Review Article

Exploring Antimalarial Herbal Plants across Communities in Uganda Based on Electronic Data

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Malaria is one of the most rampant diseases today not only in Uganda but also throughout Africa. Hence, it needs very close attention as it can be severe, causing many deaths, especially due to the rising prevalence of pathogenic resistance to current antimalarial drugs. The majority of the Ugandan population relies on traditional herbal medicines for various health issues. Thus, herein, we review various plant resources used to treat malaria across communities in Uganda so as to provide comprehensive and valuable ethnobotanical data about these plants. Approximately 182 plant species from 63 different plant families are used for malaria treatment across several communities in Uganda, of which 112 plant species have been investigated for antimalarial activities and 96% of the plant species showing positive results. Some plants showed very strong antimalarial activities and could be investigated further for the identification and validation of potentially therapeutic antimalarial compounds. There is no record of an investigation of antimalarial activity for approximately 39% of the plant species used for malaria treatment, yet these plants could be potential sources for potent antimalarial remedies. Thus, the review provides guidance for areas of further research on potential plant resources that could be sources of compounds with therapeutic properties for the treatment of malaria. Some of the plants were investigated for antimalarial activities, and their efficacy, toxicity, and safety aspects still need to be studied.

1. Introduction

Malaria, a dangerous and life-threatening disease caused by Plasmodium parasites is spread to humans through bites of infected female Anopheles mosquitoes [1]. It is one of the most widespread diseases today not only in Uganda but also throughout Africa. Hence, careful monitoring of malaria is required as the disease can be severe and can cause many deaths, especially due to the increasing prevalence of resistance to current antimalarial drugs. Among the five parasitic species that cause malaria to humans, Plasmodium falciparum and Plasmodium vivax are the deadliest [2, 3]. P. falciparum and P. vivax being the most prevalent malaria parasites in sub-Saharan Africa and regions of the Americas, respectively, were responsible for about 99.7% and 74.1% of malaria cases in 2017 [4]. In Southeast Asia, Plasmodium knowlesi is the most common cause of malaria, accounting for up to 70% of malaria cases, although it has been known to infect Old-World monkeys more [5]. Two other species of Plasmodium, Plasmodium malariae and Plasmodium ovale, generally cause mild fevers. Approximately 216 million malaria cases were registered in 2016, with a death toll of up to 445,000 [1]. According to the World Health Organization [6], the incidence of malaria in Uganda, at 47.8%, was the highest worldwide in 2005. According to Njoroge and Bussman [7], malaria is responsible for one to two million deaths annually in Africa. Typical symptoms of malaria include high fever, fatigue, headache, muscle ache, nausea, abdominal discomfort, and profuse sweating. However, in extreme cases and cases of prolonged illness without
treatment, brain tissue injury, pulmonary edema, kidney failure, severe anemia, yellow discoloration of the skin, and low blood sugar may be noted (Figure 1) [1, 2]. In Uganda, malaria is one of the major causes of illness and death [7]. Statistically, it accounts for 46% of children’s sicknesses, almost 40% of outpatient visits to hospitals and clinics, 25% of hospital admissions, 14% of inpatient deaths, and approximately 23% of infant mortalities [7].

In different parts of the world, the use of herbs and herbal extracts in the management and treatment of malaria is very common since herbs are cheap and readily available besides being effective. In fact, the use of herbal medicine for treatment worldwide is on the rise. Over 80% of the Ugandan population relies directly on herbal plants for their health care primarily [8]. A great majority of the population uses traditional herbal medicines because of their confirmed therapeutic value [8]. The increase in preference for herbal remedies coupled with resistance exhibited by pathogenic strains, including *Plasmodium* species, to the modern drugs available is the driving force behind researchers’ interest in herbal plants for possible alternatives for more effective antimalarial drugs [9, 10].

This review was aimed at providing comprehensive ethnobotanical information about various plant resources with antimalarial properties that are primarily used to manage and treat malaria across communities in Uganda, based on which further evaluation of these plants such as those of their efficacy and safety for the treatment of malaria may be based.

2. Methods and Materials

In the review, the data search processes employed by Komakech et al. [11] were modified to gather information on herbal plants for malaria treatment in Uganda from peer-reviewed articles in English published in scientific journals and other verifiable databases, with a focus on plant species and families, plant parts used, antimalarial activities of the extracts from herbal plants, and mechanisms of action of novel antimalarial phytochemicals and derivatives. Electronic literature databases such as PubMed, Medline, Scopus, SciFinder, Google Scholar, and Science Direct were carefully searched for suitable information. The following words were used as key search terms: (“Herbal medicine in Uganda” OR “Herbs in Uganda” OR “Traditional remedies in Uganda” OR “Antimalarial herbs in Uganda” OR “Antimalarial plants in Uganda” OR “Ugandan herbs” OR “Ugandan ethnomedicine” OR “Ugandan phytomedicine”), AND (“antiplasmodial activities” OR “anti-malarial activities” OR “anti-plasmodial effects” OR “anti-malarial effects” OR “malaria treatment” OR “malaria management”) OR (“Malaria in Uganda” AND “prevalence” OR “occurrence” OR “distribution” OR “herbal treatment” OR “herbal remedies” OR “phyto-medicine” OR “phyto remedy” OR “plant parts used for treatment”) OR (Phytochemicals for malaria treatment OR Artemisinins OR Quinine OR Noble anti-malarial compounds OR Plant derived anti-malarial compounds AND mechanisms of action OR modes of action) OR (“Malaria herbal medicine in Uganda” OR “Herbal medicine in Uganda” OR “Herbal malaria remedy in Uganda” OR “Natural malaria medicine in Uganda” OR “Traditional malaria herbal medicine” OR “Malaria herbal recipe” AND “dosage” OR “dose” OR “dose given” OR “mode of administration” OR “means of traditional extraction” OR “traditional extraction” OR “Toxicity” OR “Safety and toxicity” OR “Policy framework” OR “other ethno-pharmacological uses” OR “other ethno-pharmacological utilizations” OR “other ethno-medicinal uses”). The information gathered was verified separately for its reliability; any discrepancies discovered were resolved by discussions between the authors. Thereafter, these data were summarized and analyzed, and comparisons were made to draw conclusions.

3. Prevalence of Malaria

Malaria in Uganda is highly endemic because the climate is favorable for its consistently stable and year-round transmission in about 99% of the country, with the country’s entire population being at risk for contraction [12]. The most vulnerable groups of people at great risk for malaria are expectant mothers and young children under the age of 5 years [12]. The malarial parasite, *P. falciparum*, is most commonly the cause of malaria throughout Uganda, accounting for over 90% of malaria cases. However, Betson et al. [13] have warned of the potential for the emergence of infections due to *P. malariae* and *P. ovale* spp. as well, since there is much focus on countering *P. falciparum* infections. In 2016, Larocca et al. [14] indicated that Uganda was one of the leading countries in the world with malaria incidence rate as high as 478 cases per 1,000 population per year. Specifically, overall registered death cases caused by malaria in children were between 70,000 and 100,000 annually in Uganda [14]. Tremendous effort has been made to control malaria in Uganda by the government-headed Uganda Malaria Reduction Strategic Plan and Mass Action Against Malaria. These efforts have greatly reduced the malaria burden and incidence from 272 cases per 1000 population in 2016/17 to 191 cases per 1000 population in 2017/18 [12]. Although there has been a general reduction in the incidence of malaria, studies indicate that malaria prevalence along lakes, for example, Lake Victoria, and in remote areas of the country (villages) as well as areas closer to forests are much higher, with over 450 malaria cases per 1000 population (Figure 2) [12, 13, 15]. Communities around lakeshores in Uganda have always had high prevalence of malaria among children and especially the young ones despite routine treatments [12, 16]. Through the government initiative to control malaria, the prevalence in some districts remained as low as 4.3% in 2018 [12]. Malaria control strategies including indoor residual spraying along with house to house distribution of mosquito nets treated with insecticides resulted in a remarkable reduction in malaria burdens in many parts of the country [17]. Raouf et al. [18] observed that significant reductions in the levels of malaria in Uganda cannot be sustained if the current control measures are terminated.
4. Mechanisms of Actions of Novel Phytochemicals in Malaria Treatment

Herbal plants are extremely rich in phytochemicals that are highly efficacious in the treatment of malaria, such as sesquiterpenes and sesquiterpene lactones, fluoroquinolones, chalcones, flavanones, phenolics, quinones, coumarins, and alkaloids (Table 1) [35,36]. The herbal plants that are used as prophylactic measures to prevent malaria as well contain some of these compounds (Table 2). From these groups of compounds, active metabolites including quinine and artemisinin have been derived and the most successful antimalarial drugs to date have been obtained. Artemisinins from *Artemisia annua* a plant belonging to the family Asteraceae have actually been an integral part of the fight against malaria, with artemisinin-based combination therapy contributing enormously to modern day treatments [36]. They have been effective against all strains of *P. falciparum* including multi-drug-resistant ones [36,37].

The mechanism of action of artemisinin is widely debated but the most accepted theory is that of activation of the molecule by heme, which enables it to produce free radicals that then destroy the proteins needed for parasite survival [36]. The presence of an uncommon chemical peroxide linkage bridge in artemisinin, a sesquiterpene lactone, is the most probable reason for its antimalarial effects. Cleavage of the peroxide linkage bridge in the presence of iron (II) ions (from heme) forms very reactive free radicals that undergo rapid rearrangement to form more stable carbon-centered radicals, which chemically modify the parasite and inhibit various processes within the parasite molecules, resulting in its death [36]. Artemisinin acts on primarily the trophozoite parasitic phase and prevents disease progression. It kills circulating ring-stage parasites, thus increasing the therapeutic response [37]. Mok et al. [38] suggested that artemisinin is linked to the upregulation of unfolded protein response pathways, which leads to decreased parasitic growth and development. Shandilya et al. [39] suggested that artemisinin is activated by iron, which then functionally inhibits PfATP6, a calcium pump, by terminating phosphorylation, nucleotide binding, and actuator domains, eventually leading to a functional loss of PfATP6 of the *Plasmodium* parasite and its death. A study by Mbengue et al. [40] indicated that artemisinin strongly inhibits phosphoinositide-3-kinase (PfPI3K), an enzyme important in cellular activities including growth, multiplication, differentiation, and survival in *P. falciparum*.

Cinchona tree bark, from which quinine was isolated, has been used to treat malaria since 1632 [41]. The World Health Organization listed quinine as one of the important medicines needed in a health system [42]. It is however only used to treat malaria caused by chloroquine-resistant strain of *P. falciparum* in the absence of artemisinins [43]. A popular hypothesis about the mechanism of action of quinine is based on chloroquine, another quinoline drug which is closely linked to quinine and has been comprehensively
Quinine inhibits the pathway of biocrystallization of hemozoin, resulting in the accumulation of the free cytotoxic heme which eventually kills the parasite [44].

Most of the plants used in the treatment of malaria in Uganda contain alkaloids greatly implicated in antiplasmodial activity (Table 3). A number of alkaloids target apicoplast, an organelle in the *Plasmodium* parasite, while others such as benzylisoquinoline alkaloids in *Cissampelos mucronata*, a plant belonging to the family Menispermaceae inhibits protein synthesis in the parasite [99].

Flavonoids in a vast number of plants used for malaria treatment in Uganda are common to plants in the family Asteraceae such as *B. longipes*, *A. conyzoides*, and *A. africana* although other herbal plants from different families including *C. roseus* in Apocynaceae and *A. zygia* and *A. nilotica* in Mimosaceae also have them as active antiplasmodial constituents (Table 3). Flavonoids exhibit great antiplasmodial activity against different strains of the malaria parasite although the mechanism of antimalarial action is not clear [99]. Some studies suggest that flavonoids impede the influx of myoinositol and L-glutamine in erythrocytes that are infected [99]. Some flavonoids increase the level of oxidation of erythrocytes and inhibit protein synthesis in malaria parasites [99]. Furthermore, flavonoids are believed to inhibit fatty acid biosynthesis (FAS II) in *Plasmodium* [102].

Artemisinin resistance in *P. falciparum* has been reported in Vietnam, Cambodia, Muang Lao, and Thailand. A report published in 2018 showed over 30 separate cases in Southeast Asia of artemisinin resistance [36]. In case of resistance, parasitic clearance is slowed down and gametocytemia increases, resulting in greater selective pressure on other partner drugs to which resistance increases, thereby posing a great health threat. Thus, it is very important that the discovery of other drugs with novel mechanisms of action be prioritized by extensive exploration of the huge medicinal plant resources in Africa, which have been used by locals for effective malaria treatment yet have never been scientifically investigated for their antimalarial potential.

Amoa Onguéné et al. [35] emphasized that it was indeed Africa’s turn to offer a new antimalarial drug to humanity since artemisinin was discovered in Asia and quinine in Latin America.
| Plant family | Scientific name | Local name | Part used | Growth form | Mode of preparation | Dose and mode of administration for malaria | Status of antimalarial/antiplasmodial activity investigation | Other ailments treated | Reference(s) |
|-------------|----------------|------------|----------|-------------|---------------------|------------------------------------------|--------------------------------------------------|----------------------|-------------|
| Acanthaceae | Justicia betonica L. | Nalongo/quinine | Leaves/whole plant | Herb | Decoction | About 120ml every 8 hours for a week | Investigated | Diabetes, yellow fever, diarrhea | [10, 19] |
|             | Justicia amelliana (Nees) T. Anderson | Kwinini omuganda | Leaves/beig | Herb | Decoction | Orally taken, dose not specified | No record | | |
|             | Monocha subassassie C. B. Clarke | Erazzi | Leaves | Herb | Decoction | Orally taken, dose not specified | No record | Abdominal pain | [19] |
|             | Thunbergia alata Sim | Kasamunsi/meddle budo | Leaves/whole plant | Climber | Decoction | About 120ml every 8 hours for a week | No record | False teeth | [8, 10] |
| Alliaceae   | Allium cepa L. | Katungulu | Bulb | Herb | No record | | | | |
| Aloeaceae   | Aloe dawei (wild/cultivated) | Kigagi | Leaves | Herb | Decoction | A glassful once a day for 7 days | Investigated | | |
|             | Aloe kedongensis (wild) | Kigagi | Leaves | Herb | Decoction | Orally taken, dose not specified | No record | | |
|             | Aloe volkensii (cultivated) | Kigagi | Leaves | Herb | Decoction | Orally taken, dose not specified | No record | | |
|             | Aloe ferox Mill | Kigagi | Leaves | Herb | Decoction | Orally taken, dose not specified | Investigated | | |
|             | Aloe lateritica (wild) | Kigagi | Leaves/root | Herb | Decoction | Half glass every 24 hours for 7 days | No record | | [19] |
| Amaranthaceae | Amananthus hybridus L. | Bbwaga | Leaves | Herb | Decoction | About 120ml every 8 hours for a week | Investigated | False teeth | [8, 19] |
| Anacardiaceae | Mangifera indica L. | Muyembe gwakona | Leaves/bark | Tree | Decoction | 4 and 3 teaspoons after every 8 hours for adults and children, respectively, for a week | Investigated | Diarrhea, dysentery, body pain, venereal diseases, cough, syphilis | [10, 23] |
|             | Rhus natalensis Brenh. Ex Krauss | Omenoshite | Leaves | Shrub | Decoction | Orally taken, dose not specified | Investigated | | |
|             | Rhus vincana Meidler | Kalosobwosobwa/tebadda | Leaves | Shrub | Decoction | Half a glass every 8 hours for 7 days | No record | Skin rash, erectile dysfunction | [10] |
| Apioaceae   | Cenella asatica (L) Urb. | Kabo Kabakya/mbutumku | Leaves/whole plant | Herb | Decoction | 3 teaspoons thrice a day for 4 days | Investigated | | |
|             | Santania brevis De Wild. | Mubajjagabke | Bark | Tree | Decoction | Orally taken, dose not specified | No record | | |
|             | Carissa edulis (Forssk.) Vahl | Muyunza, ekamuriei | Roots | Herb | Decoction | Orally taken, dose not specified | Investigated | Epilepsy, fever, cough, syphilis, measles, dysentery | [21, 23] |
|             | Carissa spinarum Lodd. ex A. DC. | Omugulua | Roots | Herb | Decoction | About 120ml every 8 hours for a week | Investigated | | |
|             | Catharanthus roseus G. Don | Sikaigya | Leaves | Herb | Decoction | About 120ml once a day for a week | No record | | |
| Araceae     | Calatius ssp. Engl. | Ntangawuzi | Roots | Herb | Decoction | About 120ml once a day for a week | No record | | |
| Aristolochiaceae | Aristolochia elegans Mast. | Musu wa kila/ kakareso | Seeds/sap | Vine | Steeped in water and drunk | A glassful once a day | Investigated | Abdominal pain, East coast fever | [8, 19] |
|             | Aristolochia tomentosa Sims. | Kanikuku | Stem | Climber | Infusion | Oral, dose not specified | No record | Wounds, skin diseases, snake bites | [23] |
| Asclepiadaceae | Gomphocarpus physocarpus E. Mey. | Kalambo | Leaves | Herb | Decoction | Half a glass daily for a week | No record | | [10] |
| Asphodelaceae | Aloe vera (L.) Burm. f. | Kigagi/alovera | Leaves | Herb | Decoction | 1 teaspoon and 1 tablespoon 3 times a day for children and adults, respectively, for a week | Investigated | Stomach ache | [8, 25] |
| Plant family | Scientific name | Local name | Part used | Growth form | Mode of preparation | Dose and mode of administration for malaria | Status of antimalarial/antiplasmodial activity investigation | Other ailments treated | Reference(s) |
|--------------|-----------------|------------|-----------|-------------|---------------------|---------------------------------------------|-------------------------------------------------|------------------------|-------------|
| **Asteraceae** | | | | | | | | | |
| | Ageratum conyzoides L. | Namirembe | Whole plant/leaves | Herb | Decoction | A glassful thrice a day for 7 days | Investigated | Worms, weakness in pregnancy | [8, 10] |
| | Artemisia annua L. | Sweet anne | Leaves | Herb | Decoction | Oral, dose not specified | Investigated | Fever | [19] |
| | Artemisia afra Jacq. ex Willd | Pasile | Leaves | Herb | Infusion | Oral, dose not specified | Investigated | Fever | [10] |
| | Aspilia africana (Pers.) C. D. Adams | Maakayi, ekarwe | Whole plant/leaves/roots | Herb | Decoction | 8 teaspoons 3 times a day for week | Investigated | Abdominal aches, measles, diarrhea, wounds, induction of appetite | [10, 19] |
| | Baccharis raddoniensis (Sch. Bip. ex Walp.) H. Rob. | Okellokello | Leaves | Shrub | Decoction | Half a glass thrice a day for week | Investigated | Flu, skin rash, ear infections | [25, 26] |
| | Bidens grantii Sherff | Ebongwa | Leaves, flower | Herb | Decoction | Oral, dose not specified | No record | Pregnancy disorders, prehepatic jaundice | [19] |
| | Bidens pilosa L. | Sere/labika | Whole plant/leaves | Herb | Decoction | About 120 ml once a day for a week | No record | Headache | [10] |
| | Conyza bonariensis (L.) Ndasha | Ekstromana | Leaves | Herb | Decoction | Oral, dose not specified | No record | Headache | [10] |
| | Conyza floribunda H. B. K. Walker | Makalume | Leaves | Herb | Decoction | About 120 ml once a day for a week | No record | Headache | [10] |
| | Conyza sumatrensis (Retz.) E. H. Walker | Kati kati | Leaves | Herb | Decoction | Oral, dose not specified | No record | Headache | [10] |
| | Crasepappus vitellinum Kitonto | Kafugankande | Whole plant/leaves/roots | Herb | Decoction | 2 teaspoons thrice a day for 7 days | Investigated | Cough, abdominal disorders, chest pain | [10, 19, 28] |
| | Emilia javanica (Burm. F.) C. B. Rob. | Nakate | Whole plant | Herb | Decoction | Half a glass once a day for a week | No record | Cough, abdominal disorders, chest pain | [10] |
| | Guzotia saxosa Chaov | Ekstromana | Leaves | Herb | Decoction | Oral, dose not specified | Investigated | Stomach ache, HIV/AIDS opportunistic infections | [19] |
| | Gynura scandens O. Hoffm. | Ekiyogayama | Leaves | Herb | Decoction | Oral, dose not specified | No record | Febrile convulsions | [19] |
| | Miconia scandens (Schumach. & Thonn.) Roberty | Maakayi | Leaves | Herb | Decoction | Oral, dose not specified | No record | Stomach ache, body odour, yellow fever | [8] |
| | Neomarica pyrifolia (Lam.) O. Ktze | Kafugankande | Whole plant/leaves/roots | Herb | Decoction | Half a glass thrice a day for a week | Investigated | Cough, abdominal disorders, chest pain | [10, 19, 28] |
| | Schkuhria pinnata (Lam.) | Apunait | Leaves | Herb | Infusion | 1 teaspoon and 1 tablespoon 3 times a day for children and adults, respectively, for a week | Investigated | Wounds, skin diseases, diabetes, ear infections, wounds | [23, 25] |
| | Sigebeckia orientalis L. | Kyariabo | Roots | Herb | Decoction | Oral, dose not specified | Investigated | Wounds, stomach ache | [19] |
| | Solanaceae | Omasunamwe | Leaves | Herb | Decoction | Oral, dose not specified | Investigated | Fever, indigestion | [19] |
| | Tygges minuta L. | Kinsigha | Whole plant/leaves | Herb | Decoction | Half a glass thrice a day for a week | Investigated | Stomach ache, scars, anemia, diabetes | [8, 19] |
| | Tithonia diversifolia A. Gray | Kyansiga | Leaves | Herb | Decoction | Half a glass thrice a day for a week | Investigated | Flu, headache, convulsions | [10] |
| | Vernonia adonis Sch. Bip. ex Walp. | Nyakumama | Leaves/flowers | Herb | Decoction | Oral, dose not specified | Investigated | Diabetes, abdominal pain | [10, 19, 25] |
| | Vernonia amygdalina Delile | Muluhaka/ibwori | Whole plant/roots | Shrub | Decoction | Half a glass 2 times a day for 5 days | Investigated | Diarrhea, dizziness | [19] |
| | Vernonia cinerea (L.) Less. | Kayayana | Bark | Tree | Decoction | Half a glass thrice a day for a week | Investigated | Diarrhea, dizziness | [19] |
| | Vernonia lasiopus O. Hoffm. | Kafugankande | Roots/leaves | Shrub | Fresh leaf extract/root decoction | 2 teaspoons thrice a day for 7 days | Investigated | Headache, stomach ache, burns, blisters | [8, 10, 19, 20] |
| | Markhamia lutea (Benth.) K. Schum. | Musambwa/munanganda | Roots | Tree | Decoction | A glassful once a day for 7 days | Investigated | Cough, headache, convulsions | [8, 10, 19] |
| | Spathodea campanulata Buch.-Harm. ex DC. | Kifabakazi | Bark | Tree | Decoction | Half a glass 3 times a day for 5 days | Investigated | Increased vaginal fluid, skin infection, infertility, herna | [8, 10] |
| Plant family          | Scientific name                          | Local name        | Part used       | Growth form | Mode of preparation | Dose and mode of administration for malaria | Status of antimalarial/antiplasmodial activity investigation | Other ailments treated                                           | Reference(s) |
|----------------------|------------------------------------------|-------------------|-----------------|-------------|--------------------|---------------------------------------------|-------------------------------------------------------------|------------------------------------------------------------|--------------|
| Caesalpinaceae       | Cassia didymobotrya Fres.                | Mukyula           | Leaves          | Shrub       | Decoction          | About 120 ml every 8 hours for a week       | Investigated                                               | Labour induction, hypertension, retained placenta             | [10]          |
| Caesalpinaceae       | Chamaecrista nigricans Greene            | Epoduru lo didi   | Leaves          | Herb        | Infusion           | Oral, dose not specified                    | No record                                                  | Labour induction, hypertension                               | [23]          |
| Caesalpinaceae       | Erythrophleum pyrifolia                  | Omurama           | Leaves/roots    | Herb        | Infusion           | Oral, dose not specified                    | Investigated                                               | Labour induction                                           | [24]          |
| Caesalpinaceae       | Senecio spectabilis (DC.) H. Irwin & Barneby | Gacinya          | Leaves          | Tree        | Decoction          | Half a glass twice a day for 5 days         | Investigated                                               | Labour induction                                           | [10]          |
| Gaesaliaceae         | Cassia hirsuta                          | Kasagakansansi    | Roots           | Herb        | Infusion           | Oral, dose not specified                    | Investigated                                               | Labour induction, hypertension                               | [10]          |
| Canelliaceae         | Warbugia ugandensis Sprague              | Omukunanume       | Bark/leaves     | Tree        | Decoction/powder   | Half a glass once a day for a week          | Investigated                                               | Toothache, flu, skin diseases, asthma, stomach ache, body and | [10, 20, 27]  |
| Ceratopogonaceae     | Ceratopogononella                       | Kasagalansansi    | Roots           | Tree        | Decoction          | Half a glass once a day for 3 days          | Investigated                                               | Toothache, skin diseases, chest pain, wound, fever, Headache, | [23]          |
| Combretaceae         | Combretum molle G. Don                   | Ndagii            | Bark            | Tree        | Decoction          | Half a glass once a day for 3 days          | Investigated                                               | Toothache, skin diseases, chest pain, wound, fever, Headache, | [23]          |
| Combretaceae         | Combretum molle G. Don                   | Kisisasana        | Leaves          | Herb        | Decoction          | Half a glass once a day for 7 days          | Investigated                                               | Toothache, skin diseases, chest pain, wound, fever, Headache, | [21]          |
| Cucurbitaceae        | Cucurbita maxima Lam.                    | Kasuunsu          | Leaves          | Herb        | Decoction          | Oral, dose not specified                    | Investigated                                               | Toothache, skin diseases, chest pain, wound, fever, Headache, | [21]          |
| Cucurbitaceae        | Cucurbita maxima Lam.                    | Kasuunsu          | Leaves          | Herb        | Decoction          | Oral, dose not specified                    | Investigated                                               | Toothache, skin diseases, chest pain, wound, fever, Headache, | [21]          |
| Dendrocalceae        | Dendrocalceae hirsuta Eng.               | Kajyenyoyou       | Leaves          | Herb        | Decoction          | Half a glass thrice a day for a week        | Investigated                                               | Toothache, skin diseases, chest pain, wound, fever, Headache, | [21]          |
| Ebenaceae            | Eucalyptus laticeae Staff                | Emusi             | Roots           | Shrub       | Decoction          | Oral, dose not specified                    | Investigated                                               | Toothache, skin diseases, chest pain, wound, fever, Headache, | [21]          |
| Ebenaceae            | Alchornea cordifolia (Shumach.) Malv. Arg. | Lunabuba         | Leaves          | Herb        | Decoction          | Half a glass once a day for 7 days          | Investigated                                               | Toothache, skin diseases, chest pain, wound, fever, Headache, | [23]          |
| Ebenaceae            | Bridelia micrantha Bail.                 | Kataramiti        | Bark            | Tree        | Decoction          | Half a glass thrice a day for a week        | Investigated                                               | Toothache, skin diseases, chest pain, wound, fever, Headache, | [19]          |
| Ebenaceae            | Chatala abyssinica Lodd. & Spach         | Omubarama         | Leaves          | Herb        | Decoction          | Oral, dose not specified                    | Investigated                                               | Toothache, skin diseases, chest pain, wound, fever, Headache, | [23]          |
| Ebenaceae            | Oribone macrostachyus Ovile.             | Olkota            | Roots/bark      | Tree        | Decoction          | Oral, dose not specified                    | Investigated                                               | Toothache, skin diseases, chest pain, wound, fever, Headache, | [23]          |
| Ebenaceae            | Plaguea strobilis (Robb. ExWillds.) Vogt | Lukandwa/muktundla | Leaves          | Shrub       | Decoction          | Half a glass 3 times a day for a week       | Investigated                                               | Toothache, skin diseases, chest pain, wound, fever, Headache, | [8, 10, 21, 23] |
| Euphorbiaceae        | Isotropa curcas L.                       | Kirowa            | Leaves          | Shrub       | Decoction          | Oral, dose not specified                    | Investigated                                               | Toothache, weakness in pregnancy                           | [21]          |
| Euphorbiaceae        | Macaranga schweinfurthii Pax             | Kyegama           | Bark            | Tree        | Decoction          | Half a glass 3 times a day for 5 days       | No record                                                  | Toothache, weakness in pregnancy                           | [10]          |
| Euphorbiaceae        | Phyllanthus pseudoruijirui Malv. Arg.     | Nakitembe         | Leaves          | Shrub       | Decoction          | Half a glass 3 times a day for a 7 days     | Investigated                                               | Toothache, weakness in pregnancy                           | [10]          |
| Euphorbiaceae        | Shiraquisupus dillipus (Hochst.) H.-J. Esser | Musasa            | Bark            | Tree        | Decoction          | Oral, dose not specified                    | No record                                                  | Toothache, weakness in pregnancy                           | [20]          |
| Euphorbiaceae        | Tetrochordum dalymostenon (Ball.) Pax & K. Hoffm. | Ekiziranfu      | Bark            | Decoction   | Used as enema      | No record                                                  | Jaundice, measles, gastrointestinal disorders, enema       | [8, 19]       |
### Table 1: Continued.

| Plant family    | Scientific name                          | Local name       | Part used      | Growth form | Mode of preparation | Dose and mode of administration for malaria | Status of antimalarial/antiplasmodial activity investigation | Other ailments treated                                  | Reference(s) |
|-----------------|------------------------------------------|------------------|----------------|-------------|---------------------|--------------------------------------------|-------------------------------------------------------------|----------------|---------------|
| Fabaceae        | *Arachis hypogea* (NC)                   | Ebunya bwa       | Leaves         | Shrub       | Fresh extract       | Oral, dose not specified                   | No record                                                   | Diarrhea, body pain                                    | [19]          |
|                 | *Cajanus cajan* (L.) Drax               | Entonga nga      | Leaves         | Shrub       | Fresh extract       | Oral, dose not specified                   | No record                                                   | High blood pressure                                    | [10]          |
|                 | *Crotalaria agatiflora* Schweinf.        | Kijje bebe       | Whole shoot    | Shrub       | Fresh extract       | 1 teaspoon and 1 tablespoon 3 times a day  | No record                                                   | Stomach ache                                            | [28]          |
|                 | *Crotalaria ochroochra* G. Don           | Aleyo            | Leaves         | Herb        | Fresh extract       | 3 times a day for children and adults, respectively, for a week | No record                                                   | Oral wounds, body weakness, wounds, skin infections     | [8, 20, 26]   |
|                 | *Entada abyssinica* Steud. ex A. Rich   | Mswolola         | Leaves         | Tree        | Decoction           | 4 and 3 teaspoons after every 8 hours for adults and children, respectively, for a week | Investigated                                               | Fever, leprosy, burns, tuberculosis, toothache, syphilis | [10, 23]       |
|                 |                                           |                  |                |             |                     |                                            |                                                             | Wounds, candida                                         | [10]          |
|                 |                                           |                  |                |             |                     |                                            |                                                             | Abdominal pain                                          | [19]          |
|                 |                                           |                  |                |             |                     |                                            |                                                             | Oral wounds, body weakness, wounds, skin infections       | [8, 20, 26]   |
|                 |                                           |                  |                |             |                     |                                            |                                                             | Fever                                                  | [19]          |
|                 |                                           |                  |                |             |                     |                                            |                                                             | Impotence, dizziness                                     | [19]          |
|                 |                                           |                  |                |             |                     |                                            |                                                             | Fever                                                  | [19, 20, 25, 29] |
|                 |                                           |                  |                |             |                     |                                            |                                                             | Labour induction                                         | [19]          |
|                 |                                           |                  |                |             |                     |                                            |                                                             | Prolonged embryo in uterus                               | [8]           |
|                 |                                           |                  |                |             |                     |                                            |                                                             | Change of sex of child                                   | [8, 19, 20, 29] |
|                 |                                           |                  |                |             |                     |                                            |                                                             | Abdominal pain                                          | [19]          |
|                 |                                           |                  |                |             |                     |                                            |                                                             | Yellow fever                                            | [8, 10]        |
|                 |                                           |                  |                |             |                     |                                            |                                                             | Yellow fever                                            | [20, 29]       |

**Note:** Mode of preparation includes oral, decoction, and infusion. Status of antimalarial/antiplasmodial activity investigation indicates whether the activity has been investigated or not. Other ailments treated include a variety of health issues, and references are provided for further reading.
| Plant family | Scientific name | Local name | Part used | Growth form | Mode of preparation | Dose and mode of administration for malaria | Status of antimalarial/antiplasmodial activity investigation | Other ailments treated | Reference(s) |
|-------------|-----------------|------------|-----------|-------------|--------------------|-------------------------------------------|-------------------------------------------------|------------------------|--------------|
| Lamiaceae   | Aeolanthus repens Oliv. | Ntulagi | Leaves | Herb | Decoction | Half a glass 3 times a day for 3 days | No record | [10] |
|             | Ajuga remotia Benth. | Kaimwa | Leaves | Herb | Decoction | Half a glass once a day for a week | Investigated | Stomach ache | [10] |
|             | Clerodendrum myricoides R. Br. | Kikonge | Leaves | Shrub | Decoction | Half a glass daily for a week | Investigated | Syphilis, intestinal problems, induction of a labour | [10, 28] |
|             | Clerodendrum rotundifolium Oliv. | Kinsemeko | Roots/leaves | Shrub | Fresh leaf extract/root decoction | Half a glass daily for 5 days | Investigated | Diabetes | [10] |
|             | Hoslundia opposita Vahl. | Kamunye | Leaves | Herb | Decoction | Half a glass 3 times a day for a week; bath | Investigated | Ulcers | [8, 10, 25] |
|             | Leonotis nepetifolia Schimp. exBenth | Kifumufumu | Whole plant | Herb | Decoction | A glassful thrice a day for 3 days | Investigated | Stomach ache | [10, 21] |
|             | Ocimum basilicum | Emoprim | Leaves | Herb | Infusion | Half a glass 3 times a day for a week | Investigated | Fever, eye cataract | [23, 27] |
|             | Ocimum gratissimum Willd. | Muyaga | Leaves | Herb | Decoction | Half a glass 3 times a day for 5 days | Investigated | Syphilis, intestinal problems, induction of a labour | [10, 28] |
|             | Ocimum lamiifolium Hochst. | Omungya | Leaves | Herb | Decoction | Half a glass 3 times a day for a week | Investigated | Diabetes | [10] |
|             | Plectranthus barbatus | Bwirir omutano | Whole plant/leaves, roots/stem | Herb | Infusion | Oral, dose not specified | Investigated | Stomach ache, intestinal problems, induction of a labour | [10, 28] |
|             | Plectranthus caninus Roth | Kwakwakula | Leaves | Herb | Decoction | 4 and 2 teaspoons thrice a day for adults and children, respectively, for a week | No record | Fungal and bacterial infection, high blood pressure, intestinal worms and parasites | [23] |
|             | Plectranthus cf. forskohlii Ekizera | Rosemary | Leaves | Herb | Decoction | Half a glass twice a day for 5 days | Investigated | Chest pain | [10] |
|             | Tetradenia riparia (Hochst.) Codd | Kyewamala | Leaves | Herb | Decoction | One teaspoon twice a day for a week | Investigated | Other ailments treated | [10] |
| Lauraceae   | Persea americana Mill. | Ovakedo | Leaves | Tree | Decoction | About 120 ml once a day for 7 days | Investigated | Other ailments treated | [10] |
| Loranthaceae | Tapinanthus constrictiflorus (Engl.) Danser | Entrugate | Leaves | Herb | Decoction | A glass daily for 7 days | No record | Other ailments treated | [10] |
| Malvaceae   | Hibiscus sabdariffa L. | Nantyuko | Leaves | Shrub | Decoction | Half a glass thrice a day for 7 days | No record | Other ailments treated | [10] |
|             | Azadirachta indica A. Juss. | Neem | Leaves | Tree | Decoction | About 120 ml once a day for 7 days | Investigated | Other ailments treated | [10] |
| Meliaceae   | Carapa grandiflora Sprague | Omukutee | Leaves/bark | Tree | Decoction | Half a glass twice a day for 5 days | No record | Other ailments treated | [10] |
|             | Melia azedarach | Elina | Leaves | Tree | Decoction | Oral, dose not specified | Investigated | Other ailments treated | [10] |
| Menispermaceae | Cissampelos macrotanta A. Rich. | Kawawa | Leaves/whole plant | Herb | Decoction | Half a glass twice a day for 5 days | Investigated | Other ailments treated | [10] |
|             | Acacia hockii De wildl | Eksim | Roots | Tree | Decoction | Oral, dose not specified | No record | Other ailments treated | [23, 30] |
|             | Acacia nilotica | Kivumbi | Leaves | Herb | Decoction | Oral, dose not specified | No record | Other ailments treated | [23] |
|             | Albizia coriaria Wal. | Luguru | Bark | Tree | Decoction | Half a glass once a day for a week | Investigated | Other ailments treated | [10] |
| Mimosaceae  | Albizia grandibracteata Taube | Nongo | Bark | Tree | Decoction | Half a glass once a day for a week | Investigated | Other ailments treated | [8, 10, 32] |
|             | Albizia zygia (DC.) Madar. | Mafingo | Bark | Tree | Decoction | Half a glass once a day for a week | Investigated | Other ailments treated | [21] |
|             | Newtonia Buchananii (Baker) Gilb. & Per. | Mpesere | Bark | Tree | Dried, powdered, added to boiling water | Half a glass once a day for a week | No record | Other ailments treated | [10] |
| Moraceae    | Ficus natalensis Hochst. | Kirundi | Bark | Tree | Decoction | Half a glass once a day for a week | Investigated | Other ailments treated | [8, 10] |
|             | Ficus saururus DC. | Muvno | Bark | Tree | Decoction | Half a glass once a day for a week | Investigated | Other ailments treated | [8, 33] |
|             | Ficus按规定 | Mivule | Bark | Tree | Decoction | Half a glass once a day for a week | Investigated | Other ailments treated | [8, 10] |
**Table 1: Continued.**

| Plant family | Scientific name | Local name | Part used | Growth form | Mode of preparation | Dose and mode of administration for malaria | Status of antimalarial/antiplasmodial activity investigation | Other ailments treated | Reference(s) |
|--------------|-----------------|------------|-----------|-------------|---------------------|---------------------------------------------|---------------------------------------------------------------|------------------------|--------------|
| **Moringaceae** | *Moringa oleifera* Lam. | Moringa | Leaves/roots | Tree | Decoction/chewed raw | A glassful thrice a day for 7 days; a handful of fresh leaves chewed 3 times for 4 days | Investigated | Joint pains | [21, 25] |
| **Musaceae** | *Musa paradisiaca* (NG) | Kahalagala | Leaves | Herb | Decoction | Oral, dose not specified | Investigated | Jaundice, prolonged embryo in uterus | [19] |
| **Myrtaceae** | *Myrtus communis* L. | Omujujeje | Leaves | Tree | Decoction | Oral, dose not specified | Investigated | Vomiting, diarrhoea | [19] |
| **Myristicaceae** | *Pauromaceae* | Lumaba | Leaves | Tree | Decoction | Half a glass a day | No record | | [10] |
| **Myristicaceae** | *Musa lantana* Forsk. | Kivonwondo | Leaves | Shrub | Decoction | Half a glass thrice a day for 7 days | Investigated | Febrile convulsions | [10, 19, 24] |
| **Myrtaceae** | *Syzygium cordatum* Hochst. | Mugege | Bark | Tree | Decoction | Oral, dose specified | Investigated | Bloody diarrhoea, typhoid, wounds, cough | [10, 23] |
| **Musaceae** | *Syzygium jambos* L. | Jambula | Leaves | Tree | Decoction | Oral, dose specified | Investigated | Dry cough, skin rash, wounds, cough | [8, 10, 20, 29] |
| **Myrtaceae** | *Syzygium guineense* (Willd.) DC. | Kahunguri | Roots | Shrub | Decoction | Oral, dose specified | No record | Pneumonia, snake bite | [23] |
| **Papilionaceae** | *Pittosporum brachyandra* | Akuatanda | Leaves | Tree | Decoction | Oral, dose specified | No record | Diarrhoea, cough | [19] |
| **Papilionaceae** | *Pittosporum munroi* Hook. f. | Mubajjunion | Leaves | Shrub | Infusion/decoction | Half a glass a day for a week | No record | Dental caries, influenza, cough, cancer, indigestion, fever | [10, 19, 23] |
| **Papilionaceae** | * Digitaria scalarum* Chiov. | Kisuvi | Leaves | Grass | Decoction | 120ml every after 8hours for a week | Investigated | | |
| **Poeaceae** | *Imperata cylindrica* (L.) Beauv. var. africana (Anderss.) C. E. Hubbard | Lusenike | Roots | Grass | Dried, powdered, added boiling water/decoction | 120ml once a day for a week | No record | Abdominal pain | [10] |
| **Poeaceae** | *Zea mays* L. | Ntuvabasi | Flowers/husk | Cereal | Decoction | 120ml every after 8hours for a week | Investigated | Boosts immunity | [10] |
| **Polygaleaceae** | *Mucuna aemissi* Engil. | Muzini | Bark | Tree | Decoction | Half a glass thrice a day for a week | No record | | |
| **Portulacaceae** | *Talinum parviflorum* (Forssk.) Asch. ex Schweinf. | Mopina | Leaves | Herb | Decoction | Oral, dose specified | No record | | |
| **Pouzaceae** | *Prunus africana* (Hook. f.) Kalkman | Ntuvabasi | Bark | Tree | Decoction | 2 and 3 teaspoons thrice a day for children and adults respectively, for a week | Investigated | Painting, cancer | [8, 10] |
| **Pouzaceae** | *Rubus steudleri* Schweinf. | Nkemene | Leaves | Herb | Decoction | Half a glass once a day for a week | No record | | |
| **Rutaceae** | *Hallea rubrostipulata* | Nsiru | Bark | Tree | Decoction | Oral, dose specified | No record | | |
| **Rutaceae** | *Vangueria aconitifolia* K. Schum. | Matugorda | Bark | Shrub | Decoction | 2 and 3 teaspoons thrice a day for children and adults respectively, for a week | No record | | |
| **Rutaceae** | *Citrus reticulata* | Omusikwa | Roots | Herb | Decoction | Oral, dose specified | Investigated | Weight loss induction, cancer, skin diseases | [23] |
| **Rutaceae** | *Citrus sinensis* | Omukuza | Aerial parts | Climber | Decoction | Oral, dose specified | Investigated | Body cleanser | [32] |
| **Rutaceae** | *Calamondin* | Otsa | Roots | Tree | Decoction | Oral, dose specified | Investigated | Cough | [10, 23, 28] |
| **Rutaceae** | *Zanthoxylum chalybeum* Engl. | Nsungu | Bark | Tree | Decoction | Half a glass thrice a day for a week | No record | | |
| **Rutaceae** | *Zanthoxylum leprieurii* | Mubagga | Bark | Tree | Decoction | Half a glass thrice a day for a week | No record | | |
| **Rutaceae** | *Zanthoxylum chalybeum* Engl. | Nsungu | Bark | Tree | Decoction | Half a glass thrice a day for a week | No record | | |
| Plant family | Scientific name | Local name | Part used | Growth form | Mode of preparation | Dose and mode of administration for malaria | Status of antimalarial/antiplasmodial activity investigation | Other ailments treated | Reference(s) |
|--------------|----------------|------------|-----------|-------------|---------------------|------------------------------------------|----------------------------------------------------------|----------------------|--------------|
| Salicaceae   | *Trimeria grandifolia* ssp. *tropica* (Hochst.) Warb. | Omwatanshare | Leaves | Decoction | Oral, dose not specified | Investigated | | Wounds, vomiting, skin diseases, fibroids, cervical cancer | [19] |
| Sapindaceae  | *Blighia unijuga* Baker | Nkuzanyana | Bark | Tree | Decoction drunk | Half a glass twice a day for a week | Investigated | | |
| Sapotaceae   | *Manilkara obovata* (Sabine & G. Don) | Nkunya | Bark | Tree | Decoction | Oral, dose not specified | No record | | [20] |
| Scrophulariaceae | *Sopubia ramosa* (Hochst.) Hochst. | Kakulunkanyi | Whole plant | Herb | Decoction | Oral, dose not specified | No record | | [20] |
| Simaroubaceae | *Harrisonia abyssinica* Oliv. | Ekeru | Roots/leaves | Shrub | Decoction | Oral, dose not specified | Investigated | | |
| Sapindaceae  | *Datura stramonium* L. | Amadada | Leaves | Herb | Decoction drunk | Half a glass thrice a day for a week | No record | | [10] |
| Solanaceae   | *Physalis peruviana* L. | Ntununa | Leaves | Herb | Decoction drunk | Half a glass 3 times a day for a week | No record | | [8, 10, 19] |
| Solanaceae   | *Solanum nigra* L. | Nsugga | Leaves | Herb | Decoction drunk | Half a glass 3 times a day for a week | Investigated | | [8, 10] |
| Tiliaceae    | *Trumfetta rhomboidea* Jacq. | Musombanioko | Roots | Shrub | Decoction drunk | Half a glass once a day for a week | No record | | [10] |
| Umbelliferae | *Steganotania araliae* Hoehn. | Akassa | Leaves | Tree | Decoction drunk | Half a glass a day for a week | No record | | [10] |
| Verbenaceae  | *Lantana trifolia* L. | Omuhuluye | Leaves | Decoction | Oral, dose not specified | Investigated | | |
| Zingiberaceae | *Curcuma longa* L. | Binjali | Rhizome | Herb | Fresh extract | 30 ml thrice a day for 3 days | Investigated | | [28] |
5. Herbs and Plant Parts Used to Manage and Treat Malaria across Communities in Uganda

About 182 plant species from about 63 different plant families are used to treat malaria across several communities in Uganda (Table 1). Of the 63 plant families, species within the family Asteraceae are most widely used in the country to treat malaria, constituting up to 15% of all plant species used (Figure 3(a)). This is followed by species from Fabaceae (9%), Lamiaceae (8%), Euphorbiaceae (6%), and Mimosaceae (4%).

### Table 2: Some herbs used in malaria prevention amongst communities in Uganda.

| Plant family | Plant species | Local name | Plant form | Mode of use to prevent malaria | Reference(s) |
|--------------|---------------|------------|------------|--------------------------------|---------------|
| Cleomaceae   | Cleome gynandra L. | Akeyo | Herb | Leaves are cooked and eaten as a prophylactic measure | [25] |
| Cucurbitaceae| Cucurbita maxima Duchesne | Acuga | Scrambler | Leaves cooked and pasted with groundnut then eaten | [25] |
| Euphorbiaceae| Manihot esculenta Crantz | Gwana | Herb | Tuber peelings are dried then burnt in house so that smoke repels mosquitoes | [25] |
| Fabaceae     | Crotalaria ochroleuca G. Don | Alayo | Herb | Leaves are cooked and eaten as a prophylactic measure | [25] |
|              | Ocimum forsskaalii Benth. | Yat cola | Herb | Leaves dried and burnt so that smoke chases away mosquitoes; bath infusion to repel mosquito | [25] |
| Lamiaceae    | Rosmarinus officinalis L. | Rosemary | Herb | Leaves are cooked and eaten as a prophylactic measure; planted around the house to repel mosquitoes | [10] |
| Malvaceae    | Gossypium hirsutum L. | Pama | Shrub | Cotton lint is dried and burnt so that smoke keeps away mosquitoes | [25] |
| Musaceae     | Musa sp. | Labolo kwon | Shrub | Fruit peeling are dried and burnt in the house to produce smoke that keeps away mosquitoes | [25] |
| Myrtaceae    | Eucalptus grandis Maiden. | Kalitunsi | Tree | Leave and branches are burnt to repel mosquitoes | [25] |
| Poaceae      | Cymbopogon citratus Stapf. | Kisubi | Grass | Planted around the house to repel mosquitoes; taken in tea as a prophylactic measure | [19, 23] |
| Solanaceae   | Solanum americanum Mill. | Ocuga | Herb | Leaves are cooked and eaten as a prophylactic measure | [25] |

![Figure 3(a)](image1.png)  
![Figure 3(b)](image2.png)

**Figure 3:** (a) Composition of plant species in each family used to treat malaria. (b) Percentage use of plant parts for treatment of malaria.
| Plant family        | Scientific name            | Part used | Exaining solvent  | Means of traditional extraction | Report on antiplasmodial, IC50 (μg/ml)/antimalarial activity (Plasmodium strain) | Active chemical constituents                                                                 | Reference(s) |
|---------------------|----------------------------|-----------|-------------------|---------------------------------|---------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|--------------|
| Acanthaceae         | Justicia betonica L.       | Shoot     | Methanol          | Hot water                       | 69.6 (chloroquine sensitive, K39)                                               | Justetinol (indole(3,2-b)quinoline alkaloid glycoside)                                   | [20]         |
|                     | Aloe dawei A. Berger (wild/ | Leaves    | Ether             | Cold water, mashing, hot water  | Extract had anti-P. falciparum activity value of 7.97 (95% CI: 3.56 to 17.85) μg/ml with 50% schizonts suppression per 200 WBC (EC50) | Anthraquinones, aloin, lectins, Anthrone, C-glucoside homonaloin, anthraquinones, aloin, lectins, anthrones | [19, 45]    |
|                     | cultivated)                |           |                   |                                 |                                                                                  |                                                                                          |              |
| Aloeaceae           | Aloe kedongensis (wild)    | Leaves    | Methanol          | Hot water                       | 87.7 (chloroquine sensitive, D6); 67.8 (chloroquine resistant, W2)              | Anthraquinones, aloin, lectins, Anthrone, C-glucoside homonaloin, anthraquinones, aloin, lectins, anthrones | [19, 46]    |
|                     | Aloe ferox Mill             | Leaves    | Dichloromethane   | Water                           | 21 (chloroquine sensitive, D10)                                                 | Anthraquinones, aloin, lectins, Anthrone, C-glucoside homonaloin, anthraquinones, aloin, lectins, anthrones | [19, 31, 47]|
|                     |                            |           | Chloroform:Methanol| Hot water                       | >100 (chloroquine sensitive, D10)                                               | Anthraquinones, aloin, lectins, Anthrone, C-glucoside homonaloin, anthraquinones, aloin, lectins, anthrones | [19, 31, 47]|
| Anacardiaceae       | Mangifera indica L.        | Leaves    | Ethanol           | Hot water                       | >50 (chloroquine resistant, F-B1)                                               | Phenolics                                                                                   | [48, 49]    |
|                     | Rhus natalensis Bernh. Ex Krauss | Stem bark | Ethanol          | Hot water                       | 58.6 (chloroquine sensitive, D6); not detected                                  | Triterpenoids                                                                                | [54]         |
|                     |                           |           | Ethanol          | Hot water                       | 6.6 (P. falciparum)                                                            | Triterpenoids                                                                                | [54]         |
| Apocynaceae         | Alstonia boonei De Wild.   | Stem bark | Water            | Hot water                       | 80.97% suppressive activity at 200 mg/kg (P. berghoi) in combination with other two local herbs | Alkaloids, triterpenoids                                                                     | [51]         |
|                     | Carissa edulis (Forssk.) Vahl | Stem bark | Water            | Hot water                       | 14.5 (chloroquine sensitive, D6)                                               | Lignan, nortrehlenalin                                                                        | [52]         |
|                     | Carissa spinarum Lodd. ex A. DC. | Root bark | Dichloromethane  | Mashing, hot water              | 4.6 (chloroquine sensitive, D6); 5.3 (chloroquine resistant, W2)               | Saponins, sesquiterpenes                                                                     | [53]         |
|                     | Catharanthus roseus G. Don. | Leaves    | Methanol         | Hot water                       | >50 (chloroquine sensitive, D7); undetectable                                   | Sesquiterpenoids, diterpenoids, monoterpenoids, Alkaloids                                  | [19, 55]    |
|                     | Aristotlea elegans Mast.   | Seeds     | Methanol         | Cold water, mashing, hot water  | Antiplasmodial activity in terms of EC50 values 0.289 to 1.056 μg/ml (chloroquine sensitive) | Alon, anthraquinones, alo-emoindin                                                          | [56]         |
| Asphodelaceae       | Aloe vera (L.) Burm. f.    | Leaves    | Water            | Hot water                       | 67.8 (chloroquine sensitive, K39)                                               | Justetinol (indole(3,2-b)quinoline alkaloid glycoside)                                   | [20]         |
| Plant family | Scientific name | Part used | Extracting solvent | Means of traditional extraction | Report on antimalarial, IC50 (μg/ml) | Active chemical constituents | Reference(s) |
|-------------|-----------------|-----------|--------------------|---------------------------------|--------------------------------------|-----------------------------|--------------|
| Asteraceae  | Ageratum conyzoides L. | Whole plant | Methanol | Hot water | 11.5 (chloroquine sensitive, D6); 12.1 (chloroquine resistant, W2) | Flavonoids | [54] |
|             | Artemisia annua L. | Leaves | Water | Hot water | 11.1 (chloroquine sensitive, D10); 0.9 (chloroquine resistant, W2) | Sesquiterpenes and sesquiterpene lactones including artemisinin, flavonoids such as chrysopelone-D, euparoton, chrysopelone | [19, 57] |
|             | Artemisia afra Jacq. Ex Wäld | Leaves | Methanol | Hot water | 9.1 (chloroquine sensitive, D6); 3.9 (chloroquine resistant, W2) | Acacetin, genkwanin, 7-methoxyacacetin | [54] |
|             | Aspilia africana (Pers.) C. D. Adams | Leaves | Ethanol | Hot water | Significant chemo suppressive effect of 92.23% (400mg/kg) on *P. berghei* | Saponins, terpenoids, alkaloids, resins, tannins, flavonoids, sterols | [19, 58] |
|             | Baccharis aden neur (Sch. Bip. ex Walp.) H. Rob. | Leaves | Petroleum ether | Hot water | 4.6 (chloroquine resistant, K1) | Flavonoids | [26] |
|             | Aspilia africana L. | Leaves | Dichloromethane | Hot water; mashing | 8.5 (chloroquine sensitive, D10) | Flavonoids including quercetin 3,3′-dimethyl ether 7-O-a-L-rhamnopyranosyl-1′-α-ether 7-O-D-β-gluopyranose and quercetin 3,3′-dimethyl ether 5-alkylcoumarin | [52] |
|             | Bothriochline longipes N. E. Br. | Leaves | Ethanol | Hot water | 3.7 (P. falciparum); 50 (P. falciparum) | Flavonoids | [19, 24] |
|             | Crassocephalum crepidioides | Leaves | Ethyl acetate | Hot water | 40.6% inhibition of *P. falciparum* at 10μg/ml | Flavonoids | [32] |
|             | Guazatia acabra Chiov. | Whole plant | Crude ethanol | Hot water | 49.09% growth inhibition at 100 (both chloroquine sensitive, NF54 and chloroquine resistant, FCR3) | Lactones, eudesmanolone | [59] |
|             | Melanthera scandens (Schumach. & Thonn.) Roberty | Leaves | Chloroform | Hot water | 68.83% chemo suppression activity (*P. berghei*) | Triterpenoid saponins | [60] |
|             | Microllosa pyrifolia (Lam.)/O. Rzé | Leaves | Chloroform | Hot water | 5 (both chloroquine sensitive, NF54 and resistant, FCR3) | E-phytol; 6-geranylgeraniol-19-oic acid | [2, 28] |
|             | Schkuhria pinnata (lam.) | Whole plant | Water | Hot water | 22.5 (chloroquine sensitive, D6); 51.8 (chloroquine resistant, W2) | Schikhirin I and schikhirin II | [54] |
|             | Solanum muninii (Hook. f.) C. Jeffrey | Leaves | Methanol | Hot water | 1.3 (chloroquine sensitive, D6); 6.8 (chloroquine resistant, W2) | Phytosterols, n-alkanes and N-hexacosanol | [19, 55] |
|             | Tagetes minuta L. | Leaves | Ethyl acetate | Water | 21.6 (chloroquine sensitive, D7); 26.2 (chloroquine resistant, W2) | Flavonoids | [32] |
|             | Tithonia diversifolia A. Gray | Leaves | Methanol | Water | 6.0% inhibition of *P. falciparum* at 10μg/ml | Tagitinin C, sesquiterpene lactones | [55] |
|             | Vernonia adenzos Sch. Bip. ex Walp. | Leaves | Methanol | Hot water | 83.4% inhibition of parasitaemia, at 600mg/kg (*P. berghei*) | Glycosides, glycosides | [32] |
|             | Vernonia amygdalina Delile | Leaves | Methanol/ dichloromethane | Hot water, cold water | 2.7 (chloroquine resistant, K1) | Coumarin, sesquiterpene lactones including vernolepin, vernolin, vernoldin and hydroxyvernoldin, sterol glucosides | [19, 61] |
|             | Vernonia cinerea (L.) Less. | Whole plant | Water | Hot water | >50 (chloroquine sensitive, D7); 37.2 (chloroquine resistant, W2) | Sesquiterpene lactone | [62] |
|             | Vernonia lasiopus O. Hoffm. | Leaves | Methanol | Mashing; hot water | 44.3 (chloroquine sensitive, D6); 52.4 (chloroquine resistant, W2) | Sesquiterpene lactones, polyaccaresides | [19, 54] |
| Bignoniaceae | Markhamia lutea (Benth.) K. Schum. | Leaves | Ethyl acetate | Hot water | 71% inhibition of *P. falciparum* at 10μg/ml | Phenylpropanoid glycosides, cycloartane triterpenoids | [32] |
|             | Spathodea campanulata Buch.- Ham. ex DC. | Stem bark | Ethyl acetate | Water | 28.9% inhibition of *P. falciparum* at 10μg/ml | Quinone (lapachol) | [32] |
|             | Cassia didymobotrya Fres. | Leaves | Methanol | Hot water | 23.4 (chloroquine sensitive, D6; undetectable (chloroquine resistant, W2) | Alkaloids | [54] |
| Caesalpinaceae | Erythrophleum pyriforma | Leaves | Ethanol | Hot water | >50 (P. falciparum) | Piperidine alkaloids | [63] |
|             | Senecio spectabilis (DC) H. S. Irwin & Barneby | Leaves | Ethanol | Water | 59.29% growth inhibition at 100mg/kg body weight dose (*P. berghei*) | Piperidine alkaloids | [64] |
|             | Caesalpinioideae | Cassia hirsuta | Root back | Methanol | 32.0 (chloroquine sensitive D7) | Sesquiterpenes e.g. mungadiolide | [27, 54] |
|             | Warbugia ugandensis Sprague | Stem back | Methanol | Hot water | 6.4 (chloroquine sensitive, D6); 6.9 (chloroquine resistant, W2) | Sesquiterpene lactones | [27, 54] |
| Plant Family | Scientific name | Part used | Extracting solvent | Mass of traditional extraction | Means of traditional extraction | Active chemical constituents | Reference(s) |
|-------------|-----------------|-----------|-------------------|------------------------------|-------------------------------|---------------------------|--------------|
| Caricaceae  | Carica papaya L. | Leaves    | Ethyl acetate      | Hot water                    | Alkaloids, saponins, tannins, glycosides | 2.96 (chloroquine sensitive, D10); 3.98 (chloroquine resistant, D2). | [65]         |
| Celastraceae| Maytenus senegalensis | Roots   | Hot water          | 1.9 (chloroquine sensitive, D6); 2.4 (chloroquine resistant, W2) | Terpenoids, pentacyclic triterpenoids, e.g., pristimerin. | 10.8 (chloroquine sensitive, D10) | [66]         |
| Chenopodiaceae | Chenopodium ambrosioides L. | Leaves | Crude hydroalcoholic extract | Hot water | Inhibited the P. falciparum growth, exhibiting an IC₅₀ of 25.4 μg/ml. | Sesquiterpenes, monoterpenes | [67]         |
| Combretaceae | Combretum molle G. Don | Stem back | Acetone | Water | Phenolics, punicalagin | 8.2 (chloroquine sensitive, D10); 38.9 (chloroquine resistant, Dd2) | [68]         |
| Cucurbitaceae | Cucurbita maxima L. | Seeds | Crude ethanol | Hot water | Phenols, terpenoids, alkaloids, tannins | 50% reduction of parasitaemia levels in P. berghei infected mice at 500mg/kg. | [69]         |
| | Momordica foetida Schumach. | Shoots | Water | Hot water | Saponins, alkaloid, cardiac glycosides | 6.16 (chloroquine sensitive, NF54); 0.35 (chloroquine resistant, FCR3) | [28]         |
| Ebenaceae  | Euclea latideus Staff | Roots   | Hexane | Water | Triterpenoids lupeol, betulin, 3β-(5-hydroxyferuloyl)lup-20(30)-ene | 38.2 (chloroquine sensitive, 3D7); 38.9 (chloroquine resistant, Dd2) | [23]         |
| Euphorbiaceae | Alchornea cordifolia (Schumach.) Mull. Arg. | Leaves | Water | Hot water | Phenolics including ellagic acid | 4.8 (chloroquine resistant, K1) | [70]         |
| | Bridelia micrantha Baill. | Stem bark | Methanol | Hot water | Flavonoids, terpenoids | 19.4 (chloroquine sensitive, D6); 14.2 (chloroquine resistant, W2) | [50]         |
| | Clutia abyssinica Jaub. & Spach | Leaves | Methanol | Water | Diterpenes | 7.8 (chloroquine sensitive, D6); 11.3 (chloroquine resistant, W2) | [54]         |
| | Croton macrostachyus Olive. | Leaves | Chloroform | Hot water | Triterpenoids including lupeol | 83.6% inhibition of P. falciparum at 10 μg/ml. | [71]         |
| | Fluega virosa (Roxb. ExWillb.) Voigt | Leaves | Water/methanol | Hot water | bergenin | 2 (chloroquine resistant, W2) | [72]         |
| | Jatropha curcas L. | Leaves | Ethyl acetate | Hot water | Alkaloids, saponins, glycosides, tannins | 5.1 (chloroquine sensitive, NF54); 2.4 (chloroquine resistant, K1) | [73]         |
| | Phyllanthus (pseudo) niruri Mull. Arg. | Water | Hot water | Ranged from 2.9 to 4.1 (both chloroquine sensitive, 3D7 and resistant, Dd2) | Coumarins including 1-O-galloyl-6-O-luteoyl-a-D-glucose | | [74]         |
| | Tamarindus indica L. | Stem bark | Water | Hot water | Saponins (leaves), tannins | 25.1% chemosuppressive activity at 10μg/ml (P. berghei). | [78]         |
| Flacourtiaceae | Trimeria bakeri Gilg. | Leaves | Petroleum ether | Hot water | Flavonoids, terpenoids | >100 (chloroquine sensitive, K39) | [29]         |
| | Hypericaceae | Harungana madagascariensis Lam. | Stem bark | Water | Hot water | Phenolic derivatives, chrysophanol a, a-hydroxycarbazole | 26.4 (chloroquine sensitive, HB1); 28.9 (chloroquine resistant, HB2) | [79]         |
| Plant family | Scientific name | Part used | Means of traditional extraction | Extracting solvent | IC50 (μg/ml)/Report on antiplasmodial activity (strain) | Active chemical constituents | Reference(s) |
|--------------|----------------|-----------|---------------------------------|-------------------|-----------------------------------------------------|-----------------------------|--------------|
| Lauraceae    | Hoslundia opposita Vahl. | Leaves | Ethanol | Water | 66% inhibition of P. berghei at 10 μg/ml ; 55% inhibition of P. falciparum (chloroquine sensitive, FCA/GHA); 57% inhibition (chloroquine resistant, W2) | Quinones, saponins, abietane diterpenes (3-O-benzoylhosloppone) | [32] |
| Lamiaceae    | Ocimum gratissimum Willd. | Leaves | Ethanol | Water | 8.6 (chloroquine resistant, W2) | Flavonoids | [50, 80] |
| Lamiaceae    | Ocimum lamiifolium Hochst. | Leaves | Water | Water | No activity | | |
| Lamiaceae    | Plectranthus barbatus | Leaves/stem | Dichloromethane | Water | No activity | | [23, 47] |
| Lamiaceae    | Rosmarinus officinalis L. | Leaves | Ethyl acetate | Water | Essential oil at a concentration 1.8% (v/v) had no inhibitory effect against P. falciparum | | [82] |
| Lauraceae    | Tetradenia riparia (Hochst.) Codd | Root | Hot water | No activity | | | [83] |
| Lauraceae    | Milicia excels (Welw.) C. C. Berg. | Leaves | Methanol | Hot water | 76.7% chemo suppressive activity at 250mg/kg/day (P. berghei) | | [89] |
| Moringaceae  | Moringa oleifera | Leaves | Ethyl acetate | Water | 7.5 (chloroquine sensitive, Dd2); 100 (chloroquine resistant, Dd2) | Flavonoids | [49, 80] |
| Mimosaceae   | Albizia coriaria Welw. | Leaves | Ethanol | Water | 1.0% inhibition of parasitemia at 0.075mg/ml (P. berghei) | Tannins, flavonoids, terpenes | [86] |
| Mimosaceae   | Albizia grandibracteata Taube | Leaves | Ethyl acetate | Water | 22.0% inhibition of P. falciparum at 10 μg/ml | | [32] |
| Myrtaceae    | Syzygium guineense (Willd.) DC. | Leaves | Crude ethanol | Water | 49.09% chemo suppression at 400mg/kg (P. berghei) | Tannins, flavonoids, terpenoids | [94] |
| Myrtaceae    | Syzygium cumini (L.) Skeels | Leaves | Crude ethanol | Water | 0.25 to 27.1 (chloroquine-resistant strains) | | [93] |
| Myrtaceae    | Myrtus communis | Leaves | Ethyl acetate | Water | 14.7 (chloroquine sensitive, D10) | | [55] |
| Myrtaceae    | Cymbopogon citratus Stapf. | Leaves | Ethanol | Water | 99.89% suppression of parasitaemia at 1600mg/kg | Flavonoids | [20, 49, 95] |
| Myrtaceae    | Syzygium microphyllum (Welw.) Welw. | Leaves | Ethanol | Water | 9.0% inhibition of parasitemia at 100mg/kg (P. berghei) | Tannins, flavonoids, terpenoids | [92] |
| Poaceae      | Zea mays L. | Husks | Ethyl acetate | Water | 9.3 (chloroquine sensitive, 3D7); 3.7 (chloroquine resistant, INDO) | Alkaloids, flavonoids and triterpenoids | [96] |
| Myrtaceae    | Syzygium guineense (Willd.) DC. | Leaves | Ethanol | Water | 0.25 to 27.1 (chloroquine-resistant strains) | | [93] |
| Polygalaceae | Securidaca longipedunculata Fresen. | Leaves | Dichloromethane | Water | 6.9 (chloroquine sensitive, D10) | Saponins, flavonoids, alkaloids, terpenoids | [92] |
| Rosaceae     | Prunus africana | Stem bark | Hot water | Water | 0.25 to 27.1 (chloroquine-resistant strains) | Terpenoids | [54] |
Table 3: Continued.

| Plant family | Scientific name | Part used | Extracting solvent | Means of traditional extraction | Report on antiplasmodial, IC50 (μg/ml)/antimalarial activity (Plasmodium strain) | Active chemical constituents | Reference(s) |
|--------------|-----------------|-----------|--------------------|---------------------------------|--------------------------------------------------------------------------------|-----------------------------|---------------|
| Rubiaceae    | Hallea rubrostipulata (K. Schum.) J.-F. Leroy | Root | Ethanol | Water | 100 μg/ml extract had 65.54% growth inhibition (chloroquine resistant, Dd2) | Alkaloids | [59] |
|              | Pentas longiflora Oliv. | Root | Methanol | Hot water | 0.99 (chloroquine sensitive, D6); 0.93 (chloroquine resistant, W2) | Pyranonaphthoquinones, pentalongo (1) and psychorubrin (2), naphthalene derivative mollugin (3) | [97] |
|              | Citrus reticulata | Seeds (isolimonexic acid methyl ether) | Methanol | Hot water | <4.76 (both chloroquine sensitive, D6 and resistant, W2) | Limonin, isoolimonexic acid methyl ether, dicherythrine, deacetylnomilin, obacunone | [98] |
|              | Citrus sinensis | Root | 70% ethanol | Hot water | 53.27% suppression of parasitaemia at 700 mg/kg | Tannins, alkaloids, saponins, flavonoids | [20, 24, 99] |
| Rutaceae     | Tectea nobilis D. Delé | Bark | Ethyl acetate | Water | 54.7% inhibition of P. falciparum at 10 μg/ml | Limonoids, isoolimonexic acid methyl ether, dicherythrine, deacetylnomilin, obacunone | [20, 24, 99] |
|              | Toddalia asiatica Baxi. | Root bark | Methanol | Water | 6.8 (chloroquine sensitive, D6); 13.9 (chloroquine resistant, W2) | Quinoline alkaloids | [32] |
|              | Zanthoxylum chalybeum Engl. | Stem bark | Water | Hot water | 4.3 (chloroquine sensitive, NF54); 25.1 (chloroquine resistant, FCR3) | Furoquinolines (nitidine, 5,6-dihydrofuroline), coumarins | [80] |
| Salicaceae   | Salix griffithii ssp. tropica (Hochst.) Warb | Leaves | Methanol | Hot water | >50 (chloroquine sensitive, 3D7) | Chelerythrine, nitidine, methyl canadine | [28] |
| Sapindaceae  | Blighia sisyrinnum Baker | Leaves | Ethyl acetate | Hot water | 2.3% inhibition of P. falciparum at 10 μg/ml | Limonoids, steroids | [66] |
| Simaroubaceae | Harrisonia abyssinica Olive | Roots | Ethyl acetate | Hot water | 4.4 (chloroquine sensitive, D6); 10.25 (chloroquine resistant, W2) | Steroidal alkaloids, flavonoids | [100] |
| Solanaceae   | Solanum nigrum L. | Fruit | Methanol | Hot water | 10.3 (chloroquine sensitive, 3D7); 18.7 (chloroquine resistant, K1) | Sesquiterpenes, triterpenes, flavonoids | [30] |
| Ulmaceae     | Celtis africana L. | Stem bark | Ethyl acetate | Hot water | 37.5% inhibition of P. falciparum at 10 μg/ml | Steroids, terpenoids, alkaloids, saponins | [24] |
| Verbenaceae  | Lantana camara | Leaves | Dichloromethane | Hot water | 8.7 (chloroquine sensitive, 3D7); 5.7 (chloroquine resistant, W2) | Sesquiterpenes, triterpenes, flavonoids | [30] |
|              | Lantana trifolia L. | Aerial parts | Petroleum ether | Hot water | 13.2 (P. falciparum) >50 (P. falciparum) | Steroids, terpenoids, alkaloids, saponins | [24] |
| Zingiberaceae | Curcuma longa L. | Hot water, mashing | Ethanol | Water | 5 mg/kg had a significantly high chemo suppressive activity of 56.8% (P. berghei) | Polyphenolic curcumin | [100] |
Table 4: Top 17 herbal plants used locally in Uganda for malaria treatment with highest antimalarial/antiplasmodial activities (arranged alphabetically).

| Plant family | Plant species | Plant part | Extracting solvent | Report on antiplasmodial, IC50 (μg/ml)/antimalarial activity (Plasmodium strain) | Active chemical constituents | Toxicity/safety information | Reference(s) |
|--------------|---------------|------------|--------------------|----------------------------------------------------------------------------------|-------------------------------|-----------------------------|--------------|
| Asteraceae   | Artemisia afra Jaq. Ex Willd | Leaves | Methanol | 3.9 (chloroquine resistant, W2) | Acacetin, genkwanin, 7-methoxyacacetin | Cytotoxicity was observed in Vero cells Generally safe and effective; nausea may occur on drinking herbal extract; artemisinin, an active compound in the extract is safe for pregnant women at least during second and third trimesters | [54, 103] |
|              | Artemisia annua L. | Leaves | Water | 0.9 (chloroquine resistant, W2); 1.1 (chloroquine sensitive, D10) | Sesquiterpenes and sesquiterpene lactones including artemisinin | | [19, 57, 104] |
|              | Aspilia africana (Pers.) C. D. Adams | Leaves | Ethanol | Significant chemo suppressive effect of 92.23% (400 mg/kg) on P. berghei | Saponins, terpenoids, alkaloids, resins, tannins, flavonoids, sterols | No signs of toxicity in mice even at a dose as high as 5000 mg/kg Moderate toxicity on thrombocyte line and a protective effect on cardiovascular system; no signs of toxicity in mice following oral administration of 5000 mg/kg body weight (bw) dose | [19, 58] |
|              | Jatropha curcas L. | Leaves | Ethyl acetate | 2.4 (chloroquine resistant, K1) | Alkaloids, saponnins, glycosides, tannins | | [73, 105] |
|              | Microglossa pyrifolia (Lam.)O. Ktze | Leaves | Dichloromethane | 1.5 (chloroquine sensitive, 3D7; 2.4 chloroquin resistant, W2) | E-phytol; 6e-geranylgeraniol-19-oic acid | | [2, 28, 55] |
|              | Schkuhria pinnata (lam.) | Whole plant | Methanol | 1.3 (chloroquine sensitive, D6) | Schkuhrin I and schkuhrin II | | [32, 54] |
|              | Tithonia diversifolia A. Gray | Leaves | Methanol | 1.2 (chloroquine sensitive, 3D7); 1.5 (chloroquine resistant, W2) | Tagitin C, sesquiterpene lactones | Aerial parts are cytotoxic against cells from the human foetal lung fibroblast cell line | [55] |
|              | Vernonia amygdalina delile | Leaves | Methanol/dichloromethane | 2.7 (chloroquine resistant, K1) | Coumarin, sesquiterpene lactones including vernolepin, vernolin, vernolide, vernodalin and hydroxyvernodalin, steroid glucosides | Petroleum ether extract shows strong cytotoxicity | [19, 26, 32] |
| Plant family | Plant species | Plant part | Extracting solvent | Report on antiplasmodial, IC₅₀ (μg/ml)/antimalarial activity (Plasmodium strain) | Active chemical constituents | Toxicity/safety information | Reference(s) |
|--------------|---------------|------------|--------------------|---------------------------------------------|-----------------------------|-----------------------------|---------------------------|
| Caricaceae   | *Carica papaya L.* | Leaves     | Ethyl acetate      | 2.96 (chloroquine sensitive, D10); 3.98 (chloroquine resistant, DD2) | Alkaloids, saponins, tannins, glycosides | No serious toxicity reported, carpaine, an active compound against *P. falciparum* had high selectivity and was nontoxic to normal RBCs | [65, 106] |
| Celastraceae | *Maytenus senegalensis* | Roots      |                    | 1.9 (chloroquine sensitive, D6); 2.4 (chloroquine resistant, W2) | Terpenoids, pentacyclic triterpenes, e.g., pristimerin | No toxicity observed in ethanol extract | [66, 107] |
| Cucurbitaceae | *Momordica foetida* Schumach. | Shoot/Leaves | Water/Water/methanol | 0.35 (chloroquine resistant, FCR3); 6.16 (chloroquine sensitive, NF54) | Saponins, alkaloid, phenolic glycosides including 5,7,4′-Trihydroxyflavanone and kaempferol | No pronounced toxicity against human hepatocellular (HepG2) and human urinary bladder carcinoma (ECV-304, derivative of T-24) cells | [26, 28, 108] |
| Euphorbiaceae | *Alchornea cordifolia* (Schumach.) Mull. Arg. | Leaves | Water | 4.8 (chloroquine resistant, K1) | Phenolics including ellagic acid | No mortality in mice in acute toxicity test | [70, 109] |
|              | *Fluega virosa* (Roxb. ExWillb.)Voigt | Leaves | Water/methanol | 2 (chloroquine resistant, W2) | Bergenin | Nontoxic, extracts exposed to murine macrophages did not slow or inhibit growth of cells | [72, 110] |
| Lamiaceae    | *Clerodendrum rotundifolium* Oliv. | Leaves | Methanol | 0.02 (chloroquine sensitive, CQ²); 1.56 (chloroquine resistant, CQ³) | Iridoid glycosides such as serratoside A, serratoside B and monomelittoside, diterpenoids including uncinatone, derodin, and sugiol | No toxicity was observed; thus, LD₅₀ of the aqueous extract is >5000 mg/kg. b.w. | [74, 111] |
| Mimosaceae   | *Albizia zygia* (DC.) Macbr. | Stem bark | Methanol | 1.0 (chloroquine resistant, K1) | Flavonoids, mainly 3′,4′,7-trihydroxyflavone | The aqueous extract is relatively safe on subacute exposure | [87, 112] |
| Rubiaceae    | *Pentas longiflora* Oliv. | Root | Methanol | 0.99 (chloroquine sensitive, D6); 0.93 (chloroquine resistant, W2) | Pyranonaphthoquinones, pentalongin (1) and psychorubrin (2), naphthalene derivative mollugin (3) | Low cytotoxicity | [97] |
| Plant family | Plant species | Plant part | Extracting solvent | Report on antiplasmodial, IC₅₀ (µg/ml)/antimalarial activity (Plasmodium strain) | Active chemical constituents | Toxicity/safety information | Reference(s) |
|--------------|---------------|------------|--------------------|---------------------------------------------------------------------------------|----------------------------|-----------------------------|---------------|
| Rutaceae     | Citrus reticulata | Seeds (isolimonexic acid methyl ether) | <4.76 (both chloroquine sensitive, D6 and resistant, W2) | Limonin, isolimonexic acid methyl ether, ichangin, deacetylnomilin, obacunone | Dermal 50% lethal dose (LD₅₀) of undiluted leaf oil is >2g/kg in rabbits; seed extract causes respiratory distress and strong spleen contraction | [34, 113] |
families, with Myrtaceae, Aloeaceae, and Rutaceae families each contributing approximately 3% to the total number of species used for malaria treatment in Uganda (Figure 3(a)). The remaining families contribute only 49% of the total plant species used for malaria treatment (Figure 3(a)).

The plant parts greatly used to treat malaria are leaves (54.4%) followed by roots (17.4%) and bark (16%); whole plants and other plant parts are used less commonly (Figure 3(b)). A particular herbal plant is commonly used singly though some times in combination with other herbs. The most common way of use is by boiling the medicinal plant part in water and then drinking the decoction; ingestion of fresh extracts and powdered forms of the herbs is also practiced (Table 1).

Different herbal remedies are used in different communities in different parts of the country depending on the geographical distribution of the medicinal plant species, for example, Warburgia ugandensis is particularly used in the eastern part of Uganda. However, herbal plant species such as Bidens pilosa L. are spread throughout the country and thus well known for malaria treatment across the country. In a study conducted by Ssegawa and Kasenene [20], no tree species in the forests of southern Uganda were more useful than Hallea rubrostipulata and Warburgia ugandensis in the treatment of malaria. These medicinal plants are known by different local names in different parts of the country as Uganda has diverse ethnic groups, including the Luo, Baganda, Itesots, and Banyankole/Bakiga.

Among all communities in Uganda, some measures are taken to control malaria, including draining of stagnant water, clearing and burning bushes, sleeping under insecticide-treated mosquito nets, and house spraying with insecticides.

6. Mode of Preparation and Use of Herbs in Treatment of Malaria in Uganda

The mode of preparation and use of herbs among different communities vary depending on the nature of the herb and plant parts used for malaria treatment [10]. Most commonly, the herbal medicines are prepared as water extracts in the form of decoction and infusion or as steam baths (Table 1) [19, 23]. The herbal plant water extract is made mostly by boiling a handful of the medicinal plant parts such as leaves in a litre of water and then given to the patient to take orally (Table 1) [23]. The dose of the extract given is dependent on the age of the patient and the “strength” of the herbal medicine although occasionally the weight of the patient [19, 23]. The quantity of extract given ranges from 100 to 500 ml, 100 to 250 ml, and 1 to 3 tea or tablespoons for adults, older children, and young children below 5 years of age, respectively, between 1 and 3 times a day for about a week or until when patient has recovered [19, 25]. The extracts are mostly prepared from single herbal plants or from combination of two herbal plants, for example, a decoction of Tamarindus indica and Mangifera indica is common [25].

In some cases, the medicinal plant parts are dried then pulverized to powder and 2–5 tablespoons of the powder added to water and boiled to make a decoction. Some medicinal plant parts such as bark of M. indica stem and roots of V. lasiopus and their powders are boiled for long until the water is half the initial amount [25]. The herbal plant powder can also be added to cold or hot water and stirred and then drunk as recommended [10].

Medicine for malaria treatment from a herb such as B. pilosa can be made by squeezing a handful of its freshly picked leaves and drinking 1–3 teaspoons of the extract a day (Table 1) [23]. Occasionally, malaria herbal medicines can be obtained by preparing different plant parts in combination, for example, an infusion can be made from fresh leaves and pounded fresh roots of V. amygdalina [25]. This is then taken orally in a recommended dose. A handful of medicinal plant parts such as leaves can be squeezed and mixed with cold or warm water for bath, for example, leaves of B. adoensis [25]. Some common herbs are also eaten as vegetables as a prophylactic measure against malaria while others are planted in pots around houses or burnt to drive away mosquitoes (Table 2).

7. Antimalarial Activities and Toxicity of Herbs Used in Uganda for Malaria Treatment

Some studies have been performed on antimalarial activities of some of the herbal plants used in Uganda to treat malaria by using various strains of malarial parasites to confirm effectiveness as malaria treatment [26, 28]. Furthermore, a broad range of phytochemicals responsible for biological activities in some of the antimalarial herbs have been isolated and identified [23]. Of the 182 plant species used in Uganda for the treatment of malaria, 112 plant species (64%) have been investigated for antimalarial activities, of which 108 plants showed positive results and only four plant species did not give positive results when tested for antimalarial activities (Table 1). For about 70 plant species (39%) that are used among different communities in Uganda for the treatment of malaria, there was no record of investigation for antimalarial activities (Table 1).

The antimalarial activity of herbal plants is due to the presence of a number of metabolically active compounds [23]. These compounds may occur in the form of alkaloids, sesquiterpenes, quinones, triterpenoids, flavonoids, quassions, limonoids, terpenes, chalcones, coumarins, or other miscellaneous forms [85]. The solvent of extraction largely determines the concentrations of the active metabolites in the extract. For example, methanolic extracts of the herbal plants are in general more active in vitro than water extracts probably due to the presence of higher amounts of more active lipophilic compounds (Table 3) [54].

The levels of activity of the antimalarial plant extracts depend on the concentration of the active antimalarial secondary metabolites [54]. For example, gedunin, a very active compound against Plasmodium present in leaves of A. indica had an IC_{50} of 0.02 μg/ml against P. falciparum, but its concentration in the plant is in very low and thus moderate activity of its extract (Table 3) [23, 54].
The synergistic effect of the interaction of the different active secondary metabolites is a main contributing factor to the high levels of antimalarial activity of some of the herbal plant extracts, for example, in A. afr, none of the isolated flavonoids and sesquiterpenes had a high activity, yet the plant extract had an IC\textsubscript{50} of 3.9 µg/ml against P. falciparum suggesting a synergistic effect of the compounds in the extract [54]. The presence of particular active compounds in the herbal plant extracts is key in enhancing its antimalarial property. The compound 6E-geranylgeraniol-19-oic-acid a diterpene isolated from M. pyrifolia aqueous extract was considered responsible for its antimalarial activity; nitidine isolated from Z. chalybeum had an IC\textsubscript{50} as low as 0.17 µg/ml against P. falciparum 3D7 [10]; and pristimerin with an IC\textsubscript{50} 0.5 mg/ml against P. falciparum was the main active ingredient in M. senegalensis extract, making it have a very high antiplasmodial activity [54]. The presence of a moderate amount of a minimum of two secondary metabolites in the extract could explain the efficacy of the herbal extracts for malaria treatment [10]. The pathogenic strains used may be different for different in vitro studies; thus, resistance of the parasite to the active metabolites could cause a variation in the level of antimalarial activity of the extracts [10]. Herbal plants with no antimalarial activity suggest the absence of the metabolically active compounds against the Plasmodium parasites in their extracts [23]. Table 4 indicates a list of herbal plants used for malaria treatment in Uganda with high antimalarial activities (IC\textsubscript{50} < 5 µg/ml in one of its solvent extracts or high percentage inhibition of plasmodia) that could be potentially investigated further.

Although herbs are generally considered safer when used for treatment compared to conventional drugs, some of the herbs used traditionally to treat malaria in Uganda may be efficacious, but there is a need to have them used with caution as some may be toxic (Table 4). There is a variation in degree of toxicity depending on the sensitivity of animals, tissue or cells used, type of extract, nature of the test substance, dose, and mode of administration [114]. According to Lacroix et al. [32] one third of the herbs for malaria treatment in Uganda they investigated had significant antimalarial activity with low toxicity. Some of the plants parts with good antimalarial/antimalarial activities with no or low toxicity include leaves of A. annua, leaves of A. africana, S. pinnata whole plant, leaves of C. papaya, and leaves of F. virosa amongst others (Table 4). There are however extracts of some plants used for malaria treatment with very good activity against Plasmodium but with high toxicity; such plant extracts include petroleum ether leaf extract of V. amygdalina and dichloromethane leaf extract of M. pyrifolia (Table 4) [32, 55]. Clerodendrum rotundifolium is on those plants that have very good antimalarial/antiplasmodial activities but have not been investigated for their toxicity (Table 4) [33].

8. Traditional Health Care Practice and Policy Framework in Uganda

The health care system of Uganda consists of the public, private-profit oriented, and private-nonprofit oriented sectors. There is quite a large sector of informal health care including traditional medicine practitioners, drug shops, medicine vendors, and complementary and alternative practitioners. The contribution of traditional health practitioners to Uganda’s health care system was not valued until lately [115]. The negative perspective could be traced back to the colonial times when culture including use of traditional medicine such as herbs for treatment was considered primitive and so discouraged [115]. Efforts are now being made to promote the use of traditional medicine since the government has realized that traditional health practitioners are key contributors to its primary health care system [115]. The Ministry of Health created a public-private partnership with the traditional health practitioners following a recommendation that they be brought into the mainstream health system [115, 116].

A policy on Traditional and Complementary Medicine was created to regulate traditional medicine practice focusing on research and development while emphasizing the propagation, protection, and sustainable use of medicinal plant resources [115, 116]. For collaboration between the mainstream health care sector and traditional health practitioners, the Ministry of Health submitted a bill for the creation of the National Council of Indigenous and Complementary Medicine Practitioners, a semiautonomous body that shall as well protect their intellectual property rights [115, 116].

The National Drug Authority (NDA) is a body that ensures quality control of all medical products including herbal medicines in Uganda under the government statute and policy of 1993 [117]. In Uganda, there is no special regulatory measure for herbal medicines in that the same laws and policies for conventional pharmaceuticals also apply to the herbal medicinal products. A policy was introduced in 2002 to have herbal medicines registered, but so far, no registration of any herbal medicine has been made [117].

Herbal medicines though vastly used in Uganda are not sufficiently regulated. A system to license and track traditional health practitioners or their products is still lacking in the country, and the efforts to have the TCM integrated in the mainstream health care system is still a long way from being realized.

9. Conclusion

Uganda is rich in indigenous plant resources that are used by its people to treat malaria. Communities in different regions of the country use different herbs within their geographical range, though a few common herbs are used by different communities across the country. Many herbs used for
malaria treatment among several communities have not been investigated for their efficacy, and yet they could be potential sources for antimalarial remedies including drugs. Few studies have been conducted to document herbs for malaria treatment in the country, especially in the northern region. Some of the plants investigated for antimalarial/antiplasmodial activities have been found to lack efficacy, toxicity, and safety study aspects. Some plants used in the local communities had very strong antimalarial activities and could be investigated further for the identification and validation of the potential therapeutic antimalarial compounds. This review is critical in that it clearly highlights herbal plants documented in Uganda for malaria treatment but have never been investigated for their antimalarial potential, thus providing guidance for further research on potential natural plant resources that could be sources of novel compounds with therapeutic properties for the treatment of malaria.

Conflicts of Interest
The authors declare that they have no conflicts of interest.

Authors’ Contributions
Denis Okello carried out the data search and was the main contributor in writing the manuscript. Youngmin Kang technically designed and helped in writing the manuscript. Both authors read and approved the final manuscript.

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26 Evidence-Based Complementary and Alternative Medicine

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