violaceum* (Lamiaceae) leaf extract in absolute ethanol had 92.3% inhibition on day 14 after infection at a very low dose of 13 mg/kg against *P. berghei* NK65 (Balogun et al., 2009). Lastly, *Piliostigma thonningii* (Fabaceae) leaf ethanolic extract had 91.9% suppressive and 61.11% curative activities at 400 mg/kg, with an LD₅₀ of 3807.89 mg/kg, against *P. berghei* NK65 (Madara et al., 2010). These observations highlight the promise of natural plant-derived compounds, especially leaf, root, and seed extracts, for malaria treatment and necessitate further pharmacological and toxicological studies for their safe therapeutic uses.

The reviewed plants cover multiple families, with significant contributions from the Asteraceae, Euphorbiaceae, Caricaceae and Fabaceae families specifically (Table 1). The main reasons are that most of the medicinal plants belongs to these families and also due to their rich and diverse phytochemical compositions. Species from the Asteraceae family, for example, contain sesquiterpene lactones such as artemisinin and a variety of flavonoids that generate reactive oxygen species and inhibit essential parasite enzymes (Awuchi & Morya, 2023). Euphorbiaceae plants are rich in diterpenoids, alkaloids, and tannins, which disrupt parasitic membranes and interfere with critical protein functions (Benjamaa et al., 2022). In the Caricaceae family, the presence of alkaloids like carpaine and proteolytic enzymes such as papain contribute to parasite membrane disruption and enhance immune responses (Babalola et al., 2024). Similarly, members of the Fabaceae family produce isoflavonoids, lectins, and saponins that inhibit parasite DNA replication enzymes, induce membrane lysis, and stimulate host immunity (Usman et al., 2022). These phytochemical characteristics collectively explain the high representation and effectiveness of these families in antiplasmodial research.

Plant Parts, Solvents & Dosage Variations:

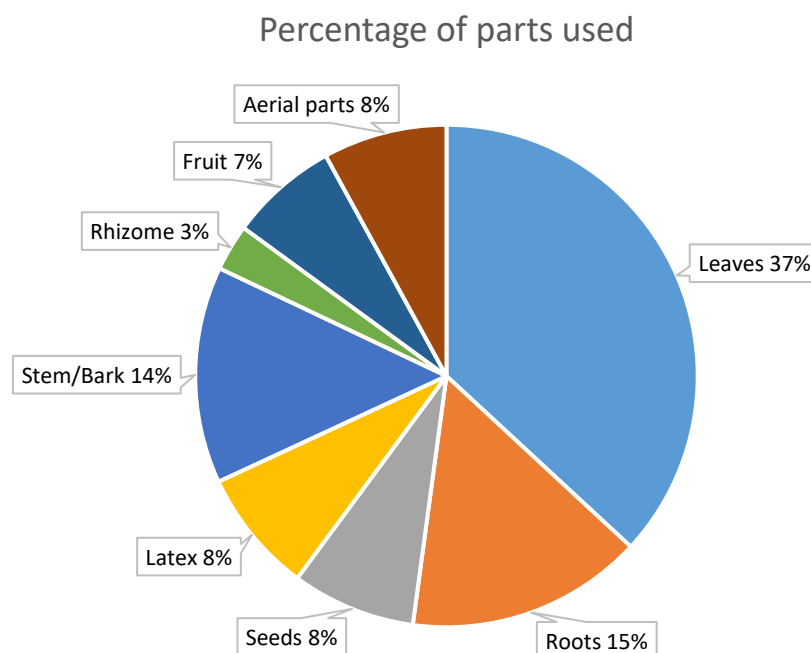
The effectiveness of therapeutic plants for antimalarial purposes depends on the plant parts being used and extraction methods and the dosage administered. On average, leaves account for about 37% of the plant materials used, attributed to their high concentration of bioactive compounds and easy accessibility., followed by roots which are 15% and seeds cover 8%. Latex is used in about 8% of cases, rhizome is 3%, while aerial parts such as stem and bark contribute 14%. Other components, including fruits and rinds, are used in roughly 7% of the cases (Figure 1). This distribution reflects the varying roles of different plant components in medicinal practices.

Extraction methods play a pivotal role in isolating bioactive compounds responsible for antimalarial activity. Methanol and hydroethanolic solvents were the most frequently employed, ensuring efficient extraction of polar and semi-polar compounds.

Extracts prepared using different solvents, such as ethyl acetate, 96% ethanol, 80% methanol, chloroform, and aqueous solutions, showed suppression rates of 100%, 100%, 91%, 75.9%, 64.2%, and 38%, respectively.

In comparison, extracts from the fruit and root demonstrated notable differences. The 80% methanolic extract of the fruit shows suppression rates of 70% and 87%, while the root extract achieved slightly higher suppression rates of 75% and 89%. These results at dosages of 400 mg/kg and 600 mg/kg suggest that the recovery rate is influenced by the plant parts being used, with the root extract generally demonstrating higher efficacy than the fruit and leaf extracts. Additionally, the choice of solvent also plays a significant role, as methanol-based extract consistently yielded higher suppression rates. The study emphasizes that optimizing the plant part, solvent, and dosage is essential for maximizing the therapeutic potential.

These findings support the continued searching of various plants and plant parts for their therapeutic potential

Figure 2 Plant Parts Used in Antimalarial Studies**Toxicity profiles & Bioactive compounds:**

Safety is a vital aspect of developing plant-based remedies. The reviewed studies indicate encouraging toxicity results for most plant extracts, with LD₅₀ values usually exceeding 2000 mg/kg. For example, *Nigella sativa* seeds, *Strychnos mitis* leaf, *Euphorbia abyssinica* roots, and *Piliostigma thonningii* leaf demonstrated an LD₅₀ of 1250 mg/kg, 2000mg/kg, 3807.89 mg/kg respectively. while achieving 94%, 95%,93.7%, 91.9% suppression.

Numerous bioactive compounds were identified as major contributors to the antimalarial effects of the reviewed plants. For instance, anthraquinones, flavonoids, and alkaloids isolated from *Aloe debrana*, *Ajuga remota*, and *Sida acuta* exhibited potent suppression of parasitemia. Compounds like Aloinoside and Pinocembrin were particularly effective, proving high activity at low concentrations. These findings support global efforts to isolate and characterize plant-derived compounds for therapeutic use.

Extraction process:

The extraction of bioactive compounds from plants typically involves various techniques depending on the plant material and intended application. Common techniques include cold percolation (Ravikumar et al., 2012), Soxhlet extraction method (Bagavan et al., 2011), and aqueous extraction (Somsak et al., 2016). Cold percolation uses solvents like ethanol to extract phytochemicals, while Soxhlet apparatus involves continuous solvent circulation for efficient extraction. Aqueous extractions, often employed for leaves, involve dispersing plant material in water followed by filtration and lyophilization. Some researchers also utilize natural sources like fruit juices or latex, such as collecting and drying leaf latex to obtain concentrated bioactive compounds (Igwenyi et al., 2024). These methods provide versatile approaches for preparing plant-based extracts for research purposes.

In vivo studies:

Most of the In-vivo studies (Table 01) were conducted using BALB/c mice infected with *Plasmodium berghei* to evaluate the antimalarial efficacy of the plant extracts. 4 day-Suppressive

tests were performed to determine the suppression of parasitemia as described in (Knight & Peters, 1980), while curative tests were conducted to assess the therapeutic potential of the substances following established protocols (Ryley & Peters, 1970). Acute toxicity was assessed by calculating the median lethal dose (LD₅₀) using the Lorke's method following the OCED guidelines (Guideline, 2001). Graded doses of the test substance were administered to groups of healthy mice, and mortality was observed over 24-48 hours to estimate the LD50 value. These in-vivo methods provided essential data on the safety and antiparasmodial efficacy of the tested plant extracts.

In vitro studies:

Most In-vitro studies (Table 02) described in this article assess the antiparasmodial efficacy of medicinal plant extracts employ a standard in vitro cultivation method for *Plasmodium falciparum* strains as described by (Trager & Jensen, 1976). CQ-resistant (3D7, Dd2 and INDO) strains are commonly used, maintained in O+ve human erythrocytes at 4-5% hematocrit in RPMI 1640 medium supplemented with 0.2% sodium bicarbonate, 0.5% Albumax (or 10% pooled human serum for INDO strain), 45 µg/L hypoxanthine, and 40-50 µg/L gentamicin. Cultures are incubated at 37°C-38°C under a gas mixture of 5% O₂, 5% CO₂, and 90% N₂, with daily medium replacement to propagate the culture. These standardized conditions ensure reproducibility and survival in evaluating the antimalarial activity of test substances (Bagavan et al., 2011; Ravikumar et al., 2012).

Future Perspectives:

The future perspectives emphasize the need to regulate extraction methods, identify active compounds, and understand their mechanisms of action for advancing plant-based malaria treatments. We can also study by combining these phytochemicals with existing antimalarial drugs such as chloroquine or artemisinin-based combination therapies (ACTs) could help overcome emerging drug resistance. Integrating traditional knowledge with modern

pharmacology can enhance the development of cost-effective therapies. This approach is particularly important for improving accessibility in resource-limited settings.

Table 1 Anti-malarial Activity (% Chemosuppression), Dosage, and Safety Profiles (LD₅₀) Across Strains (In-vivo studies).

Family	Plants	Plant part Used	Solvent	Max. Results (Suppression) %	Dosage(mg/kg)	Safe upto (mg/kg)	Strain	Referance
Acanthaceae	<i>Adhatoda schimperiana</i>	Roots	Hydroalcoholic crude extract	53.60%	600	2000	Pb	(Bobasa et al., 2018)
	<i>Acanthus polystachyus</i>	Leave	80% methanol	49.25%	400	2000	ANKA	(Kifle & Atnafie, 2020)
	<i>Acanthus polystachyus</i>	Root	80% methanol	51.48%	400	2000	ANKA	(Derebe & Wubetu, 2019)
Aloaceae	<i>Aloe pirottae</i>	Latex	80% methanol	47%	600	200	ANKA	(Dibessa et al., 2020)
	<i>Aloe citrina</i>	Leave latex	Latex extract,	60.59%	400	5000	ANKA	(B. Girma et al., 2015)
	<i>Aloe weloensis</i>	Leave latex	Leave latex extract	66.84%	400	2000	ANKA	(Teka et al., 2020)
	<i>Aloe percrassa</i>	Leave latex	Water extract,	73.60%	400	5000	ANKA	(Geremedhin et al., 2014)
	<i>Aloe megalacantha</i>	Leave	Leave latex extract	56.40%	400	2000	ANKA	(Hintsa et al., 2019)
Anacardiaceae	<i>Schinus molle</i>	Seed	Methanol crude	66.91%	400	2000	ANKA	(Habte et al., 2020)
Annonaceae	<i>Annona muricata</i>	Leaves	Aqous	85.61	1000	≥2500	ANKA	(Somsak et al., 2016)
Apiaceae	<i>Trachyspermum ammi</i>	Seed extracts	Aqous	68.76	500	LD ₅₀ =831	Pb	(Fatima et al., 2017)
Apocynaceae	<i>Alstonia boonei</i>	Leaves & Roots	Ethanol	69.23% & 67.39%	400	5000 (Atanu et al., 2021)	NK65	(Otuu et al., 2023)
Aristolochiaceae	<i>Aristolochia indica</i>	Leave	Methanol	72.00%	600	>600	NK65	(Gandhi et al., 2019)
Asclepiadaceae	<i>Periploca linearifolia</i>	Stem bark	80% Methanol	56.98%	600	2000	ANKA	(Belay et al., 2018)

Asphodelaceae	<i>Aloe otallensis</i>	Leave latex	Crude extract	60.70%	300	1500	Pb	(Paulos et al., 2011)
	<i>Kniphofia foliosa</i>	Rhizome	80% methanol	61.52%	400	2000	ANKA	(Alebachew et al., 2021)
	<i>aloe debrana</i>	Leaf latex/Aloin	Crude extract	75.0% / 78.31%	600 / 100	5000	ANKA	(Gemechu et al., 2014)
	<i>Aloe macrocarpa</i>	Leaf	Leaf exudate crude extract	74.30%	400	2000	ANKA	(Tewabe & Assefa, 2018)
Asteraceae	<i>Artemisia abyssinica</i>	Aerial part	80% methanol	82.40%	400	NE	Pb	(Adugna et al., 2014)
	<i>Artemisia annua</i>	Leaves	Aqueous extracts	>85%	400 (aqueous dry)	5000	NK65	(Apeh et al., 2024)
	<i>Echinops kebericho</i>	Roots	70% ethanol	57.29%	500	5000	ANKA	(Toma et al., 2015)
	<i>Vernonia adoensis</i>	Leaf	Methanol extract	83.36%	600	3000	ANKA	(Zemicheal & Mekonnen, 2018)
	<i>Bidens pilosa</i>	Leaves	Crude extract, and Ethyl acetate fraction	100% for both	Crude at 500 and fraction 12 at 125	NE	ANKA	(Nadia et al., 2020)
	<i>Sonchus arvensis</i>	Leaves	Ethyl acetate	77.48 %	200mg/kg	ED50 = 46.31	Pb	(Wahyuni et al., 2023)
Balanitaceae	<i>Balanites rotundifolia</i>	Leaf	80% methanol	67%	400	2000	ANKA	(Asrade et al., 2017)
Berberidaceae	<i>Berberis aristata</i>	Roots	Aqueous	67.3	350	5000	NK65	(Chandel et al., 2015)
Brassicaceae	<i>Brassica nigra</i>	Seed	80% methanol	53.13%	400	NE	ANKA	(Muluye et al., 2015)
Caricaceae	<i>Azadirachta indica</i>	Fruit juice	NA	highest at 8.6 ml/kg dose (almost = artesunate drug)	8.6 ml/Kg	NE	NK65	(Igwenyi et al., 2024)
	<i>Azadirachta indica</i>	Leaf	95% ethanol	69.60% on day 4th, 78.32% on day 6th	200	1000	NK65	(Oseni & Akwetey, 2012)

	<i>Azadirachta indica</i>	Leaf	Aqous	69.49% on day 4th, 77.41% on day 6th	200	1000	NK65	(Oseni & Akwetey, 2012)
	<i>Azadirachta indica</i>	Leaf	96% ethanol	100%	600	800	NK65	(Afolabi et al., 2021)
	<i>Carica papaya</i>	Fruit rind, and root	Petroleum ether & Chloroform extraction	fruit rind =61.78 (Petroleum ether), Root =48.11 Chloroform fraction	400	3000	ANKA	(Zelege et al., 2017)
Combretaceae	<i>Combretum molle</i>	Stem bark	80% methanol	59.7%	400	2000	Pb	(Mulaw et al., 2019)
	<i>Terminalia brownii</i>	Bark	Methanol crude extract	60.20%	400	2000	ANKA	(Biruk et al., 2020)
	<i>Combretum molle</i>	Seed	Methanol crude extract	63.50%	250	NE	ANKA	(Anato & Ketema, 2018)
Convolvulaceae	<i>Ipomoea pes-caprea</i> (L.)	Leaves and stems	Aqueous	50.89%	200	NE	NTA strain of Pb	(TIA et al., 2022)
Cucurbitaceae	<i>Zehennria scabra</i>	Leaf	80% methanolic	76.01%	400	2000	Pb	(Tesfaye & Alamneh, 2014)
Euphorbiaceae	<i>Croton macrostachyus</i>	Leaves	80% methanol/ chloroform/ methanol fraction/ aqueous	crude 91/75.9 /64.2/38 reps. & inhibition 83%, 82.3%	600	5000	ANKA	(Bantie et al., 2014)
	<i>Croton macrostachyus</i>	Fruit and root	80% methanol fruit extract and root extract	fruit extract 70% , 87% and root extract 75%, 89%	400 & 600	2000	ANKA	(Mekonnen, 2015)
	<i>Euphorbia abyssinica</i>	Roots	80% methanol	93.69%	600	2000	ANKA	(Muluye et al., 2019)
Fabaceae	<i>Cassia auriculata</i>	Leaf	Methanol	52.7	600	>600	NK65	(Gandhi et al., 2019)

	<i>Calpurnia aurea</i>	Leaves	Hydromethanolic	51.1%	60	>300	Pb	(Eyasu et al., 2013)
	<i>Piliostigma thonningii</i>	Leaves	Ethanolic	suppressive 91.9, curative 61.11%	400	LD ₅₀ 3807.89	NK65	(Madara et al., 2010)
	<i>Indigofera spicata</i>	Roots	80% methanol	53.42%	600	NE	ANKA	(Birru et al., 2017)
Lamiaceae	<i>Ajuga bracteosa</i>	Leaves	Ethanolic	86.6	1000	5000	NK65	(Chandel & Bagai, 2010)
	<i>Ajuga remota</i>	Leaves	Methanol	77.3%	100	2000	ANKA	(Nardos & Makonnen, 2017)
	<i>Clerodendrum violaceum</i>	Leaves	Absolute ethanol	92.3% on day 14 post-infection	13	NE	NK65	(Balogun et al., 2009)
	<i>Clerodendrum Myricoides</i>	Leaves	Methanol fraction and Ethyl acetate fraction	77.24%, 65.21%	300	NE	Pb	(Gebretsadik & Mekonnen, 2016)
	<i>Clerodendrum Myricoides</i>	Leaves	Methanol crude extract,	82.50%	600	3000	ANKA	(Deressa et al., 2010)
	<i>Strychnos mitis</i>	Leave	Aqueous extract and hydroalcoholic fraction	95.5% & 93.97%	600	2000	ANKA	(Fentahun et al., 2017)
Lythraceae	<i>Punica granatum</i>	Seed extracts	Aqous	77.58	500	LD ₅₀ = 1989	Pb	(Fatima et al., 2017)
Malvaceae.	<i>Sida acuta</i>	Leaf	Alkaloid, flavonoid and phenol	50.83%, 33.50% and 64.64% respectively	600	5000	NK65	(Adesina et al., 2020)
Menispermaceae	<i>Stephania abyssinica</i>	Leave	80% methanol crude extract, Ethyl acetate fraction, and Chloroform fraction	45.60% / 51.44% and 55.80%	400	NE	ANKA	(Zemene et al., 2020)

Moraceae	<i>Artocarpus communis</i>	Fruit peel	10% Ethanol	significant reduction based on histopathology study	300	NE	ANKA	(Wahyuwardani et al., 2023)
Oleaceae	<i>Olea europaea</i>	Stem bark	Methanol extract,	52.40%	400	2000	Pb	(Hailesilase et al., 2020)
Phyllanthaceae	<i>Bridelia ferruginea</i>	Stem bark	Aqueous	78.44	400	5000	Pb	(Mbah et al., 2012)
Piperaceae	<i>Piper capense</i>	Roots	Hydroalcoholic extract	48.6	600	2000	Pb	(Bobasa et al., 2018)
Ranunculaceae	<i>Nigella sativa</i>	Seeds	Methanol	94%	1250	NE	<i>P. yoelli nigeriensis</i>	(Okeola et al., 2011)
Rosaceae	<i>Hagenia abyssinica</i>	Stem bark	80% methanol	65.29%	100	2000	ANKA	(Belete & Orijino, 2019)
Rubiaceae	<i>Gardenia ternifolia</i>	Stem bark	Methanol crude	59.26%	600	2000	Pb	(Nureye et al., 2018)
Rutaceae	<i>Aegle marmelos</i>	Leaves	Methanol	67	600	ED ₅₀ = 284.73	NK65	(Gandhi et al., 2019)
	<i>Fagaropsis angolensis</i>	Stem bark	80% methanol	59.70%	600	2000	Anka	(Alemu & Misganaw, 2021)
Salvadoraceae	<i>Salvadora persica L.</i>	Leaves	Methanolic	50.6%	500	5000	Pb	(Gebrehiwot et al., 2019)
Santalaceae	<i>Osyris quadripartita</i>	Leaves	Aqueous, 98 % methanol and chloroform	21.67/ 24.4/ 41.26 % Resp.	600	600	ANKA	(S. Girma et al., 2015)
Sapindaceae	<i>Dodonaea angustifolia</i>	Root	N-butanol fraction of methanolic root extract	67.51%	600	2000	Pb	(Amelo et al., 2014)
	<i>Dodonea angustifolia</i>	Root	Methanol crude extract	84.52%	600	3000	ANKA	(Deressa et al., 2010)
	<i>Dodonaea angustifolia</i>	Leave	Acetate soluble portion of 80% aqueous MeOH	80.28%	150	NE	ANKA	(Melaku et al., 2017)

Saxifragaceae	<i>Bergenia ciliata</i>	Leaves	Ethanol	87.50%	1000	5000	NK65	(Walter et al., 2013)
Solanaceae	<i>Capsicum frutescens</i>	Fruit	80% methanolic crude fruit extract	72.65%	100	2000	Pb	(Habte & Assefa, 2020)
Zygophyllaceae	<i>Balanites rotundifolia</i>	Leave	Methanol extract	60.59%	500	5000	Pb	(Gebrehiwot et al., 2019)

NE: Not Evaluated, NA: Not Applicable

Table 2 Anti-malarial Activity (IC_{50}), Solvents, Strain and Plant Parts used (In-vitro studies).

Family	Plant Name	Plant part used	Solvent	IC_{50} (μ g/mL)	STRAIN	Reference
Acanthaceae	<i>Pseuderanthemum palatiferum</i>	Leaf	Ethanol	10.1	3D7	(Phan et al., 2003)
Amaranthaceae	<i>Achyranthes aspera</i>	Leaf	Ethyl acetate, methanol	>100	3D7/Dd2/Indo	(Bagavan et al., 2011)
Annonaceae	<i>Annona muricata</i> L	Leaf	Ethanol	12.2	3D7	(Moghadamtousi et al., 2015)
	<i>Annona squamosa</i>	Leaf	Ethyl acetate	33/20/18	3D7/Dd2/Indo	(Bagavan et al., 2011)
	–	–	Methanol	100/82/72	3D7/Dd2/Indo	(Bagavan et al., 2011)
	<i>Polyalthia longifolia</i>	Leaf	Aqueous	24	NF54	(Kwansa-Bentum et al., 2019)
	–	–	70% ethanol,	22.46	NF54	(Kwansa-Bentum et al., 2019)
	–	–	ethyl acetate	9.5	NF54	(Kwansa-Bentum et al., 2019)

	<i>Enantia polycarpa</i>	Stem bark	90% ethanol	0.126	Pf K1	(Atindehou et al., 2004)
	<i>Xylopi aromatic</i>	Aerial part	Ethanol	< 1	FcB2	(Garavito et al., 2006)
Apiaceae	<i>Centella asiatica</i>	Leaf	Ethyl acetate	>100	3D7/Dd2/Indo	(Bagavan et al., 2011)
	–	–	Methanol	>100	3D7/Dd2/Indo	(Bagavan et al., 2011)
Apocynaceae	<i>Catharanthus roseus L.</i>	Leaf/stem/flower	Ethanol	49.63/ 77.72/ 51.08	Pf	(Ravikumar et al., 2012)
	<i>Thevetia peruviana</i>	Leaf/seed	Ethanol	73.84/ 58.83	Pf	(Ravikumar et al., 2012)
Asteraceae	<i>Artemisia roxburghiana</i>	Leaves	Chloroform	0.42	Pf K1	(Dua et al., 2011)
	<i>Artemisia annua</i>	Leaves	Herbal tea extracts	1.11 (D10) and 0.88 (W2)	D10, W2	(De Donno et al., 2012)
Berberidaceae	<i>Berberis aristata</i>	Roots	aqous	67.9% at IC ₅₀ of 100	NK65	(Chandel et al., 2015)
Bromeliaceae	<i>Ananas comosus</i>	Fruit peel	Ethanol	104.1	3D7	(Pavan et al., 2012)
Celastraceae	<i>Catha edulis</i>	Roots and leaves	Cold dichloromethane	0.63 (roots) & 0.77(leaves)	D10	(Clarkson et al., 2004)
Colchicaceae	<i>Gloriosa superba</i>	Leaf	Ethyl acetate	73/77/32	3D7/Dd2/Indo	(Bagavan et al., 2011)
	–	–	Methanol	42/88/40	3D7/Dd2/Indo	(Bagavan et al., 2011)
Combretaceae	<i>Terminalia schimperiana</i>	young leaves	90% Ethanol	2.37	K1 Pf	(Atindehou et al., 2004)
Convolvulaceae	<i>Ipomoea pes-caprae</i>	Leaves	Methanol, Chloroform, Hexane, Ethyl Acetate, Aqueous	34.00, 125.33, >200, 69.67,46.33	3D7	(Pothula & Kanikaram, 2015)

	–	Stem	Methanol, Chloroform, Hexane, Ethyl Acetate, Aqueous	18.67, 23.00, 178.67, 48.67, 47.67	3D7	(Pothula & Kanikaram, 2015)
	–	Flower	Methanol, Chloroform, Hexane, Ethyl Acetate, Aqueous	42.0, 174.0, >200, 77.0, 55.67	3D7	(Pothula & Kanikaram, 2015)
	–	Root	Methanol, Chloroform, Hexane, Ethyl Acetate, Aqueous	15.00, >200, >200, 78.67, 42.33	3D7	(Pothula & Kanikaram, 2015)
Cucurbitaceae	<i>Coccinia grandis</i>	Leaf	Ethanol	69	Pf	(Ravikumar et al., 2012)
	<i>Mukia maderaspatensis</i>	Leaf	Ethyl acetate	100	3D7/Dd2/Indo	(Bagavan et al., 2011)
	–	–	Methanol	>100	3D7/Dd2/Indo	(Bagavan et al., 2011)
Euphorbiaceae	<i>Phyllanthus emblica</i>	Leaf	Ethyl acetate	7.25/15/9	3D7/Dd2/Indo	(Bagavan et al., 2011)
	–	–	Methanol	3.125/4.8/5	3D7/Dd2/Indo	(Bagavan et al., 2011)
Fabaceae	<i>Prosopis juliflora</i>	Leaf/bark/flower	Ethanol	> 100.00	Pf	(Ravikumar et al., 2012)
	<i>Acacia nilotica</i>	Leaf/ bark	Ethanol	73.36/ 59.80	Pf	(Ravikumar et al., 2012)
	<i>Abrus precatorius</i>	Seed	Ethyl acetate	34/43/35	3D7/Dd2/Indo	(Bagavan et al., 2011)
	–	–	Methanol	37/40/28	3D7/Dd2/Indo	(Bagavan et al., 2011)
	<i>Erythrina senegalensis</i>	Stem bark	90% ethanol	1.82	K1 Pf	(Atindehou et al., 2004)

Hypericaceae	<i>Harungana madagascariensis</i>	Stem bark	Ethanolic	0.052–0.517	Pf	(Iwalewa et al., 2008)
Loganiaceae	<i>Strychnos icaia</i>	Root bark	Methanolic	0.69 (3D7) and 0.42 (W2)	3D7, W2	(Lusakibanza et al., 2010)
Meliaceae	<i>Azadirachta indica</i>	Bark and Leaf	Ethanol	29.77/47.20	Pf	(Ravikumar et al., 2012)
	<i>Trichilia emetica</i>	Root bark	90% Ethanol	3.91	K1 Pf	(Atindehou et al., 2004)
	<i>Trichilia monadelpha</i>	stem bark	90% Ethanol	3.61	K1 Pf	(Atindehou et al., 2004)
Menispermaceae	<i>Arcangelisia flava</i> (L.) Merr	Stem bark	Methylene chloride	0.4	FcB1	(Nguyen-Pouplin et al., 2007)
	<i>Fibraurea tinctoria</i> Lour	Stem bark	Methylene chloride	0.5 ± 0.1	FcB1	(Nguyen-Pouplin et al., 2007)
	<i>Abuta grandifolia</i> (Mart.) Sandwith	Leaves	Alkaloid crude extract	< 1	FcB2	(Garavito et al., 2006)
Musaceae	<i>Musa sapientum</i> L	Ripe/raw fruit peel	Ethanol	2.2/3.5	3D7	(Waghmare & Kurhade, 2014)
	<i>Musa paradisiaca</i>	Flower	Ethyl acetate	75/100/>100	3D7/Dd2/Indo	(Bagavan et al., 2011)
	–	–	Methanol	>100	3D7/Dd2/Indo	(Bagavan et al., 2011)
Myrtaceae	<i>Syzygium aromaticum</i>	Flower bud	Ethyl acetate	13/20/10	3D7/Dd2/Indo	(Bagavan et al., 2011)
	–	–	Methanol	6.25/9.5/10	3D7/Dd2/Indo	(Bagavan et al., 2011)
Papaveraceae	<i>Meconopsis simplicifolia</i>	Aerial part	Chloroform	0.4	Pf TM4	(Wangchuk et al., 2011)

Piperaceae	<i>Piper holtonii</i> C. DC	Aerial part	Ethanolic	< 1	FcB2	(Garavito et al., 2006)
	<i>Piper cumanense</i> H.B. & K.	Leaves	Ethanolic	< 1	FcB2	(Garavito et al., 2006)
	<i>Pothomorphe umbellata</i>	Leaves	90% ethanol	3.74	K1 Pf	(Atindehou et al., 2004)
Poaceae	<i>Cynodon dactylon</i>	Leaf	Ethyl acetate	>100	3D7/Dd2/Indo	(Bagavan et al., 2011)
	–	–	Methanol	>100	3D7/Dd2/Indo	(Bagavan et al., 2011)
Punicaceae	<i>Punica granatum</i>	Fruit peel/ tree bark	Ethanol	2/7.4	3D7	(Shaygannia et al., 2016)
Rubiaceae	<i>Morinda pubescens</i>	Leaf/bark/flower	Ethanol	62.7/80.63	Pf	(Ravikumar et al., 2012)
	<i>Cinchona calisaya</i>	Stem bark	Decoction	0.21	Pf W2	(Bertania et al., 2005)
	<i>Nauclea latifolia</i>	Root	Infusion	0.9 (vs Nigerian) & 0.6 (vs FcB1)	Nigerian strain, FcB1/Colombia	(Benoit-Vical et al., 1998)
	<i>Morinda morindoides</i>	leaves	90% ethanol	3.54	K1 Pf	(Atindehou et al., 2004)
Salicaceae	<i>Casearia sylvestris</i> var. <i>lingua</i>	Stem bark	Hexane	0.9	FcB1/Colombia	(De Mesquita et al., 2007)
Sapindaceae	<i>Cupania vernalis</i>	Leaves	Hexane	0.9	FcB1/Colombia	(De Mesquita et al., 2007)
Simaroubaceae	<i>Quassia Africana</i>	Root	Dichloromethane	0.1	FcM29	(Mbatchi et al., 2006)
	<i>Brucea javanica</i> (L.) Merr	Root	Methylene chloride	0.1	FcB1	(Nguyen-Pouplin et al., 2007)
	<i>Simarouba glauca</i>	Cortex	Dichloromethane	0.195 (NF54), 0.184 (K1)	NF 54 & K1	(Mbatchi et al., 2006)

Stemonaceae	<i>Stemona tuberosa</i> Lour.	Roots	Ethanol	144.9	3D7	(Lin et al., 2008)
Zingiberaceae	<i>Kaempferia parviflora</i>	Rhizome	Ethanol	28.7	3D7	(Yenjai et al., 2004)

NE: Not Evaluated, NA: Not Applicable



CONCLUSION

Medicinal plants are cost-effective medicines for combating malaria, in resource-limited settings. Ethnobotanical studies have documented numerous species with significant antimalarial activity. Notably, *Bidens pilosa*, *Azadirachta indica*, and *Strychnos mitis* demonstrated parasitaemia suppression rates of 93–100% at doses of 500–600 mg/kg, with LD₅₀ values above 2000 mg/kg, indicating safety at therapeutic levels. *Calpurnia aurea* and *Clerodendrum violaceum* also showed strong efficacy at lower doses, though further toxicological evaluation is needed.

Despite these promising findings, many plant species remain underexplored. Continued research should be recommended for isolating bioactive compounds, evaluating safety profiles, and validating their potential in drug development. These efforts could support the development of accessible, plant-based antimalarials tailored to the needs of vulnerable populations.

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